# Briefly Legal: Was Kernicterus the Cause of the Adverse Outcome?

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*"At 44 hours, the serum bilirubin was evaluated as part of pre-discharge orders and found to be 13.9 mg/dL. The baby was discharged at 50 hours with an order to return to the clinic for a follow-up in 24 h. The weight at discharge was decreased by 9.3% from birth weight. The mother said in her deposition that her other child had received phototherapy before discharge."*

A 3541-gram appropriate-for-gestational age 38 5/7 week-gestation male is delivered to a 22-year-old gravida 2 para 2 Hispanic mother via vaginal delivery with vacuum assist. The prenatal course was unremarkable. Apgar scores were $8^{1}$ and $9^{5}$. The birthweight was 3541 grams, and the physical examination was unremarkable. The baby was sent to room-in with the mother, who breastfed. At 21 hours, serum bilirubin was evaluated per routine orders and was found to be 8.2 mg/dL. The mother and baby both had an A + blood type. The direct antiglobulin test (DAT) was negative. No documentation of the extent of jaundice was in the records. At 44 hours, the serum bilirubin was evaluated as part of pre-discharge orders and found to be 13.9 mg/dL. The baby was discharged at 50 hours with an order to return to the clinic for a follow-up in 24 h. The weight at discharge was decreased by 9.3% from birth weight. The mother said in her deposition that her other child had received phototherapy before discharge.

*"The mother did not keep the scheduled visit but returned to the clinic when the baby was 96 hours old. The mother stated that the baby's eyes looked yellow, and his skin was more yellow than at discharge. The physical examination revealed that the weight was the same at birth, and the physical examination was normal except for jaundice. Local laboratory blood revealed a total bilirubin of 20.1mg/dL with a direct of 0.61. "*

The mother did not keep the scheduled visit but returned to the clinic when the baby was 96 hours old. The mother stated that the baby's eyes looked yellow, and his skin was more yellow than at discharge. The physical examination revealed that the weight was the same at birth, and the physical examination was normal except for jaundice. Local laboratory blood revealed a total bilirubin of 20.1mg/dL with a direct of 0.61. An order was placed in the chart for the nurse to "call pt, if less yellow, re-draw lab if more yellow refer to hospital." In the deposition, the nurse in the pediatrician's office who received the order could not precisely explain what the order meant and did not remember the order or the patient. In her deposition, the mother stated that she did not hear from the pediatrician or the nurse until the following day ( 120 hours, day 5) when the nurse left a message on the mother's telephone to "put the baby in the sunlight."

On day 17, the baby was admitted for poor feeding, lethargy, and poor tone. His bilirubin on admission was 12.2 mg/dL with a direct of 0.2 mg/dL. Laboratory evaluations were normal, including a complete blood count, blood and urine cultures, electrolytes, and a basic metabolic panel. After admission, an evaluation revealed hypertonicity, but the medical team neither suspected bilirubin encephalopathy nor obtained neuroimaging or auditory brainstem response. On follow-up examination at two years of age, the child had developed athetoid cerebral palsy, hearing impairment, and other developmental delays. Magnetic resonant imaging (MRI) was interpreted as normal by the treating neuroradiologist but as consistent with kernicterus by the plaintiff's neuroradiologist.

The case was settled without going to a trial.

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**Discussion**

**General**

More than 80% of newborn infants will have some degree of jaundice. Since high bilirubin concentrations can cause acute bilirubin encephalopathy and kernicterus, careful monitoring of all newborn infants and adherence to Guidelines for intervention is essential. Kernicterus is a permanent disabling neurologic condition characterized by some or all of the following: choreoathetotic cerebral palsy, upward gaze paresis, enamel dysplasia, and sensorineural hearing loss. Policies must be in place and strictly enforced in hospitals and other birthing locations to ensure the proper care necessary to minimize the risk of bilirubin neurotoxicity.

**The American Academy of Pediatrics**

| Age | Bilirubin mg/dL | Issue | Plaintiff's position | Defense's position |
|---|---|---|---|---|
| 21 hours | 8.2 | Levels exceeding 5-6 mg/dL **within 24** h are abnormal. Jaundice is clinically discernible in most babies at this level | A level of 8.2 mg/dL at 21 h places this baby at high risk for dangerous hyperbilirubinemia. Clinical risk factors include: exclusive breastfeeding, vacuum extraction as well as high bilirubin level <24 h | ABO hemolytic disease was ruled out. The baby was healthy. Avoid separation of baby from mother with phototherapy. Safe to follow. |
| 44 | 13.9 | No visual **assessments** of jaundice in the chart, No assessments of transcutaneous/ laboratory testing between 21 and 44 h after birth. | Ongoing clinical assessments of jaundice by the nurses should have been made.<br><br>The rate of rise was rapid, 0.43/h | Not causally related |
| 50 | | **Discharged** with a scheduled 24 h post-discharge follow-up<br><br>**Parent education** | Negligently discharged infant while in the high-risk zone for hyperbilirubinemia<br><br>Failed to provide sufficient education to parents to safeguard infants.<br><br>Failed to institute phototherapy<br><br>Alternatively, care providers could schedule a further bilirubin level the morning after discharge.<br><br>Failed to appreciate other risk factors, including sibling with hx of jaundice, exclusive breastfeeding, and vacuum extraction.<br><br>Failed to pursue the mother for a follow-up visit vigorously. The mother says she did not know the importance of keeping the 24-hour follow-up appointment. | The mother did not keep the 24 h follow-up visit. Mother was irresponsible. The implication is that it is the mother's fault the baby had an adverse outcome |
| | | Pediatrician told the mother to place the baby in **sunlight** after discharge | While direct exposure to sunlight will decrease bilirubin levels, practical difficulties are involved in safely exposing infants. Not an appropriate intervention in U.S. Filtered sun is used in income-restricted countries. | Sunlight works. |
| 96 (4 days) | 20.1 | **Was a four-day level of 20.1mg/dL the peak?** | The trend was likely to go higher. Exclusive breastfeeding, prior sibling with jaundice & phototherapy, and sequestered blood from the vacuum indicate a higher level after day 4. High risk for bilirubin neurotoxicity | A level of 20.1mg/dL is the peak. |
| | | Pediatrician order to nurse: "call pt; if less yellow, re-draw lab. I**f more yellow,** refer to hospital." | Vague and indecipherable. Below standard to give such an order | Reasonable order |
| Three weeks | 12 | **Lethargy, poor feeding, decreased tone** | The baby had acute bilirubin encephalopathy. The bilirubin level peaked some days after being drawn at four days. Not possible to tell how high, but it peaked higher than 20 mg/dL | The admitting physicians did not suspect or diagnose bilirubin encephalopathy. The highest level was 20.1mg/dL |
| Two years | | **Athetoid cerebral palsy, cognition, and developmental delays, hearing impairmen**t | Chronic encephalopathy secondary to bilirubin toxicity | Other issues could have been responsible for these clinical findings |

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| | | **MRI** | Consistent with kernicterus. A normal MRI does not exclude kernicterus. The bilirubin probably peaked higher after being drawn on day 4. Only a postmortem examination can rule out kernicterus. More probably than not, the clinical and laboratory evaluations point to a kernicterus diagnosis. The diagnosis of kernicterus is always presumptive until postmortem. | Since MRI was normal, it cannot be kernicterus. Agree with treating neuroradiologist |

In September 2022, the Clinical Practice Committee of the AAP updated both its 2004 clinical practice Guideline and its 2009 commentary clarifying and modifying indications for the post-nursery management of bilirubin levels in healthy neonates. The Committee raised the phototherapy thresholds to a narrow range that they considered safe, revised the risk assessment approach based on the hour-specific bilirubin concentration, and defined the need for an "escalation of care" to address elevated bilirubin concentrations rapidly. The primary aim of post-discharge jaundice evaluation is to avoid severe hyperbilirubinemia and the increased risk it poses of toxicity to the central nervous system.

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The 2022 AAP clinical Guideline provides specific recommendations and evidence-based "key action statements" on:

1. prevention of hyperbilirubinemia
2. assessment and monitoring for hyperbilirubinemia.
3. treatment of hyperbilirubinemia
4. post-discharge follow-up
5. hospital policies and procedures.

Prevention begins with:

1. the identification and treatment of mothers at risk for developing antibodies to red blood cell antigens, which can lead to hemolytic disease
2. providing feeding support during birth hospitalization
3. screening 24 to 48 hours after birth or before discharge if that occurs earlier, with either transcutaneous bilirubin or total serum bilirubin level. The same approach is recommended for infants born at home.

This practice Guideline highlights risk factors such as lower gestational age, jaundice in the first 24 hours after birth, poor feeding, excessive weight loss, scalp hematoma or significant bruising (from obstetrical procedures such as operative vaginal delivery), trisomy 21, and macrosomic infant of a diabetic mother. It further points out the challenges of identifying infants with glucose-6-phosphate dehydrogenase (G6PD) deficiency, among the most important causes of hyperbilirubinemia leading to kernicterus in the U.S. worldwide.

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The evaluation of follow-up bilirubin levels should be based on the difference between the pre-discharge bilirubin level and the hour-specific phototherapy threshold, which considers the baby's age in hours and gestational age and the presence of any risk factors for neurotoxicity from hyperbilirubinemia. The closer the newborn's bilirubin level is to the newborn's risk-based phototherapy threshold, the closer follow-up the assessment needs to be.

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In the new Guideline, the phototherapy and exchange transfusion thresholds have increased slightly. These intervention thresholds consider gestational age and whether there are additional risk factors for neurotoxicity related to hyperbilirubinemia, including a low albumin level, isoimmune or other hemolytic diseases, sepsis, or clinical instability. Additional new recommendations address follow-up care after discontinuing phototherapy to assess for rebound hyperbilirubinemia. The recommendations emphasize that timely identification of hyperbilirubinemia and the appropriate use of intensive phototherapy can almost always prevent the need for an exchange transfusion. Recommendations also discuss

the circumstances under which intensive phototherapy may be provided at home.

If more than one measure of bilirubin is available (TcB or TSB), the trajectory of the increase may identify infants at higher risk of subsequent hyperbilirubinemia. A rapid rise (≥0.3 mg/dL per hour in the first 24 hours or ≥0.2 mg/dL per hour after that) is exceptional and suggests hemolysis. In this situation, performing a direct antibody test (DAT) not previously done is especially important.

As mentioned, the Guidelines include the concept of "escalation of care." This medical imperative deals with serum bilirubin levels exceeding 2 mg/dL below the gestational age and age-in-hours specific exchange transfusion threshold assessed on the appropriate exchange transfusion nomogram (with no or no, recognized hyperbilirubinemia neurotoxicity risk factors). "Escalation of care in this scenario entails admission to a pediatric hospital unit capable of providing intensive phototherapy, intravenous therapy, and exchange transfusion. An exchange transfusion is required if the infant shows signs of acute bilirubin encephalopathy (feeding difficulty, lethargy, hypertonia). The severity of the infant's symptoms can be quantified using the bilirubin-induced neurogenic dysfunction score, which assesses clinical signs (mental status, muscle tone, crying, sucking, feeding issues, visible jaundice) associated with bilirubin toxicity (hypotonia followed by hypertonia, and/or opisthotonos.

Patient education and timely follow-up are critically important and deserve emphasis, even for low-risk infants. Before discharge, all families should receive written and verbal education about neonatal jaundice and information specific to their baby, including the infant's pre-discharge bilirubin level and details about follow-up after discharge.

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**Comments on the case described above**

This baby was born before the 2022 Guidelines were published, but the plaintiff's criticisms were based on the 2004 Guidelines. It was predictable that this baby would probably develop significant hyperbilirubinemia: 1) he had a level of 8.1mg/dL within 24 hours 2); he had a significantly high level of 13.9 mg/dL at 44 hours, six hours prior to discharge, and 3) he had a vacuum assisted delivery which probably resulted in some sequestered blood which would add bilirubin production to his physiologic jaundice; 4) his bilirubin of 20.1 mg/dL was measured at 96 h before the level was likely to peak; 5) his sibling required phototherapy for jaundice.

Peak levels of bilirubin and duration of hyperbilirubinemia vary depending on racial and ethnic factors, the region of the world, and the type of feeding. White and African-American babies tend to peak 60-72 hrs with a 5-6 days duration of hyperbilirubinemia. Asian American babies tend to peak at 72-120 hours and have a duration of hyperbilirubinemia of 10-14 days. While Hispanic babies tend to peak bilirubin slightly earlier than Asian babies, there is a broader variation, perhaps related to the multicultural mixture among this group. Compared to breastfed babies, the bilirubin levels of formula-fed babies tend to peak earlier, with a lower peak and shorter duration.

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Studies using transcutaneous bilirubin (TcB) devices have developed nomograms to define the range of hour-specific normal values. Many available studies were performed in populations that included predominantly breastfed, white newborns. Possible explanations for the variability among different studies on peak bilirubin levels and time for resolution may have resulted partly from genetic variability in the hepatic conjugating ability of bilirubin, differences in breastfeeding practices, and prevalence of glucose-6 phosphate dehydrogenase (G6PD) deficiency or Gilbert syndrome in the study populations. In addition, there are differences in study design (enrollment criteria, type of TcB) and population. Skin pigmentation, for example, affects light reflectance, which can potentially impact the accuracy of the transcutaneous readings. While different methodologies have been developed to minimize this effect, the devices are imperfect. TcB generally overestimates TSB in newborns with darker skin pigmentation and underestimates TSB in newborns with lighter-pigmented skin.

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In contrast to common structural imaging modalities, ultrasonography, and computed tomography, MR imaging (MRI) has been of significant value in identifying both acute and chronic bilirubin encephalopathy. The principal findings involve bilateral and symmetric abnormalities of globus pallidus in approximately 90%, subthalamic nucleus in approximately 40%, and rarely the hippocampus. The lesions are seen best in the acute period, during the first several weeks of life on T1-weighted images, and later, chronic lesions on T2-weighted images. Abnormalities of the globus pallidus and subthalamic nucleus should be distinguished from the typical involvement in hypoxic-ischemic disease of the subcortical white matter, putamen, and thalamus. The acute lesions may be transient and, with clinical recovery, may disappear. Infants who exhibit chronic abnormality on T2-weighted images exhibit the classic clinical features of chronic post-kernicteric bilirubin encephalopathy consistently. However, the converse is not true (i.e., occasional children with the classic clinical syndrome have normal MRI findings. The MRI was normal in this case, but only postmortem evaluation can strictly confirm kernicterus.

***Suggested Reading:***


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*Disclosures: The authors have indicated no conflicts of interest.*

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