

# Neonatal Jaundice <sup>[1]</sup>

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Neonatal [jaundice](#) <sup>[2]</sup> is the yellow discoloration of the skin and eyes due to elevated bilirubin levels in the bloodstream of a newborn. Bilirubin is a byproduct of the breakdown of red blood cells. Jaundiced infants are unable to process bilirubin at a normal rate or they have an abnormally high amount of bilirubin in their bloodstream, resulting in a buildup of the yellow colored bilirubin. That build up is called hyperbilirubinemia and is the cause of [jaundice](#) <sup>[2]</sup>. Jaundice can lead to kernicterus, a rare neurological disorder that results in hearing loss, permanent brain damage, and sometimes death. Research into the causes of [jaundice](#) <sup>[2]</sup> and kernicterus began in the late eighteenth century in Paris, France. By the middle of the twentieth century, scientists developed treatments for [jaundice](#) <sup>[2]</sup> that successfully treated infants afflicted with the condition, such as phototherapy and blood exchange transfusion. Due to those treatments, the risk for an infant in developing kernicterus is very low.

In 1788, physician Jean Baptiste Timotheé Baumes gave one of the first detailed descriptions of [jaundice](#) <sup>[2]</sup>. Baumes received a prize from the [University of Paris](#) <sup>[3]</sup> in Paris, France, for his dissertation describing the progression of disease in ten jaundiced infants he autopsied. In all ten infants, he observed the yellow discoloration of their skin. Baumes argued that [jaundice](#) <sup>[2]</sup> was caused by the delayed passage of an infant's first stool and that ingestion of breast milk would treat [jaundice](#) <sup>[2]</sup>. In 1806, Baumes released a second edition of his dissertation that became the standard medical knowledge on neonatal [jaundice](#) <sup>[2]</sup> until 1847.

In 1847, physician Jacques François Édouard Hervieux submitted his own dissertation on jaundiced infants to the [University of Paris](#) <sup>[3]</sup> titled "De l'ictère des Nouveau-nés," which translates to "on the [jaundice](#) <sup>[2]</sup> of newborns." In his work, Hervieux disagreed with Baumes that a delayed first bowel movement was the cause of [jaundice](#) <sup>[2]</sup>. Hervieux meticulously described the appearance of forty-four jaundiced infants that he autopsied. Though Hervieux did not report the cause of [jaundice](#) <sup>[2]</sup>, he was one of the first people to make a connection between the breakdown of red blood cells and the development of [jaundice](#) <sup>[2]</sup>. He also remarked on the commonality of neonatal [jaundice](#) <sup>[2]</sup> and estimated that two-thirds of all infants were affected. During his autopsies, Hervieux observed yellow staining in all parts of body tissue including the brain, which later became an indicator of kernicterus, a neurological disorder that can permanently damage the brain.

In 1904, a pathologist at a city hospital in Dresden, Germany, Christian Georg Schmorl coined the term kernicterus in his article "Zur Kenntnis des ikterus neonatorum, insbesondere der dabei auftretenden gehirnveränderungen," which translates to "for information of the [jaundice](#) <sup>[2]</sup> of the newborn, especially the brain changes that occur." Schmorl had access to information from 120 infant autopsies. In 114 of those autopsies, the brain was intensely stained yellow and in six of those 114 infant autopsies very specific parts of the brain were stained. Those parts of the brain were the basal ganglia, which are a group of structures that control certain functions such as voluntary motor movements, eye control, cognitive skills, and emotion. The sharply stained basal ganglia, or nuclei, of the brain compared to the rest of the tissue led Schmorl to coin the term kernicterus, which means yellow nuclei, to describe that condition. Those stains came from the unconjugated bilirubin that had entered the brain tissue once its concentration became too high, but Schmorl claimed that staining could not just be attributed to saturation of the tissue. He claimed the staining was also due to the bilirubin binding to specific structures in the basal ganglia. Schmorl's work laid the foundation for much of the understanding of the mechanism [jaundice](#) <sup>[2]</sup> and how bilirubin toxicity affects the brain.

As of 2017, researchers claim that neonatal [jaundice](#) <sup>[2]</sup> could have at least two different causes: physiological and pathological. Physiologic [jaundice](#) <sup>[2]</sup> is the inability to process bilirubin at a normal rate, while pathologic [jaundice](#) <sup>[2]</sup> is the excessive buildup of broken down red blood cells which leads to elevated bilirubin levels. The incidence of both causes of [jaundice](#) <sup>[2]</sup> combined is fifty percent amongst term infants and eighty percent amongst preterm infants. Physicians measure the amount of bilirubin present in the infant's body using bilirubin samples taken from the blood and a range of measurements determines whether the cause of [jaundice](#) <sup>[2]</sup> is physiologic or pathologic. Physiologic [jaundice](#) <sup>[2]</sup> is also known as transient [jaundice](#) <sup>[2]</sup> because it is the more common of the two types and is much less harmful. When infants are born, their livers are not fully developed. That immaturity makes it difficult for the liver to filter all of the bilirubin, the yellow-colored byproduct of red blood cell breakdown, from the bloodstream, resulting in infants with yellow tinged skin. Physiologic [jaundice](#) <sup>[2]</sup> is the obstruction of the pathway for normal red blood cell breakdown.

During normal breakdown of red blood cells, or hemolysis, the body converts hemoglobin, a protein on the surface of red blood cells that binds to oxygen, into bilirubin, which is not soluble in water, or unconjugated, and therefore not easily excreted by the body. To become water-soluble, the unconjugated bilirubin then attaches to albumin, the blood's transport molecule, for delivery to the liver where it is absorbed by the liver cells. Through a series of reactions within the liver, the bilirubin becomes water-soluble, or conjugated, and is transported to the small intestine through bile secretion. Bacteria in the small intestine then prepare the conjugated bilirubin for excretion from the body. Physiologic [jaundice](#) <sup>[2]</sup> is attributed to the sterile gastrointestinal tract of a newborn infant and the newborn infant's immature liver, which cannot conjugate bilirubin at the normal adult rate. In addition to that, enzymes present in the infant's small intestine revert the conjugated bilirubin back to its water-insoluble state

and the bilirubin is reabsorbed into the bloodstream, starting the cycle again and increasing the levels of bilirubin as more unconjugated bilirubin is produced and not excreted by the body.

Physiologic jaundice<sup>[2]</sup> is common in many newborns and usually appears three to four days after birth and naturally passes over the course of a few weeks as the infant's liver and small intestine matures and bilirubin levels lower to adult concentration. The average range of bilirubin levels for full-term infants with physiologic jaundice<sup>[2]</sup> is 5 to 6 mg/dL of blood. When the bilirubin concentration passes 17 mg/dL, the infant's jaundice<sup>[2]</sup> is no longer considered physiologic and requires physicians to identify a pathological cause.

Infants with pathologic jaundice<sup>[2]</sup> are at higher risk for the onset of kernicterus than infants with physiologic jaundice<sup>[2]</sup>. Pathologic jaundice<sup>[2]</sup> can have several different causes. The causes include blood type incompatibility between the pregnant woman and infant, known as ABO incompatibility and Rh-factor incompatibility, and excessive red blood cell breakdown due to birth trauma. An appearance of jaundice<sup>[2]</sup> within the first twenty-four to forty-eight hours of a newborn's life is indicative of pathological origins as opposed to the delayed onset of physiologic jaundice<sup>[2]</sup>, which occurs on the third or fourth day. In infants present with jaundice<sup>[2]</sup> within the first twenty-four to forty-eight hours after birth, physicians must identify the cause of jaundice<sup>[2]</sup> to treat the condition and prevent kernicterus.

During the early twentieth century, the most common cause of pathologic jaundice<sup>[2]</sup> was *erythroblastosis fetalis*<sup>[4]</sup>, or EF. EF develops during fetal development when the antibodies of the pregnant woman attack the red blood cells of the fetus<sup>[5]</sup>. Some fetal red blood cells escape the placenta<sup>[6]</sup> and travel through the pregnant woman's bloodstream. If the fetus's red blood cell surface has Rh antigens on it, the woman's immunity system marks these red blood cells as foreign invaders. Subsequently, the immune system mounts an attack on those blood cells and can cross the placenta<sup>[6]</sup> and attack the red blood cells of the developing fetus<sup>[5]</sup>. That creates high levels of bilirubin in the fetus's blood as more red blood cells are destroyed, and the onset of hemolytic disease of the newborn at birth. With the development of Rh immunity treatments, which destroy the fetal antibodies before the pregnant woman's immune system recognized them, EF has become extremely rare. Though blood type incompatibility, which happens when the woman has type O blood and is carrying a fetus<sup>[5]</sup> with type A or B blood, can result in similar hemolytic diseases and hyperbilirubinemia at birth.

Other less common causes of pathologic jaundice<sup>[2]</sup> are those that stem from excessive red blood cell breakdown and disorders that disrupt the bilirubin metabolism pathway. Infant trauma while passing through the birth canal can result in a collection of blood underneath the skin. The breakdown of that blood can overwhelm the infant's immature liver and GI tract due to the high red blood cell turnover rate and result in jaundice<sup>[2]</sup>. Genetic causes of pathologic jaundice<sup>[2]</sup> include inherited liver and blood disorders, such as Dubin-Johnson syndrome, and the deficiency of the red blood cell enzyme glucose-6-phosphate dehydrogenase, an enzyme that assists in protecting the red blood cell from damage. Those two diseases result in a buildup of unconjugated bilirubin that can cause jaundice<sup>[2]</sup> in infants.

Because pathologic jaundice<sup>[2]</sup> does not resolve itself, physicians have developed treatments to prevent its development into kernicterus. In 1941, a group of pediatricians working at the Boston Children's Hospital in Boston, Massachusetts, originally developed exchange transfusion to treat infants that suffered from hemolytic disease of the newborn due to Rh-incompatibility. Exchange transfusion of the blood lowers the bilirubin levels in infants by half of the original amount. Physicians insert one or two catheters into a vein located in the infant's abdomen, called the umbilical vein<sup>[7]</sup>, remove small amounts of the infant's blood, and then subsequently replace it with donor blood. While the procedure occurs, physicians periodically measure the bilirubin level to ensure the infant's bilirubin levels are not rising during the transfusion. The infant continues to receive transfusions until double the amount of infant's blood volume is removed. Sometimes infants require two exchange transfusions to effectively lower the infant's bilirubin level. Complications from exchange transfusion include infection, blood clots in the vein leading to the liver, and high platelet count in the blood. Due to those potential complications, physicians tend to use exchange transfusion only if phototherapy treatment is not effective. Physicians will also use exchange transfusion if it is likely that the infant's serum bilirubin level will reach 25 mg/dL within the next twenty-four hours. At that point, the infant is at a high risk of receiving brain damage from the bilirubin because it becomes toxic to the brain at that level.

Phototherapy, which uses light wavelengths to breakdown the bilirubin into a water-soluble byproduct that is much easier for the infant's immature liver to filter and excrete from the body, has largely replaced exchange transfusion. Physician Richard Cremer in the UK first described the use of phototherapy to treat jaundice<sup>[2]</sup> in his 1958 article "Influence of Light on the Hyperbilirubinemia of Infants." Such a treatment did not become popular in the US until 1968, when Jerold Lucey and other pediatricians at the University of Vermont in Burlington, Vermont, published their own findings regarding the use of phototherapy to treat jaundiced infants. Since the 1970s, phototherapy has been the standard of care for infants with pathologic jaundice<sup>[2]</sup> in the US. Standard phototherapy uses eight white fluorescent light bulbs placed over an apparatus containing the infant. Nurses or physicians place infants under the light with as much skin surface area as possible exposed. The duration of the session depends on the severity of the jaundice<sup>[2]</sup> and the gestation<sup>[8]</sup> age of the infant. According to the American Academy of Pediatrics, physicians should use intensive phototherapy on full-term and near-term infants that have a total serum bilirubin level greater than 20 mg/dL. Performed correctly, phototherapy decreases the serum bilirubin levels by as much as thirty to forty percent. Phototherapy treatment is the least invasive treatment for neonatal jaundice<sup>[2]</sup>, but if the infant's bilirubin levels continue to rise even with intensive phototherapy treatment, physicians must perform an exchange transfusion of the infant's blood as soon as possible.

Throughout the 1950s until the 1980s in the US, pediatricians aggressively treated both physiologic and pathologic jaundice [2]. In 1992, physicians Thomas Newman and Jeffrey Maisels published an article in the journal *Pediatrics* that recommended a less aggressive treatment approach to term infants with elevated bilirubin levels from physiologic jaundice [2]. At that time, women were having shorter hospital stays after delivery than they had been in the past. As of 2017, physicians generally discharge a woman within forty-eight hours after a vaginal birth compared to the three to four day hospital stays of earlier decades. Serum bilirubin levels peak three to five days after an infant's birth, so if the infant and woman are discharged within forty-eight hours, the onset of jaundice [2] occurs after discharge. According to Maisels in a later article, the unintended consequence of early discharge resulted in the reemergence of kernicterus because physicians did not follow up with the discharged infants early enough to check for onset of jaundice [2]. By the time sick infants came to the hospital, their bilirubin levels were extremely high and the infants were become affected by kernicterus.

To combat the increase of infants affected with kernicterus, in 2004 the American Academy of Pediatrics published strict guidelines for the management of potential infant hyperbilirubinemia. Before discharge, every infant should be assessed for the risk of developing elevated bilirubin levels. Those risk factors include the presence of jaundice [2] within the first twenty-four hours after birth, hemolytic disease, prominent bruising on the infant's body, and whether the infant's sibling was jaundiced after their birth. All infants should have a follow up assessment within three days after discharge from the hospital regardless of the presence of hyperbilirubinemia risk factors in the infant. The presence of risk factors in an infant at discharge determines the timing and frequency of subsequent physician assessments.

## Sources

1. Akobeng, Anthony K. "Neonatal Jaundice." *American Family Physician* 71 (2005): 947–8.
2. American Academy of Pediatrics. "Management of Hyperbilirubinemia in the Newborn In 35 or More Weeks of Gestation" *Pediatrics* 114 (2004): 297-316. <http://www.ncbi.nlm.nih.gov/pubmed/15231951> [9] (Accessed April 11, 2016).
3. Baumes, Jean Baptiste Thimoteé. *Treatise on Icterus or Jaundice of Newborn Infants* Paris: Chez Méquignon L'aîné; 1806. <http://www.neonatology.org/classics/baumes/baumes.pdf> [10] (Accessed April 11, 2016).
4. Cremer, Richard J., P.W. Perryman, and D.H. Richards "Influence of Light on the Hyperbilirubinaemia of Infants." *The Lancet* 271 (1958): 1094–7.
5. Dennery, Phyllis A., Daniel Seidman, and David Stevenson. "Neonatal Hyperbilirubinemia." *New England Journal of Medicine* 344 (2001): 581–90.
6. Diamond, Louis K. "Historic Perspective on 'Exchange Transfusion'." *Vox sanguinis* 45 (1983): 333–5.
7. Hervieux, Jacques. "De L'ictère des Nouveau-nés." Thesis, [University of Paris](http://www.neonatology.org/classics/hervieux/hervieux.pdf) [3], 1847.
8. Hansen, Thor. "Pioneers in the Scientific Study of Neonatal Jaundice and Kernicterus." *Pediatrics* 106 (1999):15, <http://www.neonatology.org/pdf/jaundice.pdf> [11] (Accessed April 11, 2016).
9. Lucey, Jerold F. "Changing Concepts Regarding Exchange Transfusions and Neonatal Jaundice." *Clinical Obstetrics and Gynecology* 14 (1971): 586–93.
10. Maisels, Jeffrey M. "Neonatal Jaundice." *Pediatrics in Review* 27 (2006): 443–54.
11. Maisels, Jeffrey M. "What's in a Name? Physiologic and Pathologic Jaundice: The Conundrum of Defining Normal Bilirubin Levels in the Newborn." *Pediatrics* 118 (2006): 805–7.
12. Newman, Thomas J., and Maisels, Jeffrey. "Evaluation and Treatment of Jaundice in the Term Newborn: A Kinder, Gentler, Approach." *Pediatrics* (1992): 809–18.
13. Schmorl, Christian Georg. "For Information of the Jaundice of the Newborn, Especially the Brain Changes that Occur." *Verhandlungen der Deutschen Gesellschaft für Pathologie* 6 (1904) 109–15.

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## Subject

[Jaundice, Neonatal](#) [12] [Hyperbilirubinemia, Neonatal](#) [13] [Icterus neonatorum](#) [14] [Baumes, J. B. T. \(Jean Baptiste Timothee\), 1756-1828](#) [15] [Erythroblastosis fetalis](#) [16] [Phototherapy](#) [17] [Children's Hospital Medical Center \(Boston, Mass.\)](#) [18] [Maisels, M. Jeffrey](#) [19] [Lucey, Jerold F.](#) [20] [Bilirubin](#) [21] [Exchange Transfusion, Whole Blood](#) [22] [Kernicterus](#) [23]

## Topic

[Disorders](#) [24]

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[Articles](#) <sup>[25]</sup>

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- [1] <https://embryo.asu.edu/pages/neonatal-jaundice>
- [2] <https://embryo.asu.edu/search?text=jaundice>
- [3] <https://embryo.asu.edu/search?text=University%20of%20Paris>
- [4] <https://embryo.asu.edu/search?text=erythroblastosis%20fetalis>
- [5] <https://embryo.asu.edu/search?text=fetus>
- [6] <https://embryo.asu.edu/search?text=placenta>
- [7] <https://embryo.asu.edu/search?text=umbilical%20vein>
- [8] <https://embryo.asu.edu/search?text=gestation>
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- [10] <http://www.neonatology.org/classics/baumes/baumes.pdf>
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- [13] <https://embryo.asu.edu/library-congress-subject-headings/hyperbilirubinemia-neonatal>
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- [22] <https://embryo.asu.edu/medical-subject-headings/exchange-transfusion-whole-blood>
- [23] <https://embryo.asu.edu/medical-subject-headings/kernicterus>
- [24] <https://embryo.asu.edu/topics/disorders>
- [25] <https://embryo.asu.edu/formats/articles>