

Transcutaneous Bilirubin Measurements in Full-Term Infants

M. Jeffrey Maisels, MB, BCh, and Sarah Conrad, RNC

From the Division of Newborn Medicine, Department of Pediatrics, The Milton S. Hershey Medical Center, The Pennsylvania State University, Hershey

ABSTRACT. A total of 292 transcutaneous bilirubin (TcB) measurements were performed in 157 white full-term infants: 157 were obtained from the forehead and 135 from the midsternum. TcB measurements correlated well with serum bilirubin determinations ($r = .93$, $P < .0001$). The sensitivity of the test was 100% and the specificity 97%. It was possible to establish guidelines for the TcB measurement which identified all infants whose serum bilirubin concentrations exceeded 12.9 mg/100 ml (221 μ moles/liter) with no false-negative and only five false-positive determinations (3%). The positive predictive value for the TcB measurements was 58%. This implies that, in our population, an infant with a TcB index ≥ 24 has a 58% chance of having a serum bilirubin concentration >12.9 mg/100 ml. The negative predictive value was 100%. Thus, a negative test will correctly predict the absence of hyperbilirubinemia in all cases. As these measurements were obtained prospectively in a well-baby population with a prevalence of hyperbilirubinemia (>12.9 mg/100 ml) of 4.5%, the positive predictive value should be applicable to other similar populations and will, in fact, increase in populations with a higher prevalence of hyperbilirubinemia. TcB measurements can be recommended for the identification of significant neonatal jaundice in full-term infants. It is important to recognize, however, that because of potential variations in TcB meters as well as serum bilirubin measurements in different laboratories, each institution should establish its own criteria for the use of this instrument. *Pediatrics* 70:464-467, 1982; *transcutaneous bilirubin, newborn, jaundice*.

Neonatal jaundice is probably the most frequently encountered diagnostic and therapeutic problem in the newborn, but its accurate assessment still requires a measurement of the serum bilirubin concentration. Thus, the development of a screening test that will reduce the necessity for

laboratory analysis and is more reliable than visual inspection of skin color is desirable. Spectrophotometric measurement of the intensity of yellow color in the skin and subcutaneous tissue, using reflectometry, appears to be useful.¹⁻³ Yamanouchi and co-workers² first described the use of a transcutaneous bilirubin (TcB) meter, a small, hand-held, rechargeable instrument. A strobe light passes through a fiberoptic filament and penetrates the blanched skin, transilluminating the subcutaneous tissue. The scattered light comes back through a second fiberoptic filament and is carried to the spectrophotometric module where the intensity of yellow color (corrected for hemoglobin) is measured.²

PATIENTS AND METHODS

We obtained 292 TcB measurements in 157 white full-term infants admitted to the Well Baby Nursery of The Milton S. Hershey Medical Center. The study was approved by the Clinical Investigation Committee of The Milton S. Hershey Medical Center and informed consent was obtained. It has been our practice to obtain a serum bilirubin measurement on all infants on the third day of life or at other times if clinically indicated. TcB measurements were taken when blood samples for serum bilirubin concentration were obtained. In 11 instances the serum bilirubin was determined on clinical indication prior to the third day. All other determinations were performed routinely, on the third day. Total serum bilirubin concentration was measured by a modified diazo method using the DuPont automatic clinical analyzer (ACA III Instruction Manual, The DuPont Co, Clinical Systems Division, Wilmington, DE). At serum bilirubin levels of 2.5, 4.2, and 19.4 mg/100 ml, (Omega chemistry control sera, Hyland Diagnostics Corp, Bannockburn, IL) 30 repeat determinations revealed standard deviations of 0.1, 0.18, and 0.3 mg/100 ml

Received for publication Dec 28, 1981; accepted Feb 3, 1982.
Reprint requests to (M.J.M.) Department of Pediatrics, The Milton S. Hershey Medical Center, Hershey, PA 17033.
PEDIATRICS (ISSN 0031 4005). Copyright © 1982 by the American Academy of Pediatrics.

with coefficients of variation 4.6, 4.2, and 1.5%, respectively. All infants were cared for in bassinets. None of the infants received phototherapy. TcB measurements were obtained from the forehead (157) and from the midsternum (135). Both of these sites have been shown to be convenient and acceptable for its measurement.^{2,3}

RESULTS

The mean serum bilirubin concentration for all infants was 6.4 ± 3.6 (SD) mg/100 ml, range 0.5 to 16.1 mg/100 ml. For the 11 infants in whom bilirubin levels were obtained on clinical grounds, the mean bilirubin level was 4.7 ± 3.4 (SD) mg/100 ml, range 0.9 to 10.6 mg/100 ml. There was a highly significant linear relationship between serum bilirubin and TcB (Fig 1). The regression equations for measurements obtained at the forehead ($y = 7.96 + 1.33x$, $r = .93$, $P < .0001$) and sternum ($y = 7.44 + 1.35x$, $r = .93$, $P < .0001$) were similar. The coefficient of variation for repeated TcB determinations at different sites in one infant was 2.8% to 3.9%, which is similar to that reported by Hegyi et al.³

Although it has been suggested that the accuracy of TcB measurements is poorer at higher serum bilirubin levels,³ visual examination of the regression line did not seem to confirm this. We, therefore, analyzed the deviation from the regression line of each TcB measurement for each serum bilirubin measurement. The results were then grouped in increments of 5 mg/100 ml and the absolute deviation from the regression was compared for serum bilirubin levels of 0 to 4.9, 5.0 to 9.9, and ≥ 10 mg/100 ml (Table). There was no significant difference between the deviations from the regression line for any of the three ranges of serum bilirubin concentration.

DISCUSSION

The population chosen for TcB measurements, with the exception of 11 infants, represents a random sample from the well-baby nursery. In 11 infants, the serum bilirubin concentration was measured because of a clinical suspicion of significant jaundice. In fact, the serum bilirubin concentration in six of these infants was <5 mg/100 ml (85 μ moles/liter) (1 mg/100 ml = 17.1 μ moles/liter) and the mean was 4.3 ± 3.4 (SD) mg/100 ml (compared to a mean for the whole group of 6.4 ± 3.6 mg/100 ml). Thus, the inclusion of these infants (because of presumed jaundice) did not increase the number of infants in the study with significantly elevated bilirubin levels. The fact that 6/11 infants had serum bilirubin concentrations <5 mg/100 ml emphasizes the degree of error inherent in the visual diagnosis

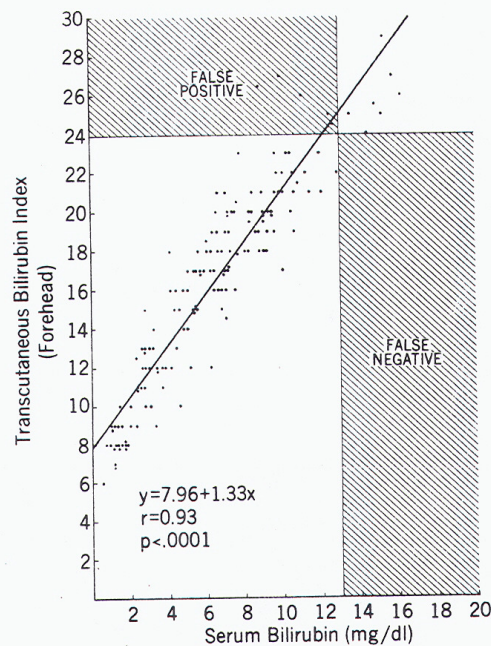


Fig 1. Serum bilirubin determinations and transcutaneous bilirubin (TcB) measurements in 157 white full-term infants. Regression line was calculated using method of least squares.

TABLE. Accuracy of Transcutaneous Bilirubin Measurements Over Range of Serum Bilirubin Measurements Obtained

n	Range of Serum Bilirubin (mg/100 ml)	Δ TcB*
55	0-4.9	1.4 ± 0.99
77	5.0-9.9	1.5 ± 0.87
25	10.0+	1.7 ± 1.20

* Values are means \pm SD. Absolute difference between actual TcB index for each serum bilirubin level and expected TcB index (from regression line). Differences between groups are not significant.

of neonatal jaundice.

As the measurement of transcutaneous bilirubin is likely to be used, primarily, as a screening technique for the identification of neonatal hyperbilirubinemia, we examined the sensitivity and specificity of the measurements. The sensitivity of a test expresses the probability that the result will be positive in the presence of the disease. The specificity expresses the probability that the test will be negative in the absence of the disease. For this purpose we assumed that it was important to identify infants whose serum bilirubin levels were greater than the physiologic range.⁴ Examination of the data suggested a forehead TcB index of 24 and

a sternum TcB index of 23 as useful dividing levels. Results obtained when the TcB index was used to identify infants with a serum bilirubin concentration >12.9 mg/100 ml (221 μ moles/liter) and >10 mg/100 ml (171 μ moles/liter) are shown in Fig 2. For infants with a serum bilirubin concentration >12.9 mg/100 ml, the sensitivity of the TcB measurement was 100% for both measurement sites, and the specificity was 97% for the forehead and 96% for the sternum.

We also calculated the positive predictive value of the TcB measurement⁵ (Fig 2). This is a measure of the probability that there is hyperbilirubinemia present (serum bilirubin concentration >12.9 mg/100 ml) in a patient with a positive test (TcB ≥ 24). The positive predictive value was .583, which implies that 58% of infants with a TcB reading ≥ 24 can be expected to have a serum bilirubin level greater than 12.9 mg/100 ml (or approximately 4/10 infants with a TcB reading ≥ 24 will have a serum bilirubin concentration ≤ 12.9 mg/100 ml). The neg-

ative predictive value is a measure of how well a negative test predicts the absence of hyperbilirubinemia (serum bilirubin level ≤ 12.9 mg/100 ml). This was 100%, implying that a negative test should always predict the absence of hyperbilirubinemia.

The importance of determining the positive and negative predictive values lies in the fact that these values will change with the prevalence of the disease studied, whereas the sensitivity and specificity will not.⁵ The prevalence of hyperbilirubinemia (serum bilirubin concentration >12.9 mg/100 ml) in our population was 4.5%. This is similar to the expected incidence of hyperbilirubinemia in a population of well babies⁴ and implies that the positive predictive value can be applied to other similar populations. In populations in which the incidence of hyperbilirubinemia is higher, the positive predictive value will increase and the number of false-positive TcB tests will, accordingly, diminish.⁵ For example, it can be calculated that if the incidence of hyperbilirubinemia in our study population of

		Forehead		
		Serum bilirubin mg/dl		
		>12.9	≤ 12.9	
TcB Index	≥ 24	7(5%)	5(3%)	12
	< 24	0	145(92%)	145
		7	150	157

Positive predictive value = 58%
Negative predictive value = 100%
Sensitivity = 100%
Specificity = 97%
Prevalence = 4.5%

		Sternum		
		Serum bilirubin mg/dl		
		>12.9	≤ 12.9	
TcB Index	≥ 23	4(3%)	5(4%)	9
	< 23	0	126(93%)	126
		4	131	135

Positive predictive value = 44%
Negative predictive value = 100%
Sensitivity = 100%
Specificity = 96%
Prevalence = 3%

		Serum bilirubin mg/dl		
		>10	≤ 10	
TcB Index	≥ 20	20(13%)	14(9%)	34
	< 20	2(1%)	121(77%)	123
		22	135	157

Positive predictive value = 59%
Negative predictive value = 98%
Sensitivity = 91%
Specificity = 90%
Prevalence = 14%

		Serum bilirubin mg/dl		
		>10	≤ 10	
TcB Index	≥ 19	11(8%)	19(14%)	30
	< 19	0	105(78%)	105
		11	124	135

Positive predictive value = 37%
Negative predictive value = 100%
Sensitivity = 100%
Specificity = 85%
Prevalence = 8.1%

Fig 2. Accuracy of transcutaneous bilirubin (TcB) measurements in predicting infants with serum bilirubin concentrations >10 mg/100 ml (171 μ moles/liter) and >12.9 mg/100 ml (221 μ mole/liter). a, true positive; b, false positive; c, false negative; d, true negative; positive predictive value = $a/(a + b)$; negative predictive value = $d/(c + d)$; sensitivity = $a/(a + c)$; specificity = $d/(b + d)$; prevalence = $(a + c)/(a + b + c + d)$.

151 infants was 10%, approximately 16 infants would have serum bilirubin concentrations >12.9 mg/100 ml. Thus, 141/157 would have serum bilirubin levels less than that range. As the sensitivity of the test is 100%, all of the infants with hyperbilirubinemia would have TcB readings ≥ 24 and because the specificity is 97%, 137/141 infants with serum bilirubin concentrations <12.9 mg/100 ml would have a TcB reading <24 . Thus, four infants would have a serum bilirubin concentration <12.9 yet have TcB levels ≥ 24 (false-positive determinations). Using these new proportions it can be calculated that the positive predictive value would rise from 58% to 80% if the incidence of hyperbilirubinemia increased from 4.5% to 10%.

These data and those previously reported^{1-3,6-9} confirm the usefulness of transcutaneous bilirubin measurements as a screening technique in full-term infants of various races. In 157 determinations at the forehead there were no false-negative and only five (3%) false-positive measurements. This means that no infant whose bilirubin level exceeded 12.9 mg/100 ml was missed and five potentially unnecessary serum bilirubin determinations were obtained. This is a highly acceptable number for a screening procedure.

If identification of a lower serum bilirubin level (eg, 10 mg/100 ml, 171 μ moles/liter) was desired in our population, a forehead TcB >20 would identify all infants with serum bilirubin concentrations >10 mg/100 ml with two false-negative (1%) and 14 (9%) false-positive determinations. No baby had a forehead TcB level ≤ 20 or a serum bilirubin concentration >11 mg/100 ml (188 μ moles/liter).

It is important to recognize that these results cannot, necessarily, be applied to other nurseries, because of the potential variation in the responses of various TcB meters as well as variation in serum bilirubin measurements from laboratory to laboratory.¹⁰ Thus, it is important for each institution to conduct its own study to determine the relationship between the TcB index, as measured with a particular instrument, and the serum bilirubin determinations obtained from a single laboratory.

Inspection of Fig 1 will show that for each TcB measurement there is a range of serum bilirubin determinations that, on occasion, may be as large as 5 mg/100 ml. Hannemann and co-workers¹¹ have

recently made similar observations and concluded, that, because of this variability, the TcB meter currently "cannot be advocated for clinical use." We cannot agree with this view. If used as a screening device, this instrument will, with a perfectly acceptable degree of accuracy, identify those infants who require a serum bilirubin determination. As with any screening test (eg, blood glucose test strips), depending on the limits established, there will be a number of false-positive determinations. Nevertheless, it is quite possible to keep false-negative determinations (failure to identify high serum bilirubin levels) close to zero. Thus, the use of a transcutaneous bilirubin meter can be recommended for the identification of significant neonatal jaundice in healthy full-term infants. Its major role will likely be to identify those infants who require a measurement of the serum bilirubin level and, if necessary, further investigation.

ACKNOWLEDGMENT

The TcB meter was provided by Narco Scientific, Air-Shields Division, Hatboro, PA.

REFERENCES

1. Hannemann RE, DeWitt DP, Wiechel JF: Neonatal serum bilirubin from skin reflectants. *Pediatr Res* 12:207, 1978
2. Yamanouchi I, Yamauchi Y, Igarashi I: Transcutaneous bilirubinometry: Preliminary studies of noninvasive transcutaneous bilirubin meter in the Okayama National Hospital. *Pediatrics* 65:195, 1980
3. Hegyi T, Hiatt IM, Indyk L: Transcutaneous bilirubinometry. I. Correlations in term infants. *J Pediatr* 98:454, 1981
4. Maisels MJ: Neonatal jaundice, in Avery GB (ed): *Neonatology, Pathophysiology and Management of the Newborn*, ed 2. Philadelphia, JB Lippincott Co, 1981, p 484
5. Haynes RB: How to read clinical journals. II. To learn about a diagnostic test. *Can Med Assoc J* 124:703, 1981
6. Lucey JF, Nyborg E, Yamanouchi I: A new device for transcutaneous bilirubinometry. *Pediatr Res* 14:604, 1980
7. Engel RR, Henis BB, Engel RE, et al: Effect of race and other variables on transcutaneous bilirubinometry. *Pediatr Res* 15:531, 1981
8. Brown AK, Kim MH, Nuchpuckdee P, et al: Transcutaneous bilirubinometry in infants: Influence of race and phototherapy. *Pediatr Res* 15:653, 1981
9. Vangyanichyakorn K, Sun S, Abubaker A, et al: Transcutaneous bilirubinometry in black and Hispanic infants. *Pediatr Res* 15:685, 1981
10. Schreiner RL, Glick MR: Interlaboratory bilirubin variability. *Pediatrics* 69:277, 1982
11. Hannemann RE, Schreiner RL, DeWitt DP, et al: Evaluation of the Minolta bilirubin meter as a screening device in white and black infants. *Pediatrics* 69:107, 1982