

Managing the jaundiced newborn: a persistent challenge

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Pediatricians and family physicians deal regularly with jaundiced newborn infants who emerge unscathed from their transient exposure to an elevated serum bilirubin level. Yet, despite published guidelines for the management of neonatal jaundice, there are rare infants in whom bilirubin encephalopathy develops. Canada currently reports the highest incidence in the developed world of 1 in 67 000 to 1 in 44 000 live births.¹

In this review, I present an approach to managing the jaundiced newborn that is based on published guidelines.^{2–5} The aim is to help clinicians identify and manage jaundice in the newborn, intervene when appropriate and, when possible, prevent bilirubin-induced brain damage. It would be ideal if the published guidelines for the management of hyperbilirubinemia, including treatment with phototherapy and exchange transfusion, were based on estimates of when the benefit of these interventions exceeded their risks and costs. These estimates should come from randomized trials or high-quality, systematic observational studies, but such studies are rare. Guidelines must therefore rely on relatively uncertain estimates of risk and benefits, often from conflicting results. In addition, use of a single peak bilirubin level to predict long-term behavioural and developmental outcomes is not reliable and will often lead to conflicting results. Because of the lack of evidence, current guidelines are mainly based on consensus, as are the recommendations included in this article.

Herein, I discuss the management of infants of 35 or more weeks of gestation, cared for in well-baby nurseries, and do not address hyperbilirubinemia in more premature infants. A complete discussion of the approach to the preterm infant can be found in a recent publication.⁶ A summary of the evidence used in this review appears in Box 1.

Why do newborns become jaundiced?

If carefully examined in the first few days after birth, more than 80% of all term and late preterm infants will have some degree of jaundice.^{7,8} Almost every infant will have a total serum bilirubin

level that is above the normal maximum adult level of 17.1 $\mu\text{mol/L}$ (1 mg/dL) because they have an increased turnover of erythrocytes, produce more than twice the amount of bilirubin produced daily by an adult⁹ and have a transient deficiency in their ability to conjugate and clear bilirubin. This imbalance between bilirubin production and conjugation is fundamental to the pathogenesis of neonatal bilirubinemia.¹⁰ It results in a steady increase in total serum bilirubin levels for the first three to five days, and sometimes more (Figure 1), followed by a decrease in levels as the rate of bilirubin production declines and conjugation improves.

What are normal and potentially harmful bilirubin levels?

By age 96 hours, the 50th percentile for total serum bilirubin levels in healthy newborns in Europe and North America is about 137–154 $\mu\text{mol/L}$ (8–9 mg/dL) and the 95th percentile is about 257–300 $\mu\text{mol/L}$ (15–17.5 mg/dL).^{11–13} These ranges are generally harmless, but if the bilirubin level should rise in excess of 425–510 $\mu\text{mol/L}$ (25–30 mg/dL), sufficient bilirubin can penetrate the blood–brain barrier, produce yellow staining and necrosis of the basal ganglia and brainstem nuclei, and lead to acute, and then chronic bilirubin encephalopathy or kernicterus. Kernicterus is a devastating form of neurologic dysfunction, characterized in its classic form by choreoathetoid cerebral palsy, auditory neuropathy and dyssynchrony with or without hearing loss,

Competing interests:

Jeffrey Maisels is a consultant to Dräger Medical Inc., the supplier of the JM-103 transcutaneous bilirubinometer.

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KEY POINTS

- Kernicterus or chronic bilirubin encephalopathy, a condition that should be largely preventable, is still occurring in the developed world.
- Serum bilirubin levels in newborns can be interpreted only according to the infant's age in hours.
- Before discharge from the nursery, every infant should have his or her total serum bilirubin or transcutaneous bilirubin level measured.
- Combining this measurement with the infant's gestational age provides an excellent prediction of hyperbilirubinemia risk.
- With few exceptions, infants who are discharged before age 72 hours should be seen within two days after discharge.

gaze palsy and enamel dysplasia of the deciduous teeth.¹⁴ Although bilirubin toxicity has been recognized for more than a century, the precise molecular mechanisms responsible for the cytotoxicity of bilirubin are not completely understood.¹⁵

How often does kernicterus occur?

Population-based studies in the United States and Europe suggest that kernicterus still occurs in about 0.5–1.0 per 100 000 infants born after

35 weeks of gestation.¹⁶ Using data from the Canadian Paediatric Surveillance Program, a voluntary reporting system that surveys Canadian pediatricians, Sgro and colleagues calculated that, from 2007 to 2008, the incidence of bilirubin encephalopathy in Canada ranged from 1 in 67 000 to 1 in 44 000 live births.¹

What do the guidelines say?

Several countries, including the US (American Academy of Pediatrics, 2004),³ Canada (Canadian Paediatric Society, 2007)⁴ and the United Kingdom (National Institute for Health and Clinical Excellence),² have published guidelines on the care of the jaundiced newborn, and an update of the American Academy of Pediatrics guideline was published in 2009.⁵ The 2009 update clarified the difference between “hyperbilirubinemia risk factors” and “neurotoxicity risk factors,” made a firm recommendation for the measurement of total serum bilirubin or transcutaneous bilirubin in every infant before discharge, and provided a structured algorithm for follow-up based on the presence of risk factors for hyperbilirubinemia and the zone in which the predischARGE levels of total serum bilirubin or transcutaneous bilirubin fell (Figure 2). The key

Box 1: Evidence used in this review

The goal of this review is to help clinicians who care for newborns to identify and manage those with jaundice. On a monthly basis over the last 40 years, I have searched MEDLINE for English-language articles using the terms “newborn jaundice,” “hyperbilirubinemia,” “phototherapy,” “bilirubin encephalopathy” and “kernicterus.” I also reviewed articles on these subjects in the Cochrane Database of Systematic Reviews, as well as recent textbooks, all published from 2000 to 2013. In addition, I reviewed the guidelines on newborn jaundice of the American Academy of Pediatrics, the Canadian Paediatric Society and the UK National Institute for Health and Clinical Excellence.

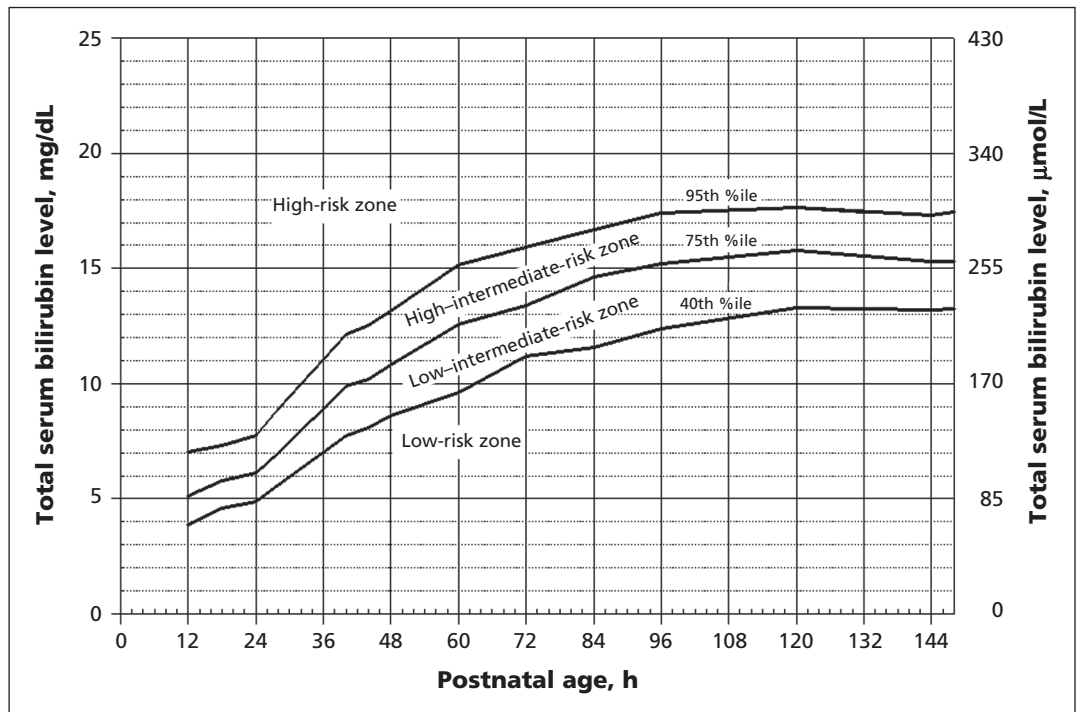


Figure 1: Nomogram for designation of risk among 2840 well newborns at ≥ 36 weeks' gestation and birth weight ≥ 2000 g, or at ≥ 35 weeks' gestation and birth weight ≥ 2500 g, based on the hour-specific serum bilirubin values. The serum bilirubin level was obtained before discharge, and the zone in which the value fell predicted the likelihood of a subsequent bilirubin level exceeding the 95th percentile. Because of sampling bias, this nomogram should not be used to represent the natural history of neonatal hyperbilirubinemia. Reproduced with permission from the American Academy of Pediatrics guidelines,³ *Pediatrics* 2004;114:297-316. Copyright © 2004 American Academy of Pediatrics.

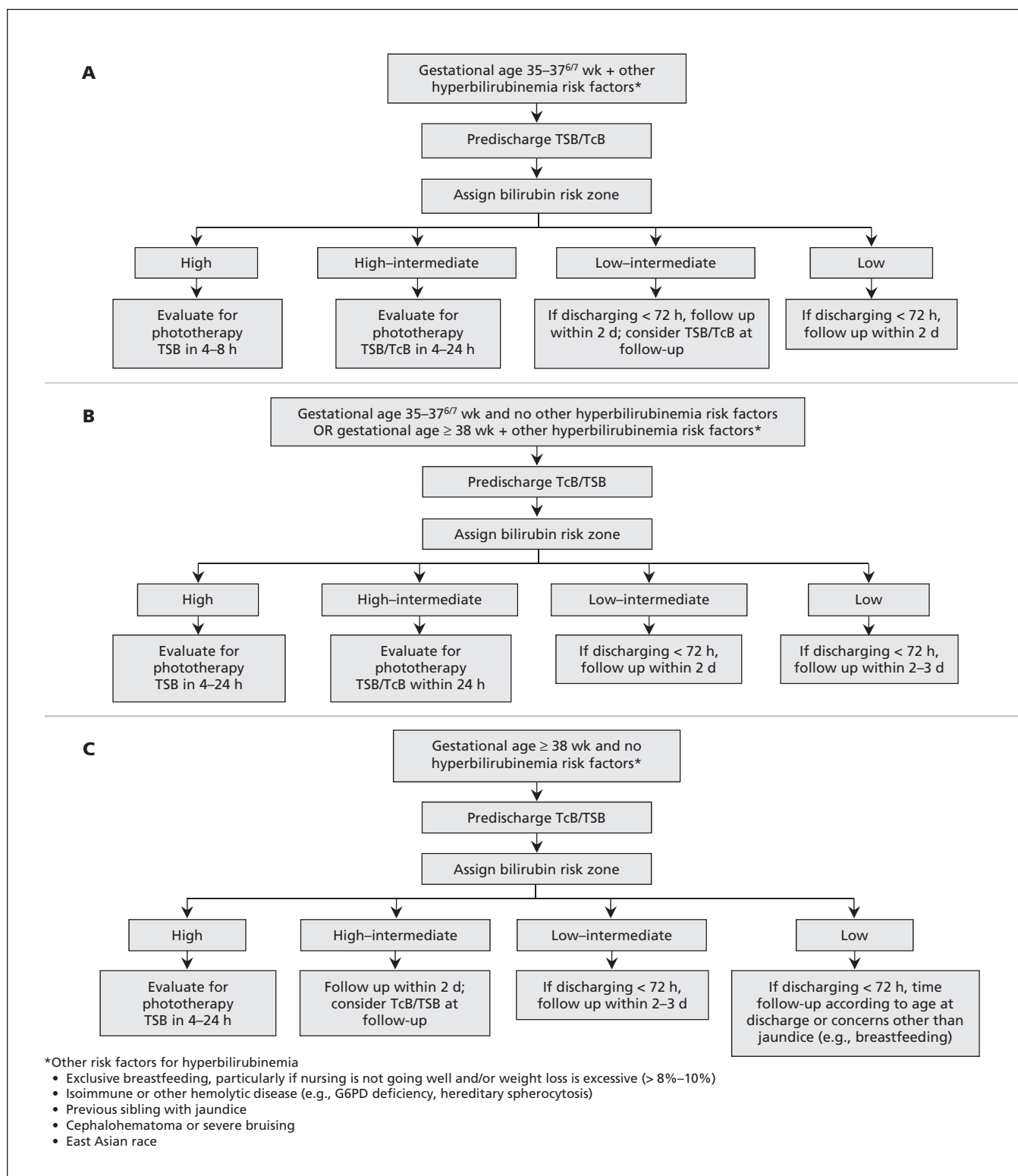


Figure 2: Algorithm providing recommendations for management and follow-up according to predischarge bilirubin measurements, gestational age and risk factors for subsequent hyperbilirubinemia. G6PD = glucose-6-phosphate dehydrogenase.

- Provide lactation evaluation and support for all breastfeeding mothers.
 - Recommendation for timing of repeat total serum bilirubin (TSB) or transcutaneous bilirubin (TcB) measurement depends on infant's age at measurement and how far the level is above the 95th percentile (Figure 1); higher and earlier initial levels require an earlier repeat measurement.
 - Perform standard clinical evaluation at all follow-up visits.
 - For evaluation of jaundice, see the 2004 American Academy of Pediatrics guideline.³
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elements of the 2004 American Academy of Pediatrics guidelines are listed in Box 2, and the hyperbilirubinemia and neurotoxicity risk factors in Boxes 3 and 4. From an analysis of the cases reported to the pilot USA Kernicterus Registry¹⁷ and the experience of those who have reviewed numerous malpractice cases involving kernicterus, the failure of clinicians to follow these guidelines accounts for most, but not all, of the kernicterus cases seen today.

Why does kernicterus still occur in the developed world?

Bilirubin levels in the newborn are unlike other laboratory measurements. The continuously shifting balance between bilirubin production and clearance produces the hourly fluctuations in total serum bili-

rubin levels that are unique to the newborn infant. Figure 1 shows why it is essential to interpret total serum bilirubin levels according to the infant's age in hours. The levels are meaningless unless they are compared with the infant's age in hours.^{3,4,18,19} Total serum bilirubin levels also vary with the racial composition of the population, the incidence of breastfeeding, and other important genetic and epidemiologic factors.¹² Total serum bilirubin levels are substantially higher in East Asian populations than in white populations, and black infants as a group have even lower levels than white infants.¹² Nevertheless, it is most important to remember that some 12% of black male infants and 4% of black female infants have a glucose-6-phosphate dehydrogenase (G6PD) deficiency,²⁰ which puts them at risk of severe hyperbilirubinemia and kernicterus (discussed later).^{1,17}

Furthermore, hospital stays are now short. It was easy to monitor jaundice and measure total serum bilirubin levels when infants remained in hospital for three or more days after birth. Today, an infant delivered vaginally is often discharged well before age 48 hours and, in some cases, before 24 hours. Figure 1 shows that bilirubin levels usually peak on the fourth or fifth day after birth. Identification and management of the jaundiced infant has therefore changed from an inpatient to an outpatient problem, which is why appropriate outpatient follow-up is so important³⁻⁵ (Figure 2).

The clinical assessment of jaundice can be difficult, and detection of jaundice by blanching the skin with digital pressure, even in a well-lit room or at a window, does not correlate well with total serum bilirubin levels.^{16,21,22} In infants discharged early, the bilirubin levels that require additional investigation, initiation of phototherapy or closer follow-up are quite low. As a result, using the degree of jaundice to estimate total serum bilirubin levels during the infant's hospital stay is not sufficient to allow these decisions about follow up and monitoring to be made with confidence. Recognizing these limitations, experts now recommend that the total serum bilirubin or transcutaneous bilirubin level be mea-

Box 2: Key elements from the American Academy of Pediatrics guideline on the management of hyperbilirubinemia in the newborn at ≥ 35 weeks' gestation³

- Promote and support successful breastfeeding
- Establish nursery protocols for the identification and evaluation of hyperbilirubinemia
- Measure the total serum or transcutaneous bilirubin level in infants with jaundice in the first 24 hours
- Recognize that visual estimation of the degree of jaundice can lead to errors, particularly in darkly pigmented infants
- Interpret all bilirubin levels according to the infant's age in hours
- Recognize that infants at less than 38 weeks' gestation, particularly those who are breastfed, are at higher risk of hyperbilirubinemia and require closer surveillance and monitoring
- Perform a systematic assessment on all infants before discharge for the risk of severe hyperbilirubinemia
- Provide parents with written and verbal information about jaundice in the newborn
- Provide appropriate follow-up based on the time of discharge and the risk assessment
- Treat jaundice in the newborn, when indicated, with phototherapy or exchange transfusion

Box 3: Important risk factors for severe hyperbilirubinemia in infants at ≥ 35 weeks' gestation

- Predischarge total serum or transcutaneous bilirubin measurement in the high-risk or high-intermediate-risk zone
- Lower gestational age
- Exclusive breastfeeding, particularly if nursing is not going well and weight loss is excessive
- Jaundice observed in the first 24 hours
- Isoimmune or other hemolytic diseases (e.g., G6PD deficiency)
- Previous sibling with jaundice
- Cephalohematoma or significant bruising
- East Asian race

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Box 4: Hyperbilirubinemia neurotoxicity risk factors [in addition to lower gestational age]

- Isoimmune hemolytic disease
- G6PD deficiency
- Asphyxia
- Sepsis
- Acidosis
- Albumin < 3.0 mg/dL [< 0.03 g/L]

G6PD = glucose-6-phosphate dehydrogenase. Reproduced with permission from Maisels et al.,⁵ *Pediatrics* 2009;124:1193-8. Copyright © 2009 American Academy of Pediatrics.

sured in all infants before discharge from the birth facility.^{4,5} In addition, nursing protocols should require measurement of total serum or transcutaneous bilirubin (without a physician's order)³ for any newborn who appears jaundiced in the first 24 hours.³⁻⁵

Because jaundice progresses cephalocaudally from face to trunk and then to the extremities, for a given bilirubin level, the skin of the face will appear more yellow than that of the foot.²³ It has been suggested that this phenomenon is the result of regional differences in skin temperature and skin perfusion,²⁴ but recent data suggest that this may not be correct.²¹ Cephalocaudal progression is graded 0 through 5.²² In a prospective cohort study of the accuracy of predischARGE visual assessment of jaundice in term and late preterm infants, only 1 of 100 infants without jaundice (cephalocaudal grade of 0) subsequently had hyperbilirubinemia, for a negative predictive value of 99%.²² Therefore, complete absence of jaundice is reassuring. But jaundice in the arms and legs below the knees (a grade of 4 or 5) was strongly associated with the development of clinically significant hyperbilirubinemia (odds ratio 6.0, 95% confidence interval [CI] 2.1–17.0).²² Nevertheless, because there is a wide range of bilirubin levels associated with each cephalocaudal grade,^{21,22} it is not possible to provide an accurate visual estimate of a bilirubin level.

How else might we assess a newborn with jaundice?

As an alternative to measuring serum bilirubin, transcutaneous bilirubin measurement is non-invasive and provides instantaneous information about the infant's bilirubin level that is superior to clinical assessment.¹⁶ There are currently two commercial devices for measuring transcutaneous bilirubin levels that are available in North America: the Konica Minolta Dräger Air-Shields JM-103 (Dräger Medical Inc., Telford, Pa.) and the BiliChek (Phillips Children's Medical Ventures, Monroeville, Pa.).¹⁶ These instruments measure the yellow colour of the blanched skin and subcutaneous tissue and convert this into an estimated total serum bilirubin level.¹⁶ The clinical utility of transcutaneous bilirubin measurements has been extensively evaluated and confirmed in hospital nurseries and outpatient settings.¹⁶ For example, a transcutaneous level above the 75th percentile¹⁸ measured with the BiliChek tool was found to be 100% sensitive in identifying infants whose total serum bilirubin levels were above the 95th percentile, for a positive predictive value of 32.9% and a negative predictive value of 100%.²⁵

In an outpatient population in which transcutaneous bilirubin was measured with the Dräger JM-103, when the transcutaneous level was less than 222 $\mu\text{mol/L}$ (13 mg/dL), the total serum bilirubin was never at or above 290 $\mu\text{mol/L}$ (17 mg/dL), for a negative predictive value of 100% and a positive predictive value of 39%.²⁶ Transcutaneous bilirubin is not a measurement of the total serum bilirubin, but when it is used as a screening tool, transcutaneous measurement can tell us (a) whether we need to measure the total serum bilirubin level and (b) whether we need to worry about the infant. Transcutaneous bilirubin measurement reduces the likelihood that a clinically significant total serum bilirubin level will be missed;^{27,28} substantially reduces the number of serum measurements needed;^{28,29} helps to estimate the risk of subsequent hyperbilirubinemia;^{8,28,30,31} and is invaluable in the outpatient setting.^{26,28,32}

Because transcutaneous bilirubin measurement tends to underestimate the total serum bilirubin level at higher serum levels, various techniques have been adopted to avoid missing a high total serum bilirubin level (i.e., a false-negative transcutaneous measurement). Investigators recommend measuring the total serum bilirubin level if the transcutaneous level is at 70% of the serum level recommended for the use of phototherapy;³³ the transcutaneous level is above the high intermediate risk line (75th percentile) on the Bhutani nomogram (Figure 1) or the 95th percentile on a transcutaneous bilirubin nomogram;^{16,34} or the transcutaneous level at follow-up after discharge is above 222 $\mu\text{mol/L}$ (13 mg/dL).^{26,32} In two outpatient studies, no infant who had a transcutaneous bilirubin level of 222 $\mu\text{mol/L}$ or less had a total serum bilirubin level equal to or greater than 290 $\mu\text{mol/L}$ (17 mg/dL).^{26,32} In one of the studies, the highest of three independent measurements with the Dräger JM-103 (not the average of three) was used for screening.²⁶ This method significantly reduced the risk of false-negative results but increased the risk of false-positive ones.

The current cost of a transcutaneous bilirubin instrument is about US\$6000, which unfortunately may deter practising physicians from purchasing one. The BiliChek also requires the use of a calibration tip (US\$10 per tip) before each measurement.

Can we predict which infant will have severe hyperbilirubinemia?

Numerous studies have identified the laboratory and clinical factors that allow us to assess the risk of subsequent severe hyperbilirubinemia in the first few days following birth. Box 3 lists the

factors that are considered relevant in helping the clinician to assess which infants will likely have hyperbilirubinemia.⁵

Absent hemolytic disease, the infant's gestational age is by far the most important single clinical risk factor for hyperbilirubinemia.⁷ When age in hours is combined with a predischarge transcutaneous or total serum bilirubin level, the effect of decreasing gestational age becomes even more important (Figure 3).^{7,31} Recent studies have shown that simply combining the predischarge bilirubin level with the infant's gestational age allows a level of positive and negative prediction that is indistinguishable from models that use all of the additional clinical risk factors.^{7,31} The utility of this parsimonious and simple method of risk prediction is illustrated in Figure 3. In a prospective cohort study, the risk of clinically significant hyperbilirubinemia in an infant whose predischarge transcutaneous bilirubin level was between the 75th and 95th percentile was 50 times greater at a gestational age of 35–37⁶⁷ weeks than at 40 or more weeks.⁷ Thus, to predict the risk of hyperbilirubinemia accurately, we need to know the gestational age and the bilirubin level for every infant before discharge.^{4,5} In addition, studies have shown that the introduction of universal bilirubin screening was associated with a significant decrease in the frequency of total serum bilirubin levels exceeding 425 $\mu\text{mol/L}$ (25 mg/dL).^{16,28,35}

There are other benefits associated with obtaining a predischarge bilirubin level for every newborn. Knowledge of the hour-specific total serum bilirubin level can alert the physician to the possibility of a problem that was not previously recognized. A level above the 95th percen-

tile (Figure 1) or consecutive measurements that cross percentiles suggest the need for increased surveillance, repeat measurement (total serum or transcutaneous bilirubin) in 4–24 hours and possibly further investigation to establish the cause of these total serum bilirubin levels.¹²

The Bhutani nomogram (Figure 1)¹⁸ has been widely used to predict which infants are or are not at risk of hyperbilirubinemia. In the original study, 39.5% of infants whose total serum bilirubin levels before discharge were in the high-risk zone subsequently had levels above the 95th percentile, as compared with none of the 1750 infants whose predischarge bilirubin level was in the low-risk zone. Nevertheless, subsequent studies have shown that some infants with a predischarge transcutaneous bilirubin level in the low–intermediate or low-risk zone will go on to have total serum bilirubin levels that meet the requirement for phototherapy.³¹ Appropriate follow-up for all infants is essential, even if they appear to be at low risk of severe hyperbilirubinemia. The algorithm in Figure 2 tells us how to manage and follow infants according to their gestational age and risk factors for hyperbilirubinemia, provided the predischarge bilirubin level is known.⁵ The early discharge of newborns following delivery makes appropriate follow-up mandatory for the prevention of severe hyperbilirubinemia and kernicterus.

What is the role of G6PD deficiency in severe hyperbilirubinemia?

A G6PD deficiency is one condition that presents an ongoing challenge to our ability to provide appropriate monitoring and surveillance of the newborn with jaundice.^{36,37} This X-linked enzymopathy has traditionally been regarded as a condition seen predominantly in the Mediterranean basin, Africa, the Middle East and Asia, but travel, immigration and intermarriage have transformed G6PD deficiency into a condition that is now encountered worldwide and has been responsible for causing extreme hyperbilirubinemia and kernicterus in the United States, Canada and Great Britain.^{1,17,37,38}

Newborns with G6PD deficiency appear completely normal and often have a normal total serum or transcutaneous bilirubin level soon after birth. However, following discharge, exposure to an oxidative stress such as naphthalene (found in mothballs), or infection or, most often, an undetermined trigger, can produce an acute hemolytic event and a rise in total serum bilirubin to a hazardous level in a matter of hours.^{36,37} Because there is no way of predicting these

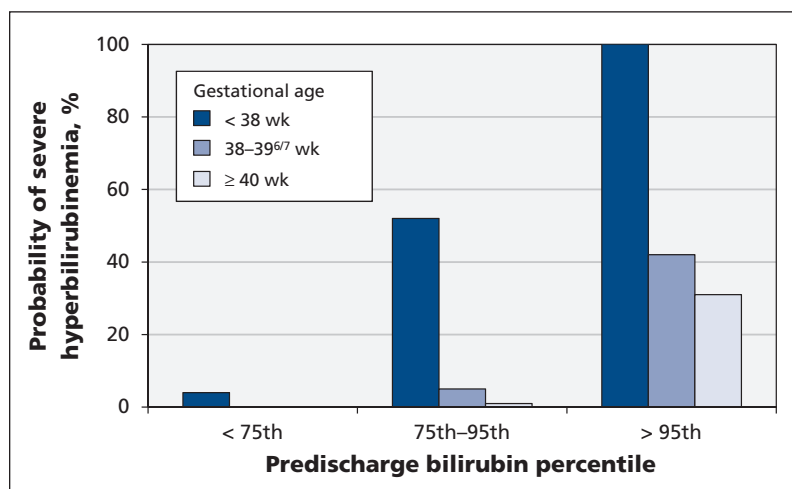


Figure 3: Probability of severe hyperbilirubinemia developing based on a newborn's predischarge bilirubin level and gestational age. Severe hyperbilirubinemia was defined as a total serum bilirubin level that exceeded or was within 1 mg/dL (17.1 $\mu\text{mol/L}$) of the hour-specific American Academy of Pediatrics threshold for phototherapy.³ Redrawn from data reported by Keren et al.⁷

exposures to oxidative stress, the current systems of monitoring and surveillance are inadequate to prevent these unpredictable events.

Can we prevent hyperbilirubinemia in breastfed infants?

The primary approach to mitigating the hyperbilirubinemia associated with exclusive breastfeeding is to ensure that breastfeeding is successful.^{3,4} Exclusive breastfeeding is strongly associated with an increased risk of hyperbilirubinemia.¹² In many breastfed infants, however, the hyperbilirubinemia appears to be primarily the result of less effective breastfeeding. A decrease in energy intake increases the enterohepatic circulation of bilirubin,³⁹ which produces a greater bilirubin load on a liver that is already compromised in its ability to clear bilirubin. Because of short hospital stays after delivery, it is increasingly difficult to

provide adequate advice and lactation support to mothers before they are discharged, and this support must be continued in the physician's office and at home.⁴⁰ Evidence for adequate intake in the breastfed infant includes four to six wet diapers in 24 hours by day 3 and the passing of mustard-coloured seedy stools by day 4 or 5.⁴⁰ The adequacy of milk production and transfer should be evaluated, and the infant monitored, if the weight loss by day 3 is greater than 7%–10%.⁴⁰

How is hyperbilirubinemia treated?

There are three ways of treating hyperbilirubinemia, but phototherapy is the treatment used today in the overwhelming majority of newborns. The other treatment methods — exchange transfusion and pharmacologic intervention — are beyond the scope of this review.

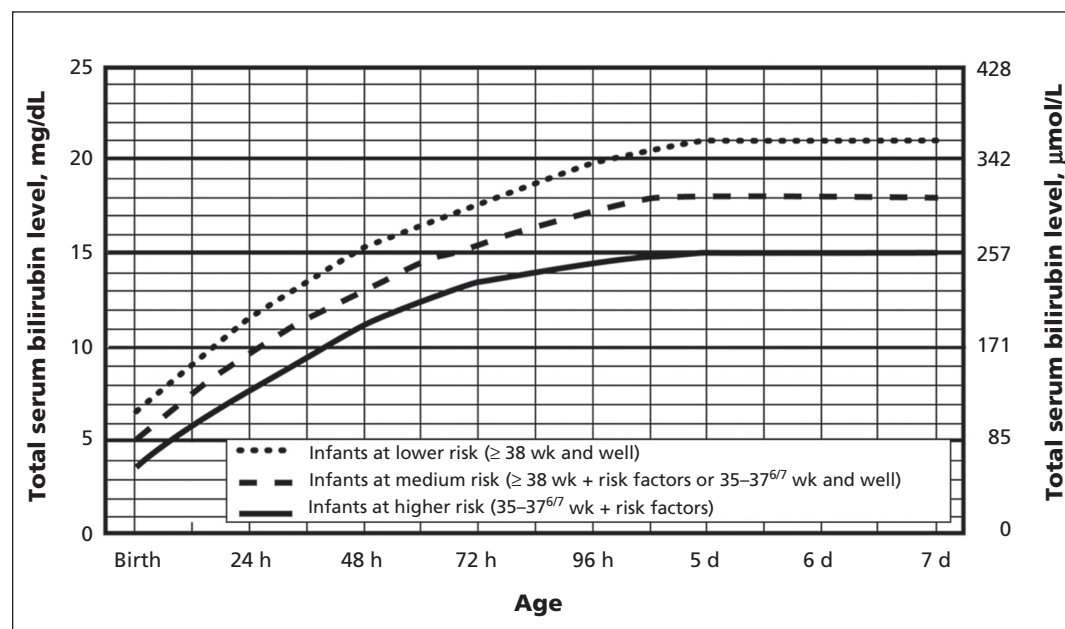


Figure 4: Guidelines for phototherapy in inpatient newborns at ≥ 35 weeks' gestation. Use total serum bilirubin. Do not subtract direct reacting or conjugated bilirubin. The lines for lower, medium and higher risk refer to risk of neurotoxicity (for neurotoxicity risk factors, see Box 4). For well infants at 35 to 37^{6/7} weeks' gestation, total serum bilirubin levels can be adjusted for intervention around the medium risk line. It is an option to intervene at lower levels for infants closer to 35 weeks' gestation and at higher levels for infants closer to 37^{6/7} weeks' gestation. Conventional phototherapy can be provided in hospital or at home at total serum bilirubin levels of 2–3 mg/dL (35–50 $\mu\text{mol/L}$) below those shown, but home phototherapy should not be used in any infant with risk factors. These guidelines refer to the use of intensive phototherapy, which should be used when the total serum bilirubin level exceeds the line indicated for each category. Infants are designated as higher risk because of the potential negative effects of the conditions listed on albumin binding of bilirubin,^{41–43} the blood–brain barrier⁴⁴ and the susceptibility of the brain cells to damage by bilirubin.⁴⁴ Intensive phototherapy implies irradiance in the blue–green spectrum (wavelengths of about 430–490 nm) of at least 30 $\mu\text{W}/\text{cm}^2$ per nanometre (measured at the infant's skin directly below the centre of the phototherapy unit) and delivered to as much of the infant's surface area as possible. Note that irradiance measured below the centre of the light source is much greater than that measured at the periphery. Measurements should be made with a radiometer specified by the manufacturer of the phototherapy system. If the total serum bilirubin level does not decrease or continues to rise in an infant who is receiving intensive phototherapy, this strongly suggests the presence of hemolysis. Reproduced with permission from Maisels et al.,⁵ *Pediatrics* 2009;124:1193–8. Copyright © 2009 American Academy of Pediatrics.

Phototherapy lowers the bilirubin level by converting the bilirubin molecule to products that can bypass the liver's conjugating system and be excreted in the bile or in the urine without further metabolism. The American Academy of Pediatrics guidelines for implementing phototherapy in infants at 35 or more weeks of gestation are shown in Figure 4^{3,5} and have been widely adopted in Canada⁴ and many other countries. The total serum bilirubin level at which intervention is recommended is based on the gestational age and other neurotoxicity risk factors (Box 4). These risk factors are the laboratory and clinical factors that might increase the risk of brain damage in an infant who has hyperbilirubinemia. Intervention is recommended at a lower total serum bilirubin level when any of the neurotoxicity risk factors are present (Figure 4).

The purpose of phototherapy in infants at 35 or more weeks of gestation is to prevent the need for an exchange transfusion, and in this respect it has been an overwhelming success.⁴⁵ But how many infants need to receive phototherapy to prevent one from requiring an exchange transfusion (the number needed to treat [NNT])? Newman and colleagues⁴⁶ estimated the number to be 10 (95% CI 6–19) for a male infant at 36 weeks' gestation who is less than 24 hours old. But for a female infant at 41 weeks' gestation who is 3 or more days old, the NNT was 3041 (95% CI 888–11 096), which strongly suggests that phototherapy could be avoided in many infants who are more mature (e.g., ≥ 39 wk).

Instead of routinely admitting infants with hyperbilirubinemia for treatment, we should consider other options, such as improved lactation support or formula supplementation.^{47,48} This latter option, although opposed by some, deserves serious consideration when one considers the alternative and cost of hospital admission and phototherapy to a blindfolded infant, an intervention that interferes with parent–infant bonding, interrupts breastfeeding and is, at the very least, disturbing for the parents. Complications associated with phototherapy include DNA damage, alterations in cytokine levels and oxidative stress,⁴⁹ and one study found an increase in the development of melanocytic nevi.⁵⁰ In one randomized controlled trial, supplementation with a whey/casein (60/40) formula significantly decreased transcutaneous bilirubin levels in breastfed newborns in the first week.⁴⁷ In another trial, substituting formula for breastfeeding for two days was as effective as phototherapy in reducing the total serum bilirubin level.⁵¹ Other options include the use of home phototherapy, or simply repeating the measurement of total serum bilirubin after several hours. In many cases, the

level will have decreased.⁴⁸ If 3000 infants need to receive phototherapy to prevent 1 from requiring an exchange transfusion, it is reasonable to ask whether, in many of these infants, phototherapy could have been avoided.

Conclusion

The management of jaundice in the newborn is a challenge because of the desire to avoid the devastating outcome of kernicterus while minimizing testing and treatment in the majority of newborns, who will do perfectly well with no interventions for jaundice. By simply combining the gestational age with the predischarge, hour-specific bilirubin level (transcutaneous or total serum level), one can, with considerable confidence, quantify the risk of severe hyperbilirubinemia in most newborns. With appropriate follow-up of infants, most cases of kernicterus can be prevented, although G6PD deficiency remains an important challenge. Continued evaluation of the screening and follow-up of newborns with jaundice will help to gauge the effectiveness of current recommendations and to determine their impact, if any, on the incidence of hyperbilirubinemia and kernicterus.

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