ARTICLE

Transcutaneous Bilirubin Levels in the First 96 Hours in a Normal Newborn Population of ≥35 Weeks' Gestation

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ABSTRACT

OBJECTIVE. To obtain transcutaneous bilirubin (TcB) measurements, at 6-hour intervals, in the first 96 hours after birth in a normal newborn population (gestational age: ≥35 weeks).

METHODS. We performed 9397 TcB measurements on 3984 healthy newborn infants (gestational age: ≥35 weeks) from 6 to 96 hours of age. All measurements were performed in the well-infant nursery with a Draeger Air-Shields transcutaneous jaundice meter (model JM-103), within 2 hours of the designated time.

RESULTS. There was a distinct pattern to the velocity of the increase in TcB levels over different time periods. TcB levels increased in a linear manner most rapidly in the first 6 to 18 hours and then less rapidly from 18 to 42 hours, followed by a much slower increase until peak levels occurred. Decreasing gestational age was associated significantly with higher TcB levels.

CONCLUSIONS. We provide data on neonatal bilirubinemia, based on TcB levels determined in a large, predominately white and breastfed, North American population. Infants who require closer evaluation and observation initially are those whose bilirubin levels are ≥95th percentile, ie, increasing more rapidly than 0.22 mg/dL per hour in the first 24 hours, 0.15 mg/dL per hour between 24 and 48 hours, and 0.06 mg/dL per hour after 48 hours. These data should be useful for detecting aberrant trends, identifying infants who need additional evaluation, and planning appropriate follow-up for jaundiced newborns.

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Key Words
bilirubin, newborn, jaundice, transcutaneous bilirubin

Abbreviations
TcB—transcutaneous bilirubin
TSB—total serum bilirubin

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ALTHOUGH THERE HAVE been many studies of bilirubin levels in normal newborn populations, the definition of what represents a "normal bilirubin level" has proved elusive. This is because total serum bilirubin (TSB) levels change rapidly in the first 48 to 72 hours and vary considerably depending on gestational age, the racial composition of the population, the proportion of breastfed infants, other genetic and epidemiological factors, and the laboratory methods used to measure bilirubin levels.[1] We now have short hospital stays, and predischarge transcutaneous bilirubin (TcB) or TSB measurements, together with the nomogram developed by Bhutani et al,[2] are being used with increasing frequency to identify when additional evaluation is necessary and to predict the risk of subsequent hyperbilirubinemia.[3] But for the reasons noted below, this nomogram does not represent the natural history of bilirubinemia in newborns. We therefore sought to define bilirubin levels in a normal newborn population (gestational age: ≥35 weeks) in the first 96 hours after birth, and the availability of TcB measurements made it possible to obtain such data. Previously we documented the accuracy of the JM-103 meter (Draeger Medical Inc, Telford, PA) in a large multiracial population.[4]

METHODS

Between November 1, 2002, and July 31, 2004, we obtained 9397 TcB measurements for 3984 infants (gestational age: ≥35 weeks) from 6 to 96 hours after birth. This was a convenience sample, obtained in cross-sectional manner from a total population of 11 796 infants admitted to the well-infant nursery of William Beaumont Hospital. TcB measurements were obtained by research nurses, from the midsternum, with the Draeger Air-Shields transcutaneous jaundice meter, model JM-103. The principles of operation of the JM-103 and the technique of measurement were as described previously.[4,5] Using a daily list of all deliveries, the nurses obtained TcB measurements between 6:30 AM and 5:00 PM, Monday through Friday, for all eligible infants whose ages were within 2 hours of one of the designated 6-hour time intervals. All infants in the well-infant nursery were eligible for the study, but we excluded those who required phototherapy before discharge (n = 139). The decision to use phototherapy was made by the attending pediatrician. Routine blood typing and Coombs' testing are not performed at our hospital; therefore, infants with positive Coombs' test results who did not require phototherapy were included. Percentiles were calculated empirically for each time interval from the array of data, with Microsoft Excel software (Microsoft, Redmond, WA).

The study was approved by the hospital's human investigation committee. Because this is a standard, completely noninvasive measurement that is performed as part of routine clinical assessment in our nursery, the committee approved a waiver of consent, and parental consent was not obtained. Demographic data on race (mother's description), delivery mode, gestational age (obstetrical estimate), and feeding were obtained from the hospital records at the time of TcB measurement. More than 90% of mothers in our hospital have full prenatal care, with first-trimester ultrasound evaluation for gestational assessment.

RESULTS

Smoothed percentile curves were drawn from the raw data (Figs 1 and 2). The full data set for this study is available with the electronic version of this article. Population demographic data are provided in Table 1, and Table 2 shows the rate of increase in TcB levels at different ages. Because there were more than twice as many TcB measurements obtained as infants studied, a possible bias might have occurred if there were many

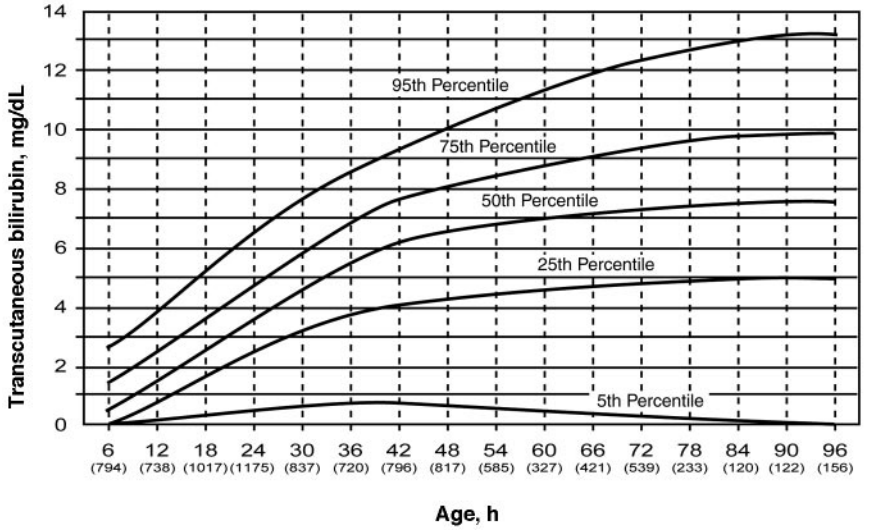

FIGURE 1
Nomogram showing smoothed curves for the 5th, 25th, 50th, 75th, and 95th percentiles for TcB measurements among healthy newborns (gestational age: ≥35 weeks). A total of 9397 TcB measurements were obtained for 3984 newborns. The number of infants studied at each interval is shown in parentheses.

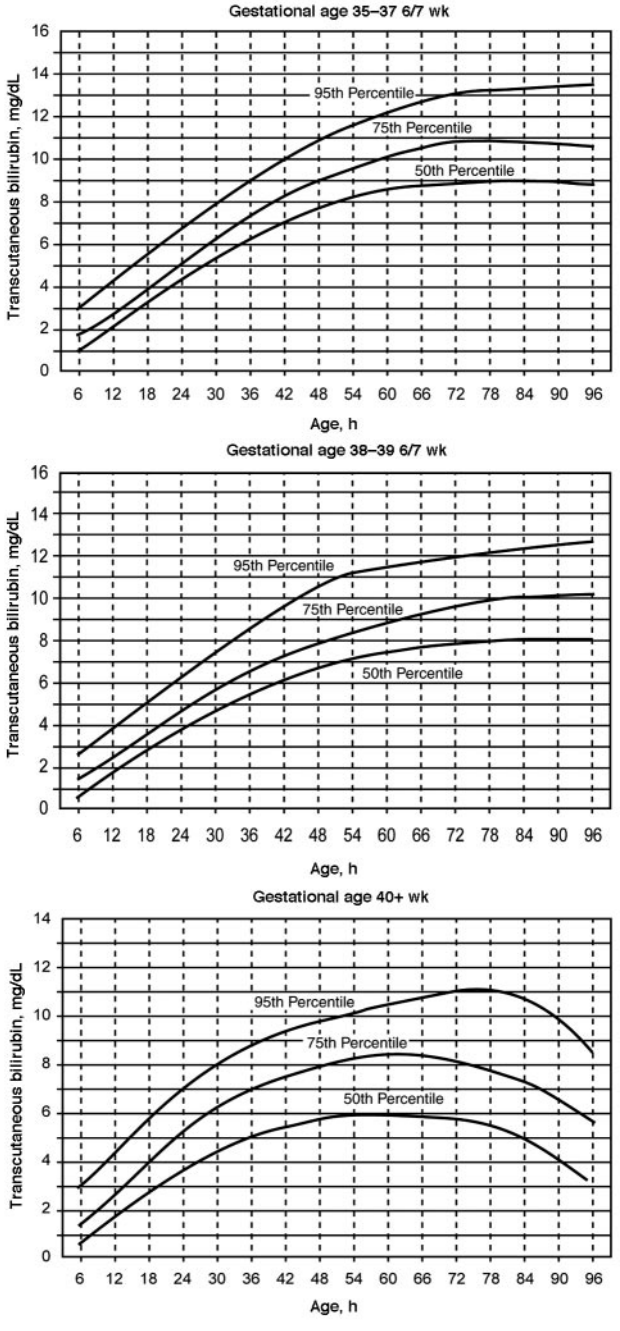

FIGURE 2
Nomograms for TcB levels according to gestational age.

more measurements for some of the demographic groups. Table 1 shows that this was not the case. Figure 3 demonstrates the normal distribution of TcB levels at different ages. The effects of gestational age on TcB levels and on the time course of bilirubinemia are illustrated in Fig 2. Decreasing gestational age and breastfeeding were associated with significantly higher TcB levels (Fig 2 and Table 3).

Short hospital stays after vaginal delivery make it difficult to obtain data on healthy infants after 48 hours.

TABLE 1 **Population Demographic Data**

	No. (%)	
	Infants	TcB Measurements
Study sample	3984	9397
Race[a]		
White	2911 (73.1)	6865 (73.1)
Black	450 (11.3)	1060 (11.3)
Middle Eastern	275 (6.9)	611 (6.5)
Indian	153 (3.9)	355 (3.8)
East Asian	143 (3.8)	333 (3.3)
Hispanic	38 (1.0)	104 (1.1)
Native American	2 (0.1)	4 (0)
Unknown	12 (0.3)	108 (1.1)
Gestational age		
35–37[6/7] wk	684 (17.2)	1646 (17.5)
38–39[6/7] wk	2036 (51.1)	4795 (51.0)
≥40 wk	1273 (32.0)	2912 (30.9)
Feeding		
Breast	2672 (67.1)	6219 (66.2)
Formula	834 (20.9)	1943 (20.7)
Both	478 (12.0)	1189 (12.7)
Delivery mode		
Cesarean section	1598 (40.1)	4239 (45.1)
Vaginal delivery	2386 (59.9)	5112 (54.4)

[a] Race was defined by mother's description.

TABLE 2 **Rate of Increase in TcB Levels in Different Percentiles at Different Ages**

Age Percentile	Increase in TcB Level, mg/dL per h			
	6–24 h	24–48 h	48–72 h	72–96 h
25th	0.14	0.08	0.01	0.02
50th	0.18	0.10	0.03	0.02
75th	0.18	0.13	0.05	0.004
95th	0.22	0.15	0.06	0.07

Increases were calculated by using linear regression analysis.

It was therefore necessary, after 48 hours, to include predominantly infants delivered via cesarean section; 40% of the study infants were delivered via cesarean section, although the total cesarean section rate in this hospital in 2004 was 33.3%. From 60 to 96 hours, 86.1% of the study infants were delivered via cesarean section.

DISCUSSION

We provide the first contemporary data, including the velocity of increase in TcB levels, for neonatal bilirubinemia in a large, predominately breastfed, North American population. The only similar published data are those of Bhutani et al,[2] although there are striking differences between their data and ours. Bhutani et al[2] developed a nomogram based on hour-specific TSB values obtained during the first 6 days after birth and used these data to help predict the likelihood of subsequent hyperbilirubinemia. The validity of this approach as a predictive tool has been amply confirmed,[2,6–11] and the nomogram is included in the hyperbilirubinemia guide-

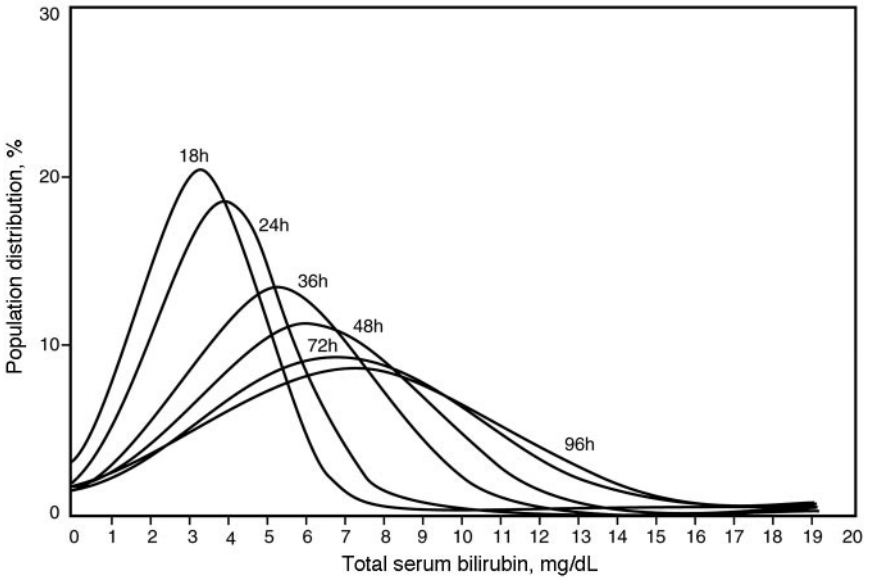

FIGURE 3
Distribution of TcB levels for selected time intervals.

TABLE 3 **Mean TcB Levels According to Delivery Mode, Gestational Age, and Feeding**

	TcB Level, Mean (SD), mg/dL			
	24 h	48 h	72 h	96 h
Delivery mode				
Vaginal delivery	3.7 (1.7)[a]	6.1 (2.9)	6.3 (3.9)	7.0 (5.1)
Cesarean section	3.5 (1.6)[a]	5.8 (2.6)	6.6 (3.4)	7.1 (3.5)
Gestational age				
35–37[6/7] wk	4.0 (1.5)[b]	6.9 (2.7)[c]	7.8 (3.1)[c]	8.3 (2.7)[c]
38–39[6/7] wk	3.6 (1.6)	6.0 (2.6)[c]	6.7 (3.1)[c]	7.4 (3.5)[c]
≥40 wk	3.6 (1.8)	5.2 (3.0)	5.4 (4.0)	3.4 (3.8)
Feeding				
Fully breastfed	3.7 (1.6)	6.0 (2.8)[d]	6.8 (3.4)[d]	7.0 (3.8)
Formula fed	3.5 (1.7)	5.6 (2.7)	6.1 (3.2)	6.0 (3.0)

Decreasing gestational age and breastfeeding have been associated consistently with higher TSB levels.[3] These data were therefore analyzed with a 1-tailed *t* test.
[a] $P < .05$ versus cesarean section (2-tailed *t* test).
[b] $P < .01$ versus 40 weeks (1-tailed *t* test).
[c] $P < .00001$ versus 40 weeks (1-tailed *t* test).
[d] $P < .05$ versus formula fed (1-tailed *t* test).

lines of the American Academy of Pediatrics.[3] Nevertheless, this nomogram does not represent the natural history of bilirubinemia in newborns.

The TSB levels used to create the nomogram of Bhutani et al[2] included measurements performed for infants both before and after discharge, up to the age of 6 days. Infants with positive direct Coombs' test results and those requiring phototherapy before the age of 60 hours were excluded.[2] But, <25% of infants who had TSB levels measured before discharge returned for follow-up care in the next few days. We do not have any clinical information on the infants who did not receive follow-up care, but it is likely that many of those who had low predischarge TSB levels or were not clinically jaundiced were not seen in follow-up visits. Therefore, the TSB values obtained after 48 to 72 hours likely represent a biased sample of more-jaundiced infants, and the data from several other studies support this conclusion.[11–17] In the nomogram of Bhutani et al,[2] the TSB levels reported for the 40th percentile after 48 hours are much higher than the mean TSB levels reported in any previous study,[11–17] including values for an exclusively breastfed Japanese population.[18]

In 6 studies of infants of predominantly northern European origin,[12–17] the mean peak TSB level between days 3 and 6 was 7.1 ± 0.89 mg/dL; in our study, the level at 96 hours was 7.2 ± 3.73 mg/dL (median: 7.7 mg/dL). In an international multicenter study of 1370 well infants (gestational age: ≥35 weeks) from nurseries in the United States, Hong Kong, and Israel, mean TSB levels at 96 ± 12.0 hours were 8.9 mg/dL for exclusively breastfed infants and 7.6 mg/dL for formula-fed infants.[11] With transcutaneous measurements, the median peak TcB level for 223 term, breastfed, Brazilian infants was 5.6 mg/dL.[19] Therefore, our data are remarkably consistent with published data and our mean levels are ~6 mg/dL lower than those of Bhutani et al.[2]

The 95th percentile for our study population is lower than that reported in other studies. In the study by Bhutani et al,[2] the 95th percentile at 96 hours was a TSB level of 17.5 mg/dL, identical to that found in 11 Kaiser Permanente northern California hospitals.[20] In the multicenter international study,[11] the 95th percentile at 96 hours was 15.5 mg/dL. We have no ready explanation for why the 95th percentile for our population is so much lower than those reported elsewhere, although it is very similar to the 95th percentile level of 12.9 mg/dL in the National Collaborative Perinatal Project.[21] One possibility is that TcB measurements underestimate TSB values at higher TSB levels, although our published data do not support this.[4] TSB levels do not reach their peak

until the 5th day or later for some infants, and exclusion of those infants would lower the 95th percentile for our population. Our mean and median values, however, are quite consistent with most published data for similar populations.[12–17]

This study has some limitations. It is not a population-based study, and it represents the data of a single center for a sample of predominately white infants. On the other hand, black infants in the United States have significantly lower TSB levels than do white infants.[22,23] Therefore, a predominance of white infants would tend, if anything, to increase TSB levels. Another limitation of this study is the relatively small sample size for infants 78 to 96 hours of age, and this could affect the validity of these data. Nevertheless, the large sample sizes for the 6- to 72-hour groups and the fact that the TcB measurements were obtained within 2 hours of the listed time make it likely that these data are quite robust. Furthermore, the shapes and characteristics of the percentile curves and the clear differences seen in the gestational age groups are all consistent with published data on the natural history of bilirubinemia in newborns. For the reasons noted above, more infants were delivered via cesarean section than normally found in the United States population, but this had no significant effect on TcB levels (Table 3). We did not compare TcB levels for the different racial groups because the number of nonwhite infants at each age was small.

CONCLUSIONS

The measurement of TSB and TcB levels for many, if not all, infants before discharge is becoming a common practice in the United States and is recommended by the American Academy of Pediatrics as the best-documented method for predicting the likelihood of subsequent hyperbilirubinemia. Normal values are needed to allow appropriate interpretation of these measurements. We provide data for neonatal bilirubinemia, based on TcB levels obtained at 6-hour intervals for 96 hours in a large, unselected, predominately breastfed, North American population. These data should be useful for detecting aberrant trends, for identifying infants who need additional evaluation, and for planning appropriate follow-up care for jaundiced newborns.

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REFERENCES

1. Maisels MJ. Jaundice. In: MacDonald MG, Seshia MMK, Mullett MD, eds. *Neonatology: Pathophysiology and Management of the Newborn*. Philadelphia, PA: Lippincott; 2005:768–846
2. Bhutani VK, Johnson L, Sivieri EM. Predictive ability of a predischarge hour-specific serum bilirubin for subsequent significant hyperbilirubinemia in healthy term and near-term newborns. *Pediatrics.* 1999;103:6–14
3. Maisels MJ, Baltz RD, Bhutani V, et al. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics.* 2004;114:297–316
4. Maisels MJ, Ostrea EJ Jr, Touch S, et al. Evaluation of a new transcutaneous bilirubinometer. *Pediatrics.* 2004;113:1628–1635
5. Yasuda S, Itoh S, Isobe K, et al. New transcutaneous jaundice device with two optical paths. *J Perinat Med.* 2003;31:81–88
6. Keren R, Bhutani VK, Luan X, Nihtianova S, Cnaan A, Schwartz JS. Identifying newborns at risk of significant hyperbilirubinaemia: a comparison of two recommended approaches. *Arch Dis Child.* 2004;90:415–421
7. Newman TB, Liljestrand P, Escobar GJ. Combining clinical risk factors with bilirubin levels to predict hyperbilirubinemia in newborns. *Arch Pediatr Adolesc Med.* 2005;159:113–119
8. Alpay F, Sarici S, Tosuncuk HD, Serdar MA, Inanc N, Gokcay E. The value of first-day bilirubin measurement in predicting the development of significant hyperbilirubinemia in healthy term newborns. *Pediatrics.* 2000;106(2). Available at: www.pediatrics.org/cgi/content/full/106/2/e16
9. Carbonell X, Botet F, Figueras J, Riu-Godo A. Prediction of hyperbilirubinaemia in the healthy term newborn. *Acta Paediatr.* 2001;90:166–170
10. Kaplan M, Hammerman C, Feldman R, Brisk R. Predischarge bilirubin screening in glucose-6-phosphate dehydrogenase-deficient neonates. *Pediatrics.* 2000;105:533–537
11. Stevenson DK, Fanaroff AA, Maisels MJ, et al. Prediction of hyperbilirubinemia in near-term and term infants. *Pediatrics.* 2001;108:31–39
12. Saigal S, Lunyk O, Bennett KJ, Patterson MC. Serum bilirubin levels in breast- and formula-fed infants in the first 5 days of life. *Can Med Assoc J.* 1982;127:985–989
13. Weakes ARL, Beazley JM. Neonatal serum bilirubin levels following the use of prostaglandin E_2 in labour. *Prostaglandins.* 1975;10:699–714
14. Calder AA, Moar VA, Ounsted MK, Turnbull AC. Increased bilirubin levels in neonates after induction of labor by intravenous prostaglandin E_2 or oxytocin. *Lancet.* 1974;2:1339–1342
15. Chew WC. Neonatal hyerbilirubinemia: a comparison between prostaglandin E_2 and oxytocin inductions. *Br Med J.* 1977;3:679–680
16. Chew WC, Swann IL. Influence of simultaneous low amniotomy and oxytocin infusion and other maternal factors on neonatal jaundice: a prospective study. *Br Med J.* 1977;1:72–73
17. Wood B, Culley P, Roginski C, Powell J, Waterhouse J. Factors affecting neonatal jaundice. *Arch Dis Child.* 1979;54:111–115
18. Yamauchi Y, Yamanouchi I. Transcutaneous bilirubinometry in normal Japanese infants. *Acta Paediatr Jpn.* 1989;31:65–72
19. Draque CM, Almeida MFB, Sanudo A, Peres CA, Santos AMN, Kopelman BI. Total serum bilirubin levels during the first 12 days of life in fully breastfed term newborn infants. *Pediatr Res.* 2002;51:343A
20. Newman TB, Escobar GJ, Gonzales VM, et al. Frequency of neonatal bilirubin testing and hyperbilirubinemia in a large health maintenance organization. *Pediatrics.* 1999;104:1198–1203
21. Hardy JB, Drage JS, Jackson EC. *The First Year of Life: The Collaborative Perinatal Project of the National Institute of Neurological and Communicative Disorders and Stroke*. Baltimore, MD: Johns Hopkins University Press; 1979
22. Linn S, Schoenbaum SC, Monson RR, et al. Epidemiology of neonatal hyperbilirubinemia. *Pediatrics.* 1985;75:770–774
23. Newman TB, Easterling MJ, Goldman ES, Stevenson DK. Laboratory evaluation of jaundiced newborns: frequency, cost and yield. *Am J Dis Child.* 1990;144:364–368