Normal Serum Bilirubin Levels in the Newborn and the Effect of Breast-Feeding

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ABSTRACT. We measured the serum bilirubin concentrations in 2,416 consecutive infants admitted to our well-baby nursery. The maximum serum bilirubin concentration exceeded 12.9 mg/dL (221 μmol/L) in 147 infants (6.1%), and these infants were compared with 147 randomly selected control infants with maximum serum bilirubin levels ≤12.9 mg/dL. In 66 infants (44.9%), we identified an apparent cause for the jaundice, but in 81 (55%), no cause was found. Of infants for whom no cause for hyperbilirubinemia was found, 82.7% were breast-fed *v* 46.9% in the control group ($P < .0001$). Breast-feeding was significantly associated with hyperbilirubinemia, even in the first three days of life. The 95th percentile for bottle-fed infants is a serum bilirubin level of 11.4 mg/dL *v* 14.5 mg/dL for the breast-fed population, and the 97th percentiles are 12.4 and 14.8 mg/dL, respectively. Of the formula-fed infants, 2.24% had serum bilirubin levels >12.9 mg/dL *v* 8.97% of breast-fed infants ($P < .000001$). When compared with previous large studies, the incidence of "readily visible" jaundice (serum bilirubin level >8 mg/dL) appears to be increasing. The dramatic increase in breast-feeding in the United States in the last 25 years may explain this observation. There is a strong association between breast-feeding and jaundice in the healthy newborn infant. Investigations for the cause of hyperbilirubinemia in healthy breast-fed infants may not be indicated unless the serum bilirubin level exceeds approximately 15 mg/dL, whereas in the bottle-fed infant, such investigations may be indicated if the serum bilirubin exceeds approximately 12 mg/dL. If phototherapy is ever indicated in healthy term infants, the overwhelming majority of such infants are likely to be breast-fed; if breast-feeding is, indeed, the cause of such jaundice, a more appropriate approach to hyperbilirubinemia in the breast-fed infant might be to treat the cause (by temporary cessation of nursing) rather than (using phototherapy to treat) the effect. *Pediatrics* 1986;78: 837–843; *bilirubin, jaundice, newborn infant, breast-feeding.*

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Serum bilirubin levels are obtained daily in every newborn nursery, and important diagnostic and therapeutic decisions are based on these measurements. But there is a paucity of appropriately conducted studies that document the distribution of bilirubin levels in normal newborn populations. Although several prospective studies of the incidence of hyperbilirubinemia in full-term infants have been published,[1–11] with two exceptions,[7,9] the data have not been presented in a manner that permits definition of the prevalence of different bilirubin levels. The National Collaborative Perinatal Project[9] was largely responsible for establishing standards for normal neonatal serum bilirubin levels. In this study, conducted from 1959 to 1966, serum bilirubin concentrations were obtained prospectively on more than 35,000 infants. However, numerous factors are known to affect serum bilirubin levels.[12] For example, although questioned in the past,[2,6,13,14] recent studies and our own data presented here, leave no doubt of the strong association between breast-feeding and jaundice in the early newborn period.[15–25] If we are to establish norms for serum bilirubin levels in newborn infants, the importance of documenting the prevalence of breast-feeding in that population is obvious. In this study, we investigated the association between serum bilirubin concentrations and breast-feeding, and we provide prospective data for a large population of infants to establish the normal distribution of serum bilirubin levels.

PATIENTS AND METHODS

We measured the serum bilirubin concentrations in 2,416 consecutive infants (95% white, 95% > 2,500 g) admitted to our well-baby nursery between January 1, 1976, and December 31, 1980. The total serum bilirubin level was measured in every case on the second or third hospital day (according to a

standard clinical protocol) and was repeated if the concentration exceeded 12.9 mg/dL (221 μmol/L [1 mg/dL = 17.10 μmol/L]) or clinical jaundice increased. When the bilirubin concentration exceeded 12.9 mg/dL (221 μmol/L), the following additional investigations were performed: blood typing, direct and indirect Coombs' tests, reticulocyte count, hematocrit, white blood cell count and differential count, smear for red cell morphology, and total and direct serum bilirubin concentrations. The maximum serum bilirubin level exceeded 12.9 mg/dL in 147 infants (6.1%). These infants constituted our "hyperbilirubinemic" group. From the remaining 2,269 infants with serum bilirubin levels ≤12.9 mg/dL, we randomly selected a control group of 147 infants and compared them with the test group for a number of variables. (Preliminary analysis of the effect of these variables on bilirubin levels has been presented[26] and will be reported in full subsequently.) Information on feeding, birth weight, and weight loss was obtained from a nursery log kept on every baby.

Serum bilirubin measurements were performed by a modified diazo method using an automatic clinical analyzer (ACA III Instruction Manual, DuPont Co, Clinical Systems Division, Wilmington, DE). At serum bilirubin levels of 2.5, 4.2, and 19.4 mg/dL (Ohmeda Chemistry Control Sera, Hyland Diagnostics Corp, Bannockburn, IL), 30 repeated determinations showed standard deviations of 0.1, 0.18, and 0.3 mg/dL with coefficients of variation of 4.6%, 4.2%, and 1.5%, respectively. The data were analyzed using the Fisher exact test for nominal data and a pooled t test for continuous data.

RESULTS

The results are shown in Tables 1 to 3. One hundred forty-seven infants (6.1%) had a serum bilirubin concentration >12.9 mg/dL. In 66 (44.9%), we identified an apparent cause for the jaundice (Table 1), but in 81 (55%), no cause was found (confirming our previous observations[13]). Of infants in whom no cause for hyperbilirubinemia was found, 82.7% were breast-fed v 46.9% in the control group ($P < .00001$). Breast-feeding was significantly associated with hyperbilirubinemia, even in the first three days of life (Table 1). The distribution of maximum total serum bilirubin levels for breast-fed and bottle-fed infants, and all infants with birth weights >2,500 is shown in Table 2 and the Figure. This information by percentile rank is shown in Table 3. The differences between the breast-fed and bottle-fed populations are obvious. Of the formula-fed infants, only 2.24% had serum bilirubin levels >12.9 mg/dL v 8.97% of the breast-fed infants ($P < .000001$). The mean maximum serum bilirubin level for 1,026 bottle-fed infants was 5.7 ± 3.3 (SD) mg/dL v 7.3 ± 3.9 mg/dL for 1,260 breast-fed infants ($P < .0001$). The 95th percentile for bottle-fed infants was a serum bilirubin level of 11.4 mg/dL v 14.5 mg/dL for the breast-fed population and the 97th percentiles were 12.4 and 15.7 mg/dL, respectively. Breast-fed infants lost, on average, 6.9% of their birth weight, whereas bottle-fed infants lost 4.2% ($P < .02$).

DISCUSSION

Our data confirm the striking association between breast-feeding and hyperbilirubinemia. Of infants for whom no apparent cause for hyperbilirubinemia was found, 83% were breast-fed. These findings and those of several other investigators,[15–25] leave no doubt that breast-feeding is strongly associated with increased serum bilirubin levels, not only on days 5 and 6 of life and later[11,14,27–29] but also in the first three to four days. Although some previous studies found no signifi-

TABLE 1. Feeding and Hyperbilirubinemia

Feeding	No. (%) of Infants With Maximum Serum Bilirubin ≤12.9 mg/dL (n = 147)	No. (%) of Infants With Maximum Serum Bilirubin >12.9 mg/dL (n = 147)		
		All Babies (n = 147)	Hyperbilirubinemia Before Discharge With No Apparent Cause (n = 81)	Hyperbilirubinemia by Day 3 With No Apparent Cause (n = 57)
Breast-fed	69 (46.9)	117 (79.6)†	67 (82.7)†	46 (80.7)†
Bottle-fed	71 (48.3)	26 (17.7)	10 (12.3)	8 (14.0)
Breast- and bottle-fed	7 (4.8)	4 (2.7)	4 (4.9)	3 (5.3)

Apparent causes include Rh incompatibility (5 patients), ABO incompatibility (16 patients), infant of diabetic mother (17 patients), asphyxia (6 patients), gestation ≤35 weeks (11 patients), bruising/cephalohematoma (45 patients), polycythemia (3 patients), cholestasis (1 patient).
† $P < .00001$ v serum bilirubin ≤12.9 mg/dL.

TABLE 2. Maximum Total Serum Bilirubin Concentrations in White Newborn Infants Weighing >2,500 Grams at Birth

Serum Bilirubin Concentration		Total Population* (N = 2,297)			Breast-Fed (N = 1,260)			Bottle-Fed (N = 1,026)		
mg/dL	μmol/L	No.	%	Cumulative %	No.	%	Cumulative %	No.	%	Cumulative %
0–0.9	0–16	51	2.22	2.22	29	2.30	2.30	22	2.14	2.14
1.0–1.9	17–33	221	9.62	11.84	90	7.14	9.44	130	12.67	14.82
2.0–2.9	34–50	180	7.84	19.68	86	6.83	16.27	94	9.16	23.98
3.0–3.9	51–67	187	8.14	27.82	82	6.51	22.78	105	10.23	34.21
4.0–4.9	68–84	186	8.10	35.92	90	7.14	29.92	95	9.26	43.47
5.0–5.9	85–102	204	8.88	44.80	98	7.78	37.70	106	10.33	53.80
6.0–6.9	103–119	241	10.49	55.29	118	9.37	47.06	122	11.89	65.69
7.0–7.9	120–136	235	10.23	65.52	135	10.71	57.78	99	9.65	75.34
8.0–8.9	137–153	225	9.80	75.32	140	11.11	68.89	85	8.29	83.63
9.0–9.9	154–170	171	7.44	82.76	104	8.25	77.14	66	6.43	90.06
10.0–10.9	171–187	117	5.09	87.85	77	6.11	83.25	39	3.80	93.86
11.0–11.9	188–204	87	3.79	91.64	59	4.68	87.94	26	2.53	96.39
12.0–12.9	205–221	54	2.35	93.99	39	3.09	91.03	14	1.37	97.76
13.0–13.9	222–238	43	1.87	95.86	35	2.78	93.81	8	0.78	98.54
14.0–14.9	239–256	30	1.31	97.17	26	2.06	95.87	2	0.19	98.73
15.0–15.9	257–273	31	1.35	98.52	24	1.91	97.78	7	0.68	99.42
16.0–16.9	274–290	16	0.70	99.22	16	1.27	99.05	0	0.00	99.42
17.0–17.9	291–307	11	0.48	99.70	8	0.63	99.68	3	0.29	99.71
18.0–18.9	308–324	4	0.17	99.87	2	0.16	99.84	2	0.19	99.90
19.0–19.9	325–341	3	0.13	100.0	2	0.16	100.0	1	0.10	100.0

* Includes 11 infants both breast- and bottle-fed.

TABLE 3. Percentile Ranks for White Newborn Infants Weighing >2,500 Grams

Percentile	Maximum Serum Bilirubin Concentration					
	Total Population* (N = 2,297)		Breast-Fed (N = 1,260)		Bottle-Fed (N = 1,026)	
	μmol/L	mg/dL	μmol/L	mg/dL	μmol/L	mg/dL
3	19	1.1	19	1.1	19	1.1
5	22	1.3	24	1.4	21	1.2
10	31	1.8	36	2.1	27	1.6
15	41	2.4	48	2.8	34	2.0
25	62	3.6	74	4.3	53	3.1
50	111	6.5	125	7.3	96	5.6
75	154	9.0	168	9.8	135	7.9
90	197	11.5	214	12.5	171	10.0
95	231	13.5	248	14.5	195	11.4
97	253	14.8	269	15.7	212	12.4
99	286	16.7	291	17.0	267	15.6

* Includes 11 infants both breast- and bottle-fed.

cant differences between breast-fed and bottle-fed infants, in these studies the breast-fed infants always had higher mean serum bilirubin levels than bottle-fed infants in the first few days of life.[5,6,13,14] Failure to show significant differences was probably the result of type II errors (sample size too small to show a significant difference, although such a difference exists). We found the mean difference for maximum serum bilirubin levels between bottle-fed and breast-fed infants was 1.6 mg/dL, a result similar to that found in other studies.[6,14] To have a 90% chance of showing a significant difference between groups of infants with these mean bilirubin levels requires at least 100 infants in each group.[30]

The described association between breast-feeding and jaundice does not, of course, imply that breast-feeding is the cause of the jaundice. Many factors that influence bilirubin levels are closely associated and, thus, confounding. For example, 15% of our breast-feeding mothers smoked *v* 41% of bottle-feeding mothers ($P < .00001$). Maternal smoking is associated with lower serum bilirubin levels in the newborn.[21,26,31,32] The association between maternal diabetes and hyperbilirubinemia is well known; 87.5% of our diabetic mothers breast-fed their infants *v* 64.4% of nondiabetic mothers ($P = .046$).

There are several reasons, however, why breast-feeding could contribute to neonatal hyperbilirubinemia. The most likely mechanisms include caloric deprivation and an increased enterohepatic circulation of bilirubin, acting separately or in concert. Breast-fed infants lose more weight (and, presumably, receive less calories) in the first few days of life than bottle-fed infants, and associations between weight loss and hyperbilirubinemia have been documented.[11,16,23,26] Caloric deprivation is known to increase the plasma bilirubin concentration in normal adults as well as those with Gilbert syndrome,[33,34] and there is an inverse relationship between oral caloric intake and serum bilirubin concentrations, particularly in infants weighing <2,000 g.[34] In the cooperative National Institute of Child Health and Human Development photother-

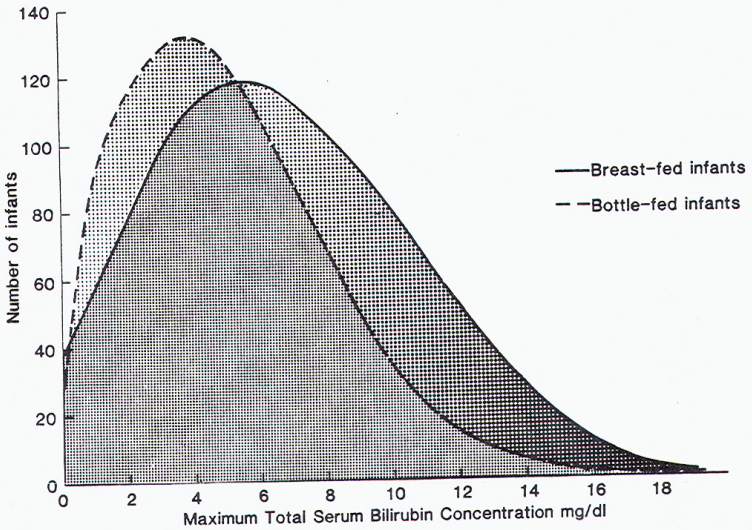

Figure. Distribution of maximum serum bilirubin concentrations in white infants weighing >2,500 g. Curves were computer generated using exponential one knot spline regression.[55]

apy study, those infants receiving ≤90 calories/kg/24 h had significantly higher peak bilirubin concentrations than those fed >90 calories/kg/24 h, and phototherapy was much less effective when caloric and fluid intakes were low.[35] Intestinal absorption of bilirubin increases dramatically in fasted rats.[36]

Breast-fed infants excrete significantly less bilirubin in their stools and pass less stool (by weight) than bottle-fed infants in the first three days of life.[37] De Carvalho et al[38] found that infants who nursed, on average, more than eight times in 24 hours for the first three days of life had significantly lower serum bilirubin levels than those fed less than eight times in 24 hours, and there was a linear, inverse relationship between the frequency of feedings and the maximum serum bilirubin levels. Unfortunately, our charts did not record the frequency of nursing in the breast-fed infants, but recently, we analyzed the feeding practices of 123 mothers who breast-fed their infants on demand while in the hospital. In spite of encouragement from nursing staff, these infants were nursed, on average, only 6.4 times in 24 hours.

Delayed passage of meconium is also associated with higher bilirubin levels,[39–42] and infants fed soon after birth have lower serum bilirubin levels than those fed later.[42,43] In adults, the predominant mechanism for fasting hyperbilirubinemia appears to be a decrease in hepatic clearance of bilirubin from the plasma,[44] and it is possible that this occurs in newborns as well. Certain breast milks also inhibit bilirubin clearance.[45,46] In babies, intestinal absorption of bilirubin appears to be enhanced by breast-feeding[37] and by a decrease or delay in the passage of meconium.[39–42]

Breast-feeding does not appear to affect bilirubin production. Measurements of the pulmonary excretion of carbon monoxide (an index of bilirubin production) showed no differences between breast-fed and bottle-fed infants, and there was no effect of caloric deprivation on bilirubin production.[47]

The values shown in Tables 2 and 3 are representative only of a population of well infants with birth weights of >2,500 g; all sick or significantly premature infants were admitted directly to our neonatal intensive care unit and were not included in this analysis. Because hyperbilirubinemia is often treated, it is not possible to document completely the natural history of neonatal jaundice. At the time of this study, many infants whose bilirubin levels exceeded 12.9 mg/dL received phototherapy, and values for the higher percentiles might be "damped." This would largely affect the values for the breast-fed infants, however, who represent 80% of babies with bilirubin levels >12.9 mg/dL. Furthermore, phototherapy appears to be relatively ineffective in the presence of a low caloric intake.[35] If caloric intake in these infants was poor (which seems likely), phototherapy may have had little or no effect.[35] No exchange transfusions were performed.

For whatever reason, clinically important differences exist between the breast-fed and bottle-fed populations. If we are satisfied with a purely statistical approach and use the 95th percentile to define the limits of physiologic jaundice, then investigations for the cause of jaundice (in an otherwise healthy, three-day-old infant, without blood group incompatibility) might be indicated when the serum bilirubin concentration exceeds 11.4 mg/dL in a bottle-fed infant but not unless it is >14.5 mg/dL in a breast-fed infant. For bilirubin, however, we are generally concerned only with the upper, and not the lower, limits of the distribution curve. Thus, the 97th percentile might be considered a more appropriate limit for physiologic jaundice, in which case we would initiate investigations in bottle-fed infants with serum bilirubin levels >12.4 mg/dL and in breast-fed infants with serum bilirubin levels >15.7 mg/dL. (Note that these "action levels" refer to a population of white infants and might not be appropriate for other racial groups.[9])

Is the Incidence of Neonatal Jaundice Increasing?

Many pediatricians who have practiced for more than 25 years are convinced that they now see more neonatal jaundice than was seen two or three decades ago. Previous investigations have suggested that one possible contribution to the apparent increase in "significant" jaundice was the increased use of oxytocin to induce labor.[48,49] As no adequate prospective studies have ever been performed during a significant time span in the same population, it is not possible to come to firm conclusions regarding this question. It is interesting to note, however, that the incidence of nonphysiologic hyperbilirubinemia (serum bilirubin level >12.9 mg/dL) in white newborns weighing >2,500 g in our study, and in the Collaborative Perinatal Project,[9] is identical—6%. However, in the collaborative project, 26.3% of infants had serum bilirubin levels ≥8 mg/dL *v* 34.5% in our nursery ($P < .0001$). Recognizing the differences in the populations, as well as laboratory techniques (although diazo methods were used in both studies), the results are nevertheless intriguing. They suggest that there has not been an increase in nonphysiologic jaundice, but there has been an increase in "readily visible" jaundice (serum bilirubin level ≥8 mg/dL). The reasons for these differences are not known, although one possibility is the dramatic increase in breast-feeding that has occurred during the last 25 years. Between 1959 and 1966 only 22% to 23% of mothers in the United States were breast-feeding their infants on discharge from the hospital,[50] whereas 55% of our infants (and 54% of infants in the United States in 1980[51]) were fully breast-fed.

Therapeutic Implications

Our data cannot address the question of a bilirubin level (if any) at which these infants should be treated to prevent possible bilirubin encephalopathy. Nevertheless, some therapeutic implications are suggested. Because eight of ten infants with serum bilirubin levels >12.9 mg/dL are breast-fed, they will certainly represent the vast majority of infants being considered for treatment (such as phototherapy). Osborn and Bolus[52] showed that, of breast-fed infants whose serum bilirubin levels reached 14 mg/dL, more than 95% could be treated successfully be temporarily interrupting nursing. Home phototherapy has arrived,[53,54] but closer inspection of infants reported to be candidates for this treatment reveals that the overwhelming majority are breast-fed—84% in one study[53] and 100% of the "study" infants in another[54] (F. Brewer, personal communication, January 1986). It seems reasonable to assume that, with rare exceptions, breast-fed infants are the only infants likely to require this form of therapy. For the sake of argument, let us further assume that phototherapy might be indicated in breast-fed infants whose serum bilirubin levels are >17.0 mg/dL. Our data show that this degree of jaundice occurs in 0.95% of the breast-fed population (Table 2) and, because 95% of these infants can be treated successfully by temporarily interrupting nursing,[52] we can further conclude that only 0.05% (or one in 2,000) breast-fed infants might be legitimate candidates for this form of treatment. Thus, if 2,000 full-term infants are born annually in a hospital, and 50% are breast-fed, we would anticipate that, every 2 years, one infant might need phototherapy.

CONCLUSIONS

Many pediatricians complain (with some justification) that we perform laboratory investigations for the diagnosis of jaundice on an excessive number of infants in our nurseries, and our results confirm this impression. Definitions of physiologic jaundice found in current texts may have created a class of healthy, jaundiced, infants with "non-disease."[56] Before being applied widely, however, our data should be confirmed in similar large studies of other populations. Future studies should also consider additional factors known to affect serum bilirubin levels in the newborn and might yield new criteria for the diagnosis of physiologic and nonphysiologic jaundice. Such criteria are more likely to be scientifically valid and clinically useful than

the existing definitions and would contribute significantly to the prevention of both investigative and therapeutic mischief.

REFERENCES

1. Beazley JM, Alderman B: Neonatal hyperbilirubinemia following the use of oxytocin in labour. *Br J Obstet Gynecol* 1975;82:265–271
2. Boylan P: Oxytocin and neonatal jaundice. *Br Med J* 1976;3:564–565
3. Calder AA, Ounsted MK, Moar VA, et al: Increased bilirubin levels in neonates after induction of labour by intravenous prostaglandin E_2 or oxytocin. *Lancet* 1974;2:1339–1342
4. Chew WC: Neonatal hyperbilirubinaemia: A comparison between prostaglandin E_2 and oxytocin inductions. *Br Med J* 1977;3:679–680
5. 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
6. Dahms BB, Krauss AN, Gartner LM, et al: Breast feeding and serum bilirubin values during the first 4 days of life. *J Pediatr* 1973;83:1049–1054
7. Davidson LT, Merritt KK, Weech AA: Hyperbilirubinemia in the newborn. *Am J Dis Child* 1953;61:958–980
8. Davies DP, Gomersall R, Robertson R, et al: Neonatal jaundice and maternal oxytocin infusion. *Br Med J* 1973;3:476–477
9. Hardy JB, Drage JS, Jackson EC: *The First Year of Life*, the Collaborative Perinatal Project of the National Institutes of Neurological and Communicative Disorders and Stroke. Baltimore, The Johns Hopkins University Press, 1979, p 104
10. Weakes ARL, Beazley JM: Neonatal serum bilirubin levels following the use of prostaglandin E_2 in labour. *Prostaglandins* 1975;10:699–714
11. Wood B, Culley P, Roginski C, et al: Factors affecting neonatal jaundice. *Arch Dis Child* 1979;54:111–115
12. Maisels MJ: Neonatal jaundice, in Avery GB (ed): *Neonatology, Pathophysiology and Management of the Newborn*, ed 2. Philadelphia, JB Lippincott Co, 1981 pp 473–544
13. Maisels MJ, Gifford K: Neonatal jaundice in full-term infants. *Am J Dis Child* 1983;137:561–562
14. McConnell JB, Glasgow JFT, McNair R: Effect on neonatal jaundice of oestrogens and progestogens taken before and after conception. *Br Med J* 1973;3:605–607
15. Adams JA, Hey DJ, Hall RT: Incidence of hyperbilirubinemia in breast- vs. formula-fed infants. *Clin Pediatr* 1985; 24:69–73
16. Butler DA, MacMillan JP: Relationship of breastfeeding and weight loss to jaundice in the newborn: Review of the literature and results of a study. *Cleve Clin Q* 1983;50:263–328
17. DeAngelis C, Sargent J, Chun MK: Breast milk jaundice. *Wis Med J* 1980;79:40–42
18. Drew JH, Barrie J, Horacek I, et al: Factors influencing jaundice in immigrant Greek infants. *Arch Dis Child* 1978;53:49–52
19. Johnson CA, Lieberman B, Hassanein RE: The relationship of breastfeeding to third-day bilirubin levels. *J Fam Pract* 1985;20:147–152
20. Kuhr M, Paneth N: Feeding practices and early neonatal jaundice. *J Pediatr Gastroenterol Nutr* 1982;1:485–488
21. Linn S, Schoenbaum SC, Monson RR, et al: Epidemiology of neonatal hyperbilirubinemia. *Pediatrics* 1985;75:770–774
22. Maisels MJ, Gifford KL: Breast feeding contributes to neonatal jaundice, abstracted. *Pediatr Res* 1983;17:324A
23. Osborn LM, Reiff MI, Bolus R: Jaundice in the full-term neonate. *Pediatrics* 1984;73:520–526
24. Saigal S, Lunyk O, Bennett KJ, et al: Serum bilirubin levels in breast- and formula-fed infants in the first five days of life. *Can Med Assoc J* 1982;127:985–989
25. Lascari AD: "Early" breast feeding jaundice: Clinical significance. *J Pediatr* 1986;108:156–158
26. Maisels MJ, Leib G, Gifford K, et al: The "yellow baby syndrome" (or why well babies are jaundiced), abstracted. *Pediatr Res* 1985;19:240A
27. Hall RT, Braun WJ, Callenbach JC, et al: Hyperbilirubinemia in breast-versus-formula-fed infants in the first six weeks of life: Relationship to weight gain. *Am J Perinatol* 1983;1:47–51
28. Kivlahan C, James EJP: The natural history of neonatal jaundice. *Pediatrics* 1984;74:364–370
29. Maisels MJ, D'Arcangelo MR: Breast feeding and jaundice in the first six weeks of life, abstracted. *Pediatr Res* 1983;17:324A
30. Cohen J: *Statistical Power Analysis for the Behavioral Sciences*, New York, Academic Press, 1977
31. Hardy JB, Mellits ED: Does maternal smoking during pregnancy have a long-term effect on the child? *Lancet* 1972;2:1332–1336
32. Nymand G: Maternal smoking and neonatal hyperbilirubinemia. *Lancet* 1974;2:173
33. Barrett PVD: Hyperbilirubinemia of fasting. *JAMA* 1971; 217:1349–1353
34. Felsher BF, Rickard D, Redeker AG: The reciprocal relation between caloric intake and the degree of hyperbilirubinemia in Gilbert's syndrome. *N Engl J Med* 1970;283:170–172
35. Wu PYK, Hodgman JE, Kirkpatrick BV, et al: Metabolic aspects of phototherapy. *Pediatrics* 1985;75(suppl):427–433
36. Gartner LM: Breast milk jaundice, in Levine RL, Maisels MJ (eds): *Hyperbilirubinemia in the Newborn*, report of the 85th Ross Conference on Pediatric Research. Columbus, OH, Ross Laboratories 1983, pp 75–91
37. De Carvalho M, Robertson S, Klaus M: Fecal bilirubin excretion and serum bilirubin concentration in breast-fed and bottle-fed infants. *J Pediatr* 1985;107:786–790
38. De Carvalho M, Klaus MH, Merkatz RB: Frequency of breast-feeding and serum bilirubin concentration. *Am J Dis Child* 1982;136:737–738
39. Rosta J, Makoi Z, Kertesz A: Delayed meconium passage and hyperbilirubinemia. *Lancet* 1968;2:1138
40. Weisman LE, Merenstein GB, Digirol M, et al: The effect of early meconium evacuation on early-onset hyperbilirubinemia. *Am J Dis Child* 1983;137:666–668
41. Wirth FH Jr, Davis SE: The effect of early meconium evacuation on the serum bilirubin levels in healthy term infants, abstracted. *Pediatr Res* 1973;7:341
42. Wu PYK, Teilman P, Gabler M, et al: "Early" versus "late" feeding of low birthweight neonates: Effect on serum bilirubin, blood sugar and responses to glucagon and epinephrine tolerance tests. *Pediatrics* 1967;39:733–739
43. Wennberg RP, Schwartz R, Sweet AY: Early versus delayed feeding of low birth weight infants: Effects on physiologic jaundice. *J Pediatr* 1966;68:860–866
44. Bloomer JR, Barrett PV, Rodkey FL, et al: Studies of the mechanisms of fasting hyperbilirubinemia. *Gastroenterology* 1971;61:479–487
45. Foliot TA, Ploussard JP, Housset E, et al: Breast milk jaundice: In vitro inhibition of rat liver bilirubinuridine diphosphate glucuronyl transferase activity and Z protein-bromosulfophthalein binding by human breast milk. *Pediatr Res* 1976;10:594–598
46. Poland RL, Schultz GE, Garg G: High milk lipase activity associated with breast milk jaundice. *Pediatr Res* 1980; 14:1328–1331
47. Stevenson DK, Bartoletti AL, Ostrander CR, et al: Pulmonary excretion of carbon monoxide in the human infant as an index of bilirubin production: IV. Effects of breast-feeding and caloric intake in the first postnatal week. *Pediatrics* 1980;65:1170–1172
48. Campbell N, Harvey D, Norman AP: Increased frequency of neonatal jaundice in a maternity hospital. *Br Med J* 1975;2:548–552
49. Sims DG, Neligan GA: Factors affecting the increasing

incidence of severe non-haemolytic neonatal jaundice. *Br J Obstet Gynecol* 1975;82:863–867
50. Foman SJ: *Infant Nutrition*, ed 2. Philadelphia, WB Saunders Co, 1974, pp 7–12
51. Martinez GA, Krieger FW: 1984 milk-feeding pattern in the United States. *Pediatrics* 1985;76:1004–1008
52. Osborn LM, Bolus R: Breastfeeding and jaundice in the first week of life. *J Fam Pract* 1985;20:475–480
53. Eggert LD, Pollary RA, Folland DS, et al: Home phototherapy treatment of neonatal jaundice. *Pediatrics* 1985;76:579–584
54. Slater L, Brewer MF: Home versus hospital phototherapy for term infants with hyperbilirubinemia: A comparative study. *Pediatrics* 1984;73:515–519
55. Tektronix Inc 1977: Plot 50. *Statistics* 1977;4:6-1–6-7
56. Meador CK: The art and science of nondisease. *N Engl J Med* 1965;272:92–95