Conseil *d'*Évaluation *des* Technologies *de la* Santé *du* Québec

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TRANSCUTANEOUS BILIRUBINOMETRY IN THE CONTEXT OF EARLY POSTNATAL DISCHARGE

Report submitted to

The Minister of Research, Science and Technology of Québec

Conseil d'évaluation des technologies de la santé du Québec

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SUMMARY

INTRODUCTION

In February 1998, the Conseil des directeurs de la santé publique asked the *Conseil d'évaluation des technologies de la santé* (CETS) to examine the usefulness of providing each region in Québec with transcutaneous bilirubinometers. These devices are used to screen for the presence of jaundice in newborns, a sign of an elevated blood bilirubin level. Specifically, CETS was asked to examine the usefulness of instituting the utilization of this instrument, in light of the precision and accuracy of its results, the benefits of its use and the economic and organizational implications of purchasing and using it both during follow-up visits after early postnatal discharge and in hospitals.

Problem

Most Québec hospitals have undertaken to reduce the length of postpartum stays, with discharge taking place about 48 hours postpartum (two days) for a normal, uncomplicated vaginal delivery or 96 hours (four days) for an uncomplicated cesarean. Hyperbilirubinemia is a significant problem in the context of early discharge, since the bilirubin level usually peaks between the third and fifth day of life in term newborns, that is, after discharge from the institution of birth. Yet, when above a certain level, hyperbilirubinemia can cause irreversible neurological damage in newborns. Early detection is therefore extremely important, since this neurological damage can be prevented with phototherapy or other medical treatments.

Strategy recommended in Québec

In Québec, a systematic home visit two or three days after discharge from the institution of birth is one of the approaches recommended to counter the risks associated with the practice of early postnatal discharge. During the visit, special attention is given to examining the infant for the presence of jaundice and to determining its level. This is done by means of a visual assessment, using a transcutaneous bilirubinometer or an icterometer, or by taking a blood specimen for the purpose of measuring the serum bilirubin concentration. Often, a combination of these is used.

Role of transcutaneous bilirubinometry

The published data regarding transcutaneous bilirubinometry basically concerns an instrument that has been commercially available since the early 1980s. The data concerning this technology indicate that, in healthy term newborns, the transcutaneous bilirubin measurement (TcB), or transcutaneous bilirubin index, usually correlates well with the blood bilirubin concentration and that there is a linear relationship between these two parameters. Since several factors affect this relationship, transcutaneous bilirubinometer readings cannot be used directly to make a decision as to the need to administer phototherapy or undertake an exchange transfusion. In healthy term newborns, this technology is, however, a more effective tool than the eye and the icterometer in detecting cases where a serum bilirubin test is required.

Utility of transcutaneous bilirubinometry

The instrument in question has the advantage of being compact, battery-powered and extremely simple and fast to operate, and it gives an instant readout. It is therefore handy both in clinical settings, nurseries and in the home, and results in a smaller number of blood specimens being taken for serum bilirubin measurements. Thus, one can reduce the risks (risk of accidental bone

puncture and of osteomyelitis when the procedure is performed improperly, risk of infection) and the discomfort and pain associated with obtaining blood specimens, in addition to the costs that this test entails.

Several factors argue in favour of using transcutaneous bilirubinometry in the context of post-discharge follow-up, especially the need to identify newborns at risk for significant hyperbilirubinemia after being discharged from the institution of birth, the fact that it is more difficult to detect jaundice by a visual examination outside a hospital setting, and the waiting period associated with serum bilirubin tests. With operating conditions very similar to those recommended in a clinical setting, which include rigorous quality control for the procedure and adequate user training, this technology should maintain its efficacy when used outside of hospitals.

Limitations of transcutaneous bilirubinometry

According to the available data, this technology is ineffective when used in newborns subjected to phototherapy or who have undergone an exchange transfusion and is of limited efficacy in premature, sick or low-birthweight newborns, and in multiethnic populations because of the variation in skin pigmentation. Although its use in multiethnic populations has few consequences, apart from a larger number of serum bilirubin tests, it may sometimes be necessary to adopt a particular strategy in order to optimize its utility*. Also, the use of this technology requires close ties with a clinical laboratory in order to ensure optimal and safe utilization (e.g. determination of a decision level for eliminating practically all potential false negatives and reducing as much as possible the number of serum bilirubin tests performed).

Economic implications and potential benefits of using transcutaneous bilirubinometry

The use of transcutaneous bilirubinometry in the context of early postnatal discharge could lead to an increase in direct costs to the health-care system. These higher costs than those presently incurred for screening for neonatal hyperbilirubinemia could be offset by different benefits whose value cannot be determined at this time. Thus, they could be justified by:

- The near-guarantee of detecting all cases of excessive hyperbilirubinemia and therefore of preventing the risk of bilirubin encephalopathy or nuclear jaundice.
- The earlier detection of hyperbilirubinemia, which could result in lower serum bilirubin levels in cases of neonatal readmission for jaundice.
- The decrease in the number of serum bilirubin tests with the concurrent reduction in the risks, discomfort and pain associated with obtaining blood specimens.
- The validation of the assessment of the degree of jaundice by nursing personnel, which would give them the assurance of not missing any cases of jaundice, in addition to a sense of security against possible legal action.

Conclusion

This assessment report brings out the importance of making early postnatal discharge part of a perinatal program that includes a systematic, early visit (no later than the third day after discharge from hospital) to the mother and infant. Since transcutaneous bilirubinometry is effective in detecting cases where a serum bilirubin meas-

* Although the information on this subject is limited, it seems that this limitation on the use of transcutaneous bilirubinometers has been corrected in recent models, which have not necessarily been approved by Health Canada.

urement is required, making this technology part of a well-established perinatal program presents numerous benefits that could offset the costs associated with it.

However, even if transcutaneous bilirubinometry may play a useful role, the published data on this technology are insufficient to recommend a wide-scale program for the systematic purchase of these devices. The appropriateness of using transcutaneous bilirubinometry must therefore be assessed by the regional and local authorities on the basis of the following:

- The benefit of an objective measurement of the degree of jaundice, which is especially useful outside hospitals.
- The considerable ease of use in different settings.
- The instrument's relatively high cost.
- The limited or zero effectiveness of the most commonly used models in certain circumstances (highly multiethnic population, during treatment by way of phototherapy or exchange transfusion) compared to more recent models.
- The need for strict quality control for its utilization, for assessing its long-term effectiveness and for adequate user training.
- The need to assess, at the local level, the budget impact of purchasing one or more instruments.

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LIST OF ABBREVIATIONS

AAP:	American Association of Pediatrics, United States
ACOG:	American College of Obstetricians and Gynecologists, United States
CETS:	Conseil d'évaluation des technologies de la santé du Québec
CLSC:	Centre local de services communautaires (local community service centre)
ECRI:	Emergency Care Research Institute, United States
SB:	Serum bilirubin
TB:	Transcutaneous bilirubinometer or transcutaneous bilirubinometry
TcB:	Transcutaneous bilirubin

GLOSSARY

Accuracy: The degree to which a measurement represents the true value that one is attempting to determine [62].

Antiglobulin test or direct Coombs' test: A test for detecting antibodies bound to an individual's red blood cells. Washed red blood cells are treated with an antiserum and observed for agglutination. This test is performed on the cord blood of newborns of Rh-negative mothers and in newborns suspected of having hemolytic disease of the newborn, which can be due to maternal antibodies. The test is also used to investigate anemias. A positive result suggests autoimmune hemolytic anemia [76].

Bilirubin: A tetrapyrrolic compound with the formula $C_{33}H_{36}N_4O_6$. A red bile pigment present in the form of sodium bilirubinate in bile and as calcium bilirubinate in the gallbladder. It can be found in the urine and in tissues in patients with jaundice. It results from the breakdown of erythrocyte hemoglobin by reticuloendothelial cells. Bilirubin is transported into the blood in a water-insoluble form bound to albumin. This is free, or indirect, bilirubin. In the liver, it is conjugated with glucuronic acid. This is conjugated, or direct, bilirubin, which may be excreted in the bile [30].

Blood bilirubin level: The concentration of bilirubin in the blood. Bilirubin occurs in the blood in an unconjugated form (free or indirect bilirubin) and in a conjugated form (direct bilirubin). When the bilirubin level peaks in a healthy term newborn, the average total blood bilirubin level is 105 μmol/L (range, 34 to 205 μmol/L). In older children and in adults, it is usually less than about 20 μmol/L, the upper limit depending on the technique used to determine the concentration and on the population of interest* [37, 110].

Choreoathetosis: A motor disorder characterized by a combination of choreiform† and athetotic movements‡ [30].

Icterus or jaundice: A yellow discoloration of the skin and mucous membranes due to the presence of bile pigments in the blood and tissues. ♦- **visible jaundice:** Occurs when the blood bilirubin level is greater than 85 μmol/L in newborns or 34 μmol/L in older children [110].

Negative predictive value: The likelihood that the individual does not have the disease when the test result is negative [53].

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* Written personal communication from P. Leclerc, medical biochemist, CHA - Hôpital du Saint-Sacrement, July 7, 1999.

† **Chorea:** Abrupt, brief, rapid, irregular and noncoordinated movements affecting one or more parts of the body and occurring at no specific rate. Chorea, which usually affects the face, tongue and distal part of the limbs, is often accompanied by hypotonia [30].

‡ **Athetosis**: Motor disorders characterized by slow, noncoordinated, wide, involuntary movements, predominantly in the limbs, and associated with a dysfunction of the systems inhibiting motor neuron activity [30].

Normal newborn: An infant born at term, with an adequate weight (generally ≥ 2,500 g) and a normal physical examination [25].

Nuclear jaundice of the newborn, or kernicterus: A severe form of neonatal jaundice characterized by staining of the basal nuclei of the brain and of the bone marrow by bilirubin, causing late neurological complications [30].

Oculogyric: Controlling the coupled movements of the eyes, especially their rotation [30].

Opisthotonos: Spasmodic contraction of the muscles of the nape and back, mainly of the extensor muscles, observed especially in tetanus, and where the body forms an arc from the occiput to the heels [30].

Plethora: An excess of blood [30].

Positive predictive value: The likelihood that the individual has the disease when the test result is positive [53].

Precision: As a property of a measurement, the dispersion of the values that it provides on either side of its mean for a given dimension. The standard deviation of this distribution provides an estimate of the absolute precision. Dividing the standard deviation by the mean gives the coefficient of variation, which is an estimate of the relative precision [62].

Sensitivity: Indicates the proportion of affected individuals confirmed by a positive test result [53]. In this report, sensitivity refers to the proportion of newborns with significant hyperbilirubinemia for whom the screening test, using transcutaneous bilirubinometry, was positive as well.

Specificity: Indicates the proportion of healthy individuals confirmed by a negative test result [53]. In this report, specificity refers to the proportion of newborns without significant hyperbilirubinemia for whom the screening test, using transcutaneous bilirubinometry, was negative as well. Its complement, 1 - specificity, is the proportion of false-positive results.

Spherocytosis: A form of hemolytic anemia characterized by the presence of spherocytes in the blood.♦**- spherocyte**: An erythrocyte in the form of a biconvex (instead of biconcave) disk of increased thickness and reduced diameter, but of normal volume [30].

Term newborn: An infant that has completed 37 weeks of gestation [2].

1. INTRODUCTION

Most Québec hospitals have undertaken to reduce the length of postpartum stays in the case of healthy term newborns. Although the length of stay in early discharge programs varies, it is usually about 48 hours postpartum (two days) for a normal vaginal delivery and 96 hours (four days) for an uncomplicated cesarean [25].

Jaundice is a major concern in the context of early discharge. This condition is, in fact, the most frequent cause of readmission [17, 52, 72], accounting for 70 to 85% of cases [23, 39]. Also, the increasing number of isolated cases of nuclear jaundice or of other morbid conditions associated with hyperbilirubinemia is raising concerns about their possible resurgence [23]. This situation is due to the fact that the bilirubin concentration usually peaks between the third and fifth day of life in term newborns [16, 32], i.e. after their discharge from the institution of birth in the case of early discharge. Yet, above a certain level, jaundice can cause irreversible neurological damage in newborns, mainly extrapyramidal disturbances (especially athetosis), gaze abnormalities and sensorineural hearing loss. Early detection of jaundice is therefore extremely important, since such neurological damage can be prevented with phototherapy or other medical treatments [28].

In Québec, different follow-up modalities are presently available to mothers, infants and their families after early postnatal discharge. One of these modalities is a follow-up visit at an outpatient clinic or in the home during the first few days after discharge from hospital. The home visit, which is becoming more and more common, may be done on a systematic basis or for only a certain proportion of patients who have been discharged early.

One important thing to check for during this visit is the presence of jaundice in the infant, a sign of an elevated blood bilirubin level. This verification often consists of a visual assessment, which is affected significantly by the observer's experience and skill, and the ambient lighting and colours [21]. In the home, these factors are much more variable than in a hospital, which makes the assessment more difficult. In addition, and as pointed out by Leduc and Ouellet [64], a nurse who examines a newborn in the home does not have the option of comparing her clinical impression with that of other nurses or of physicians, which also makes this assessment more difficult.

This being said, a noninvasive technology is now available, that is transcutaneous bilirubinometry, which permits an estimate of the blood bilirubin level so that one can quickly screen for newborns at risk for too high a level and for whom an accurate serum bilirubin measurement is required. The only model that was commercially available in Canada when this study began was the Minolta/Air Shields Jaundice Meter™. The major drawback with this device is its relatively high price, which varies, depending on how many are purchased, from $5,000 to $7,000 each, which would result in a significant outlay if most Québec hospitals, CLSCs and their points of service decided to purchase them.

This situation led the Conseil des directeurs de la santé publique to ask the *Conseil d'évaluation des technologies de la santé (CETS)*, in February 1998, to determine if it would be useful to provide each region in Québec with this instrument, in light of the precision and accuracy of its results, the benefits of its use and the economic and organizational implications of purchasing it and using it both in the context of follow-up visits and in hospitals.

This assessment is based on a review of the scientific literature on transcutaneous bilirubinometry. The main databases searched were MEDLINE, COCHRANE, EMBASE, PASCAL and HSTAR (articles published from 1978 to April 1998). Other articles were found by reviewing the bibliographies of the articles identified during the initial search and the lists in *Current Contents*. This information was updated on a regular basis (up to December 1999) and was complemented, among other things, with searches on the Internet and consultations with health-care professionals and manufacturers of medical devices.

2. NEONATAL HYPERBILIRUBINEMIA

2.1 NORMAL ROUTES OF BILIRUBIN EXCRETION

During pregnancy, the low oxygen tension delivered to the fetus through the placenta results in a greater need for hemoglobin in order to transport oxygen *in utero* and therefore in a two-to-three-fold increase in erythrocyte production in the fetus [123], in erythrocytes being produced three to four times faster than in an adult, and in a two-thirds decrease in their lifespan [34]. When the newborn starts to breathe at the beginning of its life outside the uterus, this need diminishes, and in a few days, the reticuloendothelial system destroys the excess erythrocytes.

Bilirubin is a metabolic breakdown product of hemoglobin. In the bloodstream, bilirubin is found both in the free and conjugated forms. Bilirubin (unconjugated) bound to serum albumin is transported to the liver, where it is transferred to acceptor proteins (proteins Y and Z) inside hepatocytes. Glucuronyl transferase then conjugates the bilirubin with uridine diphosphoglucuronic acid (UDPGA), producing bilirubin diglucuronide (direct, or conjugated, bilirubin), which is then excreted actively through the bile ducts into the intestine. The newborn does not have the intestinal bacteria oxidizing bilirubin to urobilinogen in the intestine. As a result, bilirubin is excreted intact in the stool, giving the latter its typical bright yellow colour. However, the digestive system of the newborn (and of the fetus) contains β-glucuronidase, which deconjugates a portion of the bilirubin, thus permitting the unconjugated bilirubin to be reabsorbed and to reenter the bloodstream via the intestinal lumen (enterohepatic circulation of bilirubin) [76].

2.2 ETIOLOGY OF NEONATAL HYPERBILIRUBINEMIA

Nearly 90% of healthy term newborns have a blood bilirubin level greater than 35 μmol/L the first week after birth. In fact, there are two distinct phases. During the first phase, the blood bilirubin level increases to about 105 μmol/L on the third day, then gradually decreases to 35 to 50 μmol/L on the fifth day. Subsequently, the blood bilirubin level remains relatively stable for a few days, then gradually diminishes to less than 15 μmol/L on the eleventh or twelfth day [14]. Clinically, jaundice in a newborn becomes visible when the blood bilirubin level exceeds 85 μmol/L [110]. Neonatal icterus presents in a cephalocaudal fashion, appearing consecutively in these five regions: 1) the head and neck; 2) the trunk to the umbilicus; 3) the groin and hips; 4) the knees, shoulders, heels and wrists; and 5) the feet and hands, including the soles and palms.

The jaundice can be one of two types: physiologic or pathologic. The exact cause of physiologic jaundice is not known, even though increased erythrocyte destruction, the limited binding capacity of bilirubin in hepatocytes, the level of bilirubin conjugation with glucuronic acid and the level of excretion into the bile have all been blamed, as has been the enterohepatic circulation of bilirubin. Physiologic jaundice usually occurs more than 24 hours after birth and is observed in 45 to 60% of term newborns and in an even higher percentage (80%) of premature infants [14]. The jaundice is said to be "physiologic" if the increase in the blood bilirubin concentration is less than 85 μmol/L/day and the peak (observed between the third and fifth day) does not exceed 225 μmol/L in term newborns. In general, there are no associated signs (lethargy, poor feeding or tempera-

ture variations), and it usually disappears in one week. However, the accumulation of bilirubin, whatever its origin, can lead to nuclear jaundice, especially in premature or sick newborns.

Breast-feeding apparently promotes jaundice. In breast-fed infants, jaundice manifests according to one of the following two patterns. One is what is referred to as "exaggerated physiologic jaundice", which is characterized by a serum bilirubin level of 175 μmol/L or more during the first three to four days following birth. This level usually returns to normal between the 7th and 10th day after birth [19]. Although the causes of exaggerated jaundice have not been clearly identified, it is believed to be attributable to an insufficient frequency of breast-feeding and to an insufficient quantity of breast milk being ingested. Inadequate breast-feeding apparently decreases stool excretion, slows intestinal transit and increases intestinal stasis and enterohepatic bilirubin circulation[1]. This type of jaundice is observed in 6 to 25% of breast-fed infants [19]. Earlier and more frequent breast-feeding is therefore recommended in order to reduce the incidence of jaundice and its severity [76].

In the other pattern, the jaundice is sometimes referred to as "late", since it occurs within four to seven days after birth. The serum bilirubin level peaks between the 10th and 15th postnatal day and often remains high (260 to 435 μmol/L) for close to two weeks, then slowly declines toward normal levels within 4 to 16 weeks after birth [6, 19]. Late jaundice might be associated with the presence of substances in breast milk that have an inhibitory effect on the hepatic enzyme glucuronyl transferase, thus preventing the conjugation of bilirubin [6]. Approximately 1 to 2% of breast-fed infants are reported to develop this type of jaundice [3]. Despite the fact that no cases of bilirubin encephalopathy have been associated with this type of jaundice, there is no reason why a significant increase in the serum bilirubin concentration in breast-fed infants would pose less of a risk than a similar increase in formula-fed infants. Consequently, if the serum bilirubin level in a breast-fed infant increases and is likely to reach 25 mg/dL (428 μmol/L), the breast-feeding might be discontinued temporarily (48 hours). Afterward, the mother should, however, be strongly encouraged to continue breast-feeding [3].

Pathologic jaundice is usually associated with pathologic disturbances that lead to increased bilirubin production (e.g. certain isoimmune hemolytic diseases, such as an Rh or ABO incompatibility, or enzyme abnormalities, such as of glucose-6-phosphate dehydrogenase) and/or decreased bilirubin excretion (e.g. in the case of hepatitis or bile duct atresia). Pathologic jaundice generally manifests within 24 hours after birth and/or lasts for more than eight days. The serum bilirubin concentration increases quickly, i.e. more than 8.5 μmol/L/hour. In this type of jaundice, the serum bilirubin level frequently exceeds 215 μmol/L within the first 48 hours following birth [6]. According to the American Academy of Pediatrics [2], term neonates 24 hours of age or younger who have clinical jaundice are not considered healthy and should undergo a more thorough evaluation to rule out the possibility of a pathologic cause. Phototherapy or an exchange transfusion may be indicated in order to quickly reduce the total serum bilirubin concentration within the first 24 hours of life.

2.3 OCCURRENCE OF NEONATAL HYPERBILIRUBINEMIA

In North America, significant hyperbilirubinemia (serum bilirubin ≥ 290 μmol/L) reportedly occurs in about 5% of newborns within the first five days after birth [12]. Since this proportion depends, among other things, on the population's

[1] Information provided in writing by R C. Walker, pediatrician, Children's Hospital of Eastern Ontario, Ottawa (July 16, 1999).

Table 1: Percentage of newborns with significant serum bilirubin concentrations (≥ 290 μmol/L) during the first five days following birth[a]

Source	% jaundiced newborns	% breast-fed
Seidman et al, 1996 [97] (Jerusalem)	1.7 (n = 1,220)	93
Bhutani et al, 1997 [12] (Philadelphia)	4.5 (n = 1,097)	65
Martinez et al, 1996 [77] (Buenos Aires)	12.0 (n = 164)	100

[a] From Maisels and Newman [74].

ethnic composition, the incidence of breast-feeding and the interlaboratory variation in serum bilirubin measurements, the actual prevalence of significant hyperbilirubinemia in a given population can, however, differ significantly from this value. The results of three recent prospective studies (Table 1) show the significant differences between the blood bilirubin levels observed in three various populations of term neonates.

Although this phenomenon may be attributable to increased vigilance, different studies conducted in the United States indicate that the proportion of newborns with excessively high serum bilirubin levels has increased over the years (Table 2). Thus, 6% of infants born between 1959 and 1966 had a blood bilirubin level greater than or equal to 13 mg/dL (225 μmol/L) in the Collaborative Perinatal Project study [47]. Newman et al [84] observed that 10% of infants of Caucasian origin born between 1980 and 1982 had a peak blood bilirubin level greater than or equal to 13 mg/dL (225 μmol/L), and this figure increased to 14% from 1986 to 1987 (unpublished data from Newman; reported by Maisels and Newman [74]). The Collaborative Perinatal Project study also indicated that 0.8% of the newborns had a blood bilirubin level greater than or equal to 20 mg/dL (345 μmol/L) from 1959 to 1966 compared to 2% from 1995 to 1996 for the subjects in the Kaiser Permanente Northern California Study, which involved 11 hospitals [85]. Although all the causes of this increase were not identified, the reduction in the length of postnatal hospital stays, the increase in the percentage of breast-fed children and an increase in the number of Asian children in the population[2] have been identified as influencing factors.

The data available on these factors indicate a similarity between the situation in Canada [26, 112] or Québec [25, 102, 109] and the United States. Consequently, it could be expected that the proportion of cases of hyperbilirubinemia is on the increase here as well.

Despite the fact that jaundice is very common in neonates, severe hyperbilirubinemia (a blood bilirubin level greater than 435 μmol/L) is very rare. Thus, in the Kaiser Permanente Northern California Study [85], one child in 770 had a peak serum bilirubin level greater than 435 μmol/L, and levels greater than 520 μmol/L were observed in only one case in 10,000.

2.4 CONSEQUENCES OF NEONATAL HYPERBILIRUBINEMIA

Nuclear jaundice is one of the possible consequences of hyperbilirubinemia. This syndrome results from the deposition of unconjugated bilirubin in the basal ganglia, which gives them a jaundiced hue and causes cerebral lesions. The first symptoms of nuclear jaundice in term new-

[2] Higher-than-normal bilirubin production is reported in a larger proportion of Asians (e.g. Japanese, Koreans, Chinese) and certain native populations in North America than in other ethnic groups [123].

Table 2: Percentage of newborns with different serum bilirubin concentrations

Source	Percentage of newborns
Collaborative Perinatal Project (Hardy et al, 1979 [47])	**1959-1966**: (n = 31,904) 6% with a serum bilirubin level ≥ 225 μmol/L 0.8% with a serum bilirubin level ≥ 345 μmol/L
Newman et al, 1990 [84] Newman (unpublished data in Maisels and Newman, 1998 [74])	**1980-1982**: (n = 2,443**)** 10% with a serum bilirubin level ≥ 225 μmol/L **1986-1987**: 14% with a serum bilirubin level ≥ 225 μmol/L
Kaiser Permanente Northern California Study (Newman et al, 1997 [85])	**1995-1996**: (n = 37,340**)** 2% with a serum bilirubin level ≥ 345 μmol/L 0.13% with a serum bilirubin level > 435 μmol/L 0.0001% with a serum bilirubin level > 520 μmol/L

borns are lethargy, poor feeding and vomiting. These can be followed by opisthotonos, oculogyric crisis, seizures and death. In premature infants, nuclear jaundice may not be associated with any recognizable signs. During childhood, the late signs of nuclear jaundice may be manifested as choreoathetosis, sensorineural hearing loss, vertical gaze paralysis [76] and (rarely) mental retardation [29]. It is not known if minor degrees of bilirubin encephalopathy can result in less severe neurological impairment (e.g. perceptual-motor handicaps and learning disorders at school) [76].

The determining factors of bilirubin toxicity in neonates are many and complex and are still obscure. However, it is known that, in order to have a harmful effect, bilirubin must cross the cerebromeningeal barrier, which does not occur unless it is bound to serum albumin. The factors that apparently determine the toxicity of bilirubin are therefore those that affect the serum albumin concentration and the binding of bilirubin to albumin, the penetration of bilirubin into the brain, and the vulnerability of brain cells to the toxic effects of bilirubin [3].

It is still not known if there exists a toxicity threshold for bilirubin or a continuum of injury for low or moderate bilirubin concentrations. Also, it is reported that healthy term neonates are not necessarily affected by high bilirubin concentrations (about 520 or 690 μmol/L) [86, 87, 92, 93]. However, although extremely rare[3], nuclear jaundice in healthy term or near-term neonates has been reported in cases of extreme hyperbilirubinemia (> 520 μmol/L). According to Maisels and Newman [75], by preventing extreme hyperbilirubinemia in healthy term neonates, almost all potential cases of nuclear jaundice should be prevented.

2.5 BRIEF DESCRIPTION OF THE SCREENING AND DIAGNOSTIC METHODS

The following sections briefly describe the methods for screening for and diagnosing hyperbilirubinemia in healthy newborns.

[3] Although it was thought that the problem of nuclear jaundice had practically been eliminated in the United States, 22 cases were reported there between 1991 and 1995 in healthy term or near-term infants who had been discharged less than 48 hours after birth [23].

Table 3: Serum bilirubin concentration as a function of body region in cases of jaundice[a]

Region	Mean serum bilirubin concentration
1. Head and neck	105 μmol/L
2. Trunk to umbilicus	155 μmol/L
3. Groin including upper thighs	210 μmol/L
4. Knees and elbows to ankles and wrists	260 μmol/L
5. Feet and hands including the soles and palms	260 μmol/L

[a] From Banks et al, 1996 [6].

2.5.1 Visual assessment

The most commonly used method for checking for the presence of jaundice in newborns is the visual assessment. The presence of visible jaundice is used as a criterion for the need for a blood bilirubin determination. To detect signs of jaundice, the baby's skin on a bony prominence (forehead, nose, sternum) is blanched by pressing firmly with the thumbs. If there is jaundice, the skin assumes a yellow colour when the pressure is released, then assumes its normal colour again. In newborns with dark skin, yellow pigmentation is looked for on the buccal mucosa, the posterior portion of the roof of the mouth and the conjunctival sacks. It is advisable to perform the examination in daylight in order to prevent the colour of the walls, especially blue, and the artificial light from masking the yellow pigmentation. Jaundice appears first in the face and gradually spreads to the trunk and limbs as the total blood bilirubin level increases. This phenomenon, the cephalocaudal progression of visible jaundice, is sometimes used to estimate the serum bilirubin concentration (see Table 3). The sensitivity of this procedure has been called into question [6].

The visual assessment is strongly affected by the observer's experience and skill, the degree of plethora, anemia and the ambient lighting and colours [21]. Consequently, this technique can sometimes be ineffective in detecting those cases of jaundice requiring a closer follow-up. In any event, this seems to be what the results by Tayaba et al [108] indicate, which were obtained in a clinical setting. These authors report a few cases of newborns visually assessed as having little or no jaundice (i.e. 0 to 5 on a scale of 20) but who actually had hyperbilirubinemia greater than or equal to 225 μmol/L. The study by Ruchala et al [91], which was conducted in the home, also revealed the difficulty of detecting jaundice by a visual assessment. They report that of 17 neonates, 7 cases were assessed visually as being slightly jaundiced (i.e. 1 to 2 on a scale of 5) but who actually had significant hyperbilirubinemia (≥ 290 μmol/L). At least one of these cases (observed value: 21 mg/dL, or 357 μmol/L) was above the level at which the Canadian Paediatric Society [36] recommends initiating phototherapy. According to what is indicated in the study, this case of hyperbilirubinemia would not normally have been detected, since a serum bilirubin test was performed only in newborns with an index of 3 or higher.

2.5.2 Icterometry

The difficulty posed by the visual assessment led to the development of more elaborate techniques using reference instruments. In 1960, Gossett described the use of an icterometer for assessing

the degree of jaundice in newborns. This instrument is referred to in the literature as the "Perspex icterometer", the "Ingram icterometer" or the "Gossett icterometer". It consists of a strip of Plexiglas on which five stripes of graded yellow colour are painted, each separated from the other by a transparent stripe, and each stripe is assigned a value (1 to 5). The device is pressed against the infant's nose until the skin is blanched[4]. The yellow colour of the skin thus pressed, which appears in the transparent stripes, is matched with the band of similar intensity. A reading higher than 3 indicates the need for a serum bilirubin determination.

Since the development of the icterometer in 1960, there have been several studies on its usefulness in predicting the degree of jaundice in newborns. Most of the studies carried out have major flaws that make it difficult to compare their results. Nonetheless, these studies usually show a high linear correlation between serum bilirubin levels and icterometer values. The coefficient of correlation varies from 0.63 to 0.99 [13, 43, 78, 96, 111]. The icterometer has been used for jaundice screening in Caucasian, Oriental and black populations. Very wide variation is observed in the results of the different studies. The mean serum bilirubin concentration associated with each icterometer reading varies from 92 to 154 μmol/L for an icterometer reading of 2.5 and from 191 to 330 μmol/L for a reading of 4.5 (see Table 4). As shown by Merritt and Coulter [78], this variability is also reflected in the coefficients of variation for these concentrations for different icterometer readings: 40% at 2, 30% at 3 (usual decision level) and 20% at 5.

This imprecision of the icterometer is too great to be attributable only to the variation associated with serum bilirubin quantization, to the differences between the populations of infants studied (in the publications considered, all were of Caucasian origin) or to interobserver variation. According to Dai et al [29], this imprecision might be attributable to variation in the intensity of the colours between different icterometers. To avoid this problem, they recommend checking the results of each icterometer and plotting a calibration curve at each institution rather than relying on published values for describing the relationship between serum bilirubin concentrations and icterometer values. This suggestion is similar to that made by Merritt and Coulter [78].

The results documenting interobserver variability are contradictory. Merritt and Coulter [78] did not observe any significant difference between the results by different observers, whether they were experienced or not. However, Waterston and Taputaira [111] reported a significant difference in interobserver performance, the more experienced observers obtaining better results. After examining the results concerning the use of the icterometer by 14 observers, Morrison and Wilkerson [83] noted such a large variation that they could not recommend the use of this instrument.

Unlike what was noted by Waterston and Taputaira, the observers' accuracy did not seem to improve with experience.

The effect of the type of lighting on icterometer performance is another critical factor in the use of this instrument in the context of neonatal examinations after early postnatal discharge. Merritt and Coulter [78] observed that the light from two types of fluorescent lights widely used in nurseries did not significantly affect the icterometer readings. However, Schumacher [91], who used the icterometer in artificial light and daylight in 103 newborns, reports that a difference in icterometer reading of 0.5 units occurred

[4] In black infants, this procedure is performed on the gums [95].

Table 4: Serum bilirubin concentrations associated with different icterometer readings

Icterometer reading	Mean blood bilirubin level in μmol/L (range of values)	Source*
2,5	Not specified (min.: 65.87; max.: 190.67)	Gosset, 1960 [41]
	131.21 (standard deviation: 39.35)	Culley, 1960 [27]
	154.09 (standard deviation: 31.72)	Schumacher, 1985 [96]
	91.86 (min.: 38.13; max.: 168.13)	Merritt and Coulter, 1994 [78]
3,0	Not specified (min.: 104.00; max.: 346.67)	Gosset, 1960 [41]
	173.85 (standard deviation: 39.17)	Culley, 1960 [27]
	178.01 (standard deviation: 34.84)	Schumacher, 1985 [96]
	109.20 (min.: 58.93; max.: 221.87)	Merritt and Coulter, 1994 [78]
4,5	Not specified (min.: 104.00; max.: 424.67)	Gosset, 1960 [41]
	330.37 (standard deviation: 62.75)	Culley, 1960 [27]
	256.53 (standard deviation: 23.05)	Schumacher, 1985 [96]
	190.67 (min.: 81.47; max.: 306.80)	Merritt and Coulter, 1994 [78]

* Sample size: Gosset, 1960 [41], n = 229; Culley, 1960 [27], n = 183; Schumacher, 1985 [96], n = 106; Merritt and Coulter, 1994 [78], n = 536.
N.B.: min. = minimum ; max. = maximum.

27 times. The newborns exposed to fluorescent light had the highest values on 22 occasions. It cannot be determined from the data presented in this article if the type of lighting in which newborns are examined may be associated with a risk of not detecting those with excessive hyperbilirubinemia.

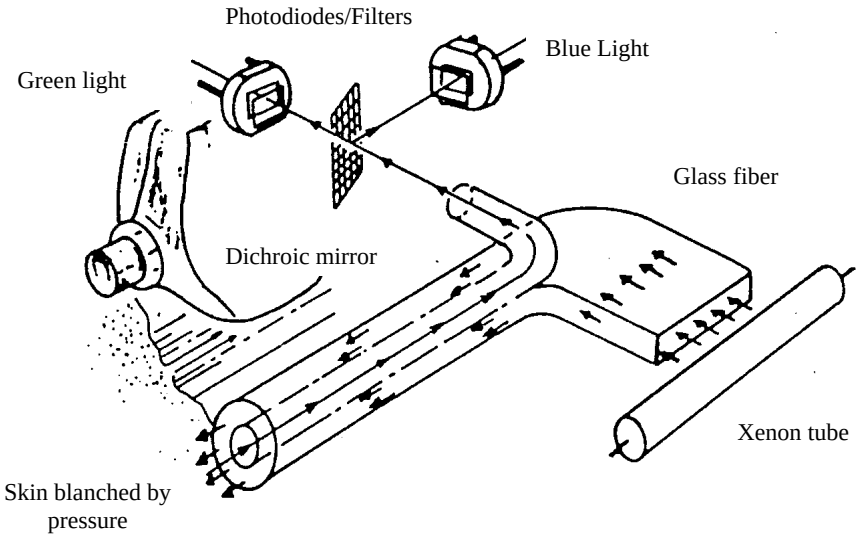
In short, according to published literature, the icterometer is useful in screening for jaundice in different populations of newborns in a clinical setting. This instrument offers the huge advantage of being inexpensive (under $20). However, on the downside, there is considerable imprecision because, as with the visual assessment, this method does not provide an objective measurement of the degree of jaundice. It may be difficult to offset this major drawback in the context of early postpartum discharge, where the operating conditions are highly variable (multiple users, variable lighting, etc.).

2.5.3 Transcutaneous bilirubinometry

There are two types of bilirubinometers. One, which is described in the following section, is based on spectrophotometric techniques and is used to measure bilirubin concentrations in samples of whole blood or serum. Transcutaneous, or indirect, bilirubinometry is a noninvasive technique which usually measures light reflection at the surface of a newborn's skin and which establishes the correlation between this measurement and the blood bilirubin concentration. The only model of transcutaneous bilirubinometer that was commercially available in Canada when this study began[5] was the Minolta/Air Shields Jaundice Meter™. It contains a fiberoptic photocell [1]. When the instrument is pressed against the infant's skin firmly enough, a xenon tube emits a light pulse. The light ray is reflected by the skin and thus transmitted to a dichroic mirror (a mirror that reflects light of a given wavelength while allowing a second colour to pass through) via a second group of fiber optic filaments (see Figure 1). The mirror separates the

[5] According to information provided by F. Jacques, Medical Devices Bureau, Health Canada, during a telephone conversation on October 16, 1998.

Figure 1: Descriptive diagram of the operation of the transcutaneous bilirubinometer [95]



colour into two light spectra, which pass through a blue (complementary colour of yellow) filter and a green (complementary colour of red) filter, respectively. The instrument can thus measure the intensity of reflected yellow light by correcting for absorption attributable to the red colour of skin (mainly hemoglobin) [29, 56]. The instrument's readout is a unitless figure that increases with the intensity of the reflected yellow light. Under controlled conditions, this value correlates with the tissue bilirubin level, which, in turn, correlates with the blood bilirubin level. The device does not, therefore, permit a direct measurement of the blood bilirubin concentration, but rather an objective measurement of the degree of jaundice. Consequently, the expression "jaundice meter" is more accurate than the expression "cutaneous bilirubinometer" or "transcutaneous bilirubinometer". The Minolta/Air Shields Jaundice Meter™ has been the subject of numerous clinical studies aimed at documenting its efficacy.

According to recent publications, other models of transcutaneous bilirubinometers for screening for hyperbilirubinemia are commercially available. They include the Bili*Check*™ and the ColorMate™ TLc-BiliTest™ (or Chromatics ColorMate III). According to information found on the Internet[6] and completed by other information provided by the company in April 2000, the former instrument, which was developed by SpectRx, has the advantage of accurately measuring the total bilirubin level in newborns, regardless of skin colour, the length of pregnancy, the postnatal age or the use of phototherapy. An older source[7] states that this device was the subject of a multinational clinical trial in France, Germany, United Kingdom and Italy in 1997. No articles on this study were identified in the main bibliographic databases consulted (MEDLINE, EMBASE, PASCAL, etc.). Since then, this instrument has been approved for sale

[6] On February 2, 1999 at http://www.healthyne.com/ interact…/infant_management/bilicheck1.html.

[7] Information found on the Internet at http://www. prnewswire.com/, press release dated October 3, 1997 and entitled "SpectRx, Inc. announces launch date for hand-held infant jaundice product Bili*Check* to be introduced at Medica 97: units also shipped for U.S. FDA clinical trials".

in Canada. Health Canada files[8] indicate that it is manufactured by Respironics Georgia. On this company's Web site it is stated that it is based in Pittsburgh, Pennsylvania[9]. No study on this device's efficacy was found in the scientific literature.

The other device, the ColorMate™ TLc-BiliTest™, differs from the previously mentioned instruments by the fact that data processing is an integral part of the measurement-taking process and that mathematical algorithms are used to take different parameters into account. Thus, race, weight and the use of phototherapy reportedly do not interfere with the relationship between the transcutaneous bilirubin measurement and the blood bilirubin concentration [108].

This instrument has been approved by the U.S. Food and Drug Administration. According to information obtained from the company (Chromatics Color Sciences International, Inc., New York, NY)[10], its sales price in the United States is approximately the same as that of the Minolta/Air Shields Jaundice Meter™, i.e. about $3,000 US. This figure does not include the cost (which was not specified) of the individual calibration tips that automatically adjust the device before taking a measurement. The manufacturer says that it plans to seek approval to sell the device on the Canadian market. It also expressed great interest in and said it was willing to collaborate actively in any project aimed at validating the instrument. The device has been subject of a scientific publication, which deals with its efficacy in a clinical setting [108]. The results of the study are presented in Section 4.

[8] Information received by e-mail (May 19, 1999) from C. Choquet, head of In Vitro Diagnostic Instruments, Medical Devices Bureau, Health Canada.

[9] Consulted on May 14, 1999 at http://www. respironics.com/.

[10] Information e-mailed (December 1998) by Sheila Kempf, vice-president of this company's medical division.

2.5.4 Bilirubinometry based on the principles of spectrophotometry

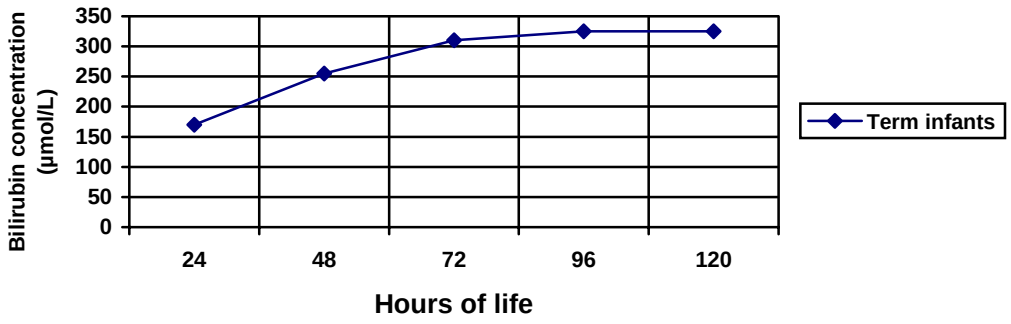
In clinical laboratories, the use of instruments that operate on the principles of spectrophotometry to measure blood bilirubin levels is the standard for diagnosing hyperbilirubinemia. Blood bilirubin tests are usually performed on a multiple analyzer, which is used to measure other parameters as well, such as enzymes, blood glucose and electrolytes.

Bilirubin can occur in four forms in the blood: unconjugated, monoconjugated, diconjugated, and conjugated and irreversibly bound to albumin. Clinical biochemistry laboratory techniques are used to measure the total bilirubin level (sum of the four fractions), the indirect bilirubin level, the result of this test being an estimate of the concentration of the unconjugated form, and the direct bilirubin level, which is an estimate of the concentration of the other three forms. The measurement of the direct and indirect fractions is used with other tests to identify the different causes of hyperbilirubinemia both in newborns and in children and adults. However, in newborns, an elevated indirect bilirubin is by far the cause most frequently observed, and it is usually on the basis of the total serum bilirubin that a decision is made as to whether phototherapy is required.

2.6 TREATMENTS FOR NEONATAL HYPERBILIRUBINEMIA

The early detection of hyperbilirubinemia in newborns is extremely important because bilirubin encephalopathy or nuclear jaundice can be prevented with phototherapy or exchange transfusion. Although exchange transfusion was a common practice in the 1950s to 1970s and is still sometimes necessary, phototherapy has become the usual method of managing hypebilirubinemia. Phototherapy, whose efficacy has been demonstrated [20, 92], results in the isomeriza-

Figure 2: Serum bilirubin concentrations: decision levels for initiating phototherapy for hyperbilirubinemia in infants without risk factors[a]



[a] Source: The Fetus and Newborn Committee, Canadian Paediatric Society (1999) [36].

tion of unconjugated bilirubin to water-soluble derivatives that are more easily excreted by the body, which prevents the occurrence of the high bilirubin levels associated with permanent sequelae. Exchange transfusion is used to control bilirubin concentrations that have reached the level where nuclear jaundice can result. Such treatment is aimed at preventing any additional bilirubin formation due to hemolysis or at eliminating the existing bilirubin [29, 76].

In Canada, the risks associated with hyperbilirubinemia led the Fetus and Newborn Committee of the Canadian Paediatric Society [36] to propose a detailed plan for managing hyperbilirubinemia in healthy term infants. It includes guidelines concerning the bilirubin levels at which phototherapy might be initiated in healthy term infants and those with risk factors. The bilirubin levels specified in this organization's statement are more conservative than those previously recommended by the American Academy of Pediatrics [2]. In the case of a healthy term infant, phototherapy should be initiated as indicated in Figure 2. Recommendations are also provided for infants with the following risk factors:

- Gestational age younger than 37 weeks and a birthweight less than 2,500 g.
- Hemolysis due to maternal isoimmunization, a glucose-6-phosphate dehydrogenase (G6PD) deficiency, spherocytosis or other causes.
- Jaundice at less than 24 hours of age.
- Septicemia.
- Resuscitation at birth.

These risk factors are contraindications for early neonatal discharge. Consequently, the curve for infants with one or more risk factors is not included in this report.

3. HYPERBILIRUBINEMIA AND EARLY POSTNATAL DISCHARGE

3.1 RISK OF READMISSION FOR NEONATAL HYPERBILIRUBINEMIA

One of the consequences of early discharge is a higher hospital readmission rate. Studies on the subject report readmission rates ranging from 0 to 6%, and nearly three quarters of these readmissions were due to hyperbilirubinemia [25, 69]. Decreasing the length of neonatal hospital stays increases the risk of not detecting cases of significant hyperbilirubinemia in healthy term infants, because the bilirubin level peaks after discharge. Apart from the reduction in the length of neonatal hospital stays, the proportion of infants who are breast-fed is on the rise [26, 66], as is the number of people of Asian origin in the Canadian population [102, 109] (and possibly, therefore, the number of Asian infants). It is known that breast-feeding is associated with an increased risk of hyperbilirubinemia and that Asian neonates have higher bilirubin levels than white or black infants [74].

Furthermore, early postnatal discharge as such is reported to be associated with an increased risk of readmission for significant hyperbilirubinemia. Soskolne et al [101] and Maisels and Newman [74] observed that, in effect, a gestational age younger than 38 weeks, a neonatal hospital stay shorter than 72 hours and the occurrence of jaundice in the nursery were major risk factors for readmission for jaundice. These two teams do not make a distinction between the risk associated with a neonatal stay shorter than 48 hours and that associated with discharge within 72 hours after birth. They therefore conclude that any discharge that takes place within 72 hours after birth significantly increases the risk of readmission for jaundice compared to a postnatal discharge occurring after 72 hours (Table 5).

Presently, the role of early postnatal discharge in the increased risk of readmission for hyperbilirubinemia cannot be explained. The results of the U.S. studies by Maisels and Kring [72] and Newman et al [84] invalidates the hypothesis that the decrease in the risk of readmission for hyperbilirubinemia associated with a postnatal discharge after 72 hours results from screening for and treating jaundice before infants are discharged.

As an alternative hypothesis, Maisels and Newman [74] suggest the possibility that mothers who receive instructions from staff over a longer period of time are better able to breast-feed their infants. Also, there are indications that mothers' ability to assimilate information concerning breast-feeding and infant care is reduced when they are discharged early. This could also have a negative impact on infants' health and well-being in the days following their discharge. It should be pointed out that certain guidelines include recommendations aimed specifically at ensuring adequate breast-feeding of infants after they are discharged from the institution of birth, e.g. the guidelines issued by the Perinatal Committee of Eastern Ontario, which were drafted in 1996 within the framework of the Perinatal Education Program of Eastern Ontario.

Together, these various factors (decrease in the length of postnatal hospital stays, increase in the proportion of breast-fed infants, increase in the number of Asian infants in the population) point to the need for a strategy aimed at screening infants at risk for very high bilirubin levels after their discharge.

Table 5: Risk of readmission for jaundice according to length of stay[a]

Length of stay	Odds ratio	95% confidence interval
< 48 hours[b]	2.40	1.09 – 5.30
48 to < 72 hours[b]	3.15	1.40 – 7.09

[a] From Maisels and Kring, 1998 [72].
[b] Compared to a length of stay of 72 hours or longer.

3.2 SAFETY MEASURES CONCERNING EARLY POSTNATAL DISCHARGE

One common approach consists in screening for hyperbilirubinemia during a follow-up visit for each newborn discharged early after birth, the visit taking place within the first few days after the infant leaves the institution of birth. The visit can take place in the home, in a physician's office or at an outpatient clinic. If each newborn who meets the criteria for early discharge is examined during this visit, the health-professional would note any visible jaundice (if present) and see to it that a follow-up and, if need be, the appropriate treatment are provided. In actual fact, a systematic postnatal examination poses certain problems. This practice necessarily requires cooperation between the families involved and the medical personnel. Furthermore, in certain situations, in certain places during the winter, for example, it is unreasonable or even risky to ask a mother to make a trip when she has only been home for a short while. It should also be noted that a significant proportion of mothers choose not to return for a follow-up visit, even if they are asked to do so. Home visits by nursing personnel are an increasingly widespread practice, but resource availability and the safety of these health-professionals in certain locations prevent the use of this strategy. In addition, some mothers decline home visits, even if they are free of charge [71].

3.2.1 Measures recommended by different organizations

To ensure a safe early-discharge policy, professional medical organizations, such as the American Academy of Pediatrics and the American College of Gynecologists [3], the Society of Obstetricians and Gynaecologists of Canada [100] and the Association des pédiatres du Québec [4], have developed selection and follow-up criteria. Briefly, selected infants must be full-term and healthy, they must have undergone two physical examinations more than 24 hours apart, and their parents must be adequately prepared. A follow-up program must also be developed, and it should involve a reassessment two or three days (48 to 72 hours) after discharge from hospital. During the out-of-hospital follow-up (physician's office, clinic or home), special emphasis is placed on assessing the degree of jaundice.

The Council of the Society of Obstetricians and Gynaecologists of Canada [100] specifically recommends “[t]hat the normal length of stay for normal labour and vaginal delivery be two days for hospitals without availability of home care and nursing services and that it be one to two days with home care nursing services” and

"[t]hat the length of stay after a Caesarian section be four or more days for hospitals without availability of home care nursing services and three days for hospitals with home care nursing services." A joint statement with the Canadian Paediatric Society [22] maintains that "[w]hen discharge occurs before 48 hours after birth, this must be part of a programme that ensures appropriate ongoing assessment of the mother and baby. This evaluation should be carried out by a physician or other qualified professional with training and experience in maternal/infant care. A personal assessment in the home is preferred for all mothers and babies. Relying on newly delivered mothers to travel to a clinic or office may result in many families being inadequately followed due to a lack of compliance. The visit is not intended to replace a complete evaluation by a physician, but should focus on those aspects that require early intervention (e.g., feeding problems, jaundice, signs of infection, etc.)."

The Conseil des directeurs de la santé publique and the Comité des directrices and directeurs généraux des Régies régionales de la Santé et des Services sociaux du Québec formally recommends systematic home visitation after early postnatal discharge [24].

Lastly, more recently, the Minister of Health and Social Services [82] recommended that the practice of early postnatal discharge be part of a program ensuring the continuity of services after such discharge. In a document prepared as a guide, for the regional boards and the various players, for instituting such early discharge programs, the conditions deemed essential for their organization, the conditions likely to facilitate the organization of care and services in such programs, and the responsibilities of physicians (in private clinics, hospitals or CLSCs), hospitals and CLSCs during the pre-, intra- and postnatal periods are outlined. Early (no later than the third day after discharge from hospital), systematic home visitation is recommended. The presence of jaundice in the infant is one of the items to be checked for during the visit [82].

Other organizations have issued recommendations specifically concerning hyperbilirubinemia. Thus, the Canadian Paediatric Society [36] recommends that testing for bilirubin levels in newborns be readily available on an outpatient basis. Since there is no direct relationship between the intensity of jaundice and the degree of hyperbilirubinemia, it is sometimes recommended that a serum bilirubin test be performed in all jaundiced infants [9, 90]. Other authors [5, 88] believe that, after postnatal discharge, jaundice and other factors should be taken into consideration in assessing the need for a serum bilirubin determination. The American Academy of Pediatrics [2] states that a direct serum bilirubin test is indicated in healthy, breast-fed infants with jaundice lasting more than two weeks after birth and whose urine is dark or whose stool is light. If the infant's history (especially the appearance of the stool and urine) and physical examination are normal, observation should be continued. If the jaundice persists for more than three weeks, the urine bilirubin and total and direct serum bilirubin levels should be measured.

3.2.2 Description of the practice in Québec

In 1997, CETS observed that, in practice, there did not seem to be uniformity in the application of the recommendations concerning early discharge programs, especially with regard to the medical visit 48 hours after discharge, which is generally left to the attending physician's discretion. The discharge follow-up can assume different forms—a telephone call a few hours after discharge, a 24-hour telephone line, one or more follow-up appointments at an outpatient clinic, one or more systematic home visits or selective home visits for cases where there are some concerns, or some combination thereof [25].

Table 6: Relationship between systematic or nonsystematic visitation by CLSCs as part of early postnatal discharge and the time of the visit[a]

	Breakdown of CLSCs according to the time of the visit			
	24-48 hours	**3-5 days**	**6 days and +**	**Variable**
Systematic visitation (18 CLSCs)	22%	39%	33%	11%
Nonsystematic visitation (17 CLSCs)	12%	12%	35%	41%

[a] From Ste-Marie, 1998 [103]. It is stated in that report that the percentages indicated are based on the number of responses obtained for each question, not on the total number of questionnaires received. Some questions were not answered by all the respondents. The percentages have been rounded off.

One publication describes the postnatal services at some of Québec's CLSCs [103]. The description is based on answers to a questionnaire distributed to 49 CLSCs on whose territory there is a hospital with a short-term obstetrical program or a length of stay meeting the criteria for a short stay, more than three years ago (in February 1997). At the time, 47% of the CLSCs (18 of the 40 CLSCs that responded) carried out systematic visitation to all mothers. Nearly two thirds of the CLSCs that practiced systematic visitation made the visits within the first five days following discharge as opposed to only 24% for the CLSCs that did not practice systematic visitation. The time of the visit varied much more in the latter group (Table 6).

Furthermore, according to this report, more than 50% (27/40) of the CLSCs screened for physiologic jaundice at the time. The method used varied according to the CLSC. Eighteen of these 27 CLSCs opted only for a clinical examination or observation, the others using a bilirubinometer, an icterometer or a blood test (often a combination of the above).

More-detailed data on 40 CLSCs[11] indicate that, in November 1998, 31 of them systematically screened for physiologic jaundice. Of those that did such screening (systematically or not), 16 opted for a clinical examination or observation, while ten others used a bilirubinometer alone or in conjunction with an icterometer or a blood test. The method used by the other CLSCs varied or is not specified (Table 7). This information is an indication only, since this list is not exhaustive and is no longer up to date. Other institutions may now screen for physiologic jaundice, or others may have changed their approach.

According to Ste-Marie's report [103], all of Québec's CLSCs that had an early discharge program as at February 1997 believed that the task of screening for physiologic jaundice could be entrusted to them and performed during the first home visit. At the time, the conditions deemed necessary for doing this were to ensure equipment availability, provide prior training, ensure that there are memoranda of understanding between the CLSCs and hospitals, and secure the cooperation of physicians. The report's authors also recommend that the visits be done systema-

[11] According to a written communication from L. Rocheleau, senior consultant, Association des CLSC et des CHSLD du Québec, November 1998.

Table 7: Overview of the screening method used by CLSCs or health centres[a] (November 1998)

Screening method	Number of CLSCs or health centres
Observation/clinical examination	16[b]
Bilirubinometer/heel pad puncture	10[c]
Other method	10[d]

[a] According to a written communication from Lucille Rocheleau, senior consultant, Association des CLSC et des CHSLD du Québec, November 1998.
[b] Three of them stated that jaundice screening was not done systematically.
[c] Two of them stated that jaundice screening was not done systematically.
[d] Most did not specify the method used.

tically and that, in the case of several CLSCs, they take place sooner after postnatal discharge.

3.3 ASSESSING HYPERBILIRUBINEMIA IN THE CONTEXT OF POSTNATAL FOLLOW-UP

In a clinical setting, neonatal hyperbilirubinemia is usually assessed by systematically performing a serum bilirubin test in all infants with visible jaundice only. The identification of those cases where a blood bilirubin determination is actually required involves the use of qualitative (presence or absence of visible jaundice as determined by a visual assessment) or semiquantitative (determination of the degree of jaundice using an icterometer or a transcutaneous bilirubinometer) methods for measuring jaundice.

As regards the practice of early postnatal discharge, the bilirubin concentration usually peaks after discharge from the institution of birth in cases of healthy term infants. In this context, the ability to assess hyperbilirubinemia quickly, easily, effectively and inexpensively has become more important.

3.3.1. Predictive approaches

Consideration has been given to using predictive methods in a clinical setting in order to identify, shortly after birth, those infants more at risk for subsequently developing significant hyperbilirubinemia and for whom a closer follow-up is required. A number of tests have been investigated: maternal blood bilirubin concentration at birth [60], cord bilirubin concentration at birth [51, 57, 58], the measurement of or increase in yellow skin colour during the first 24 postnatal hours[12] (using transcutaneous bilirubinometry) [57, 114], a serum bilirubin test during the first few hours after birth [11, 12, 97] and estimating bilirubin production by measuring carbon monoxide levels [99, 104]. Generally, when these tests are used alone in healthy term infants, their clinical value is limited because of their low positive predictive value and their low specificity when precedence is given to high sensitivity.

The methodology developed by Bhutani et al [11] seems more promising in this regard. Their approach is based on the association observed between serum bilirubin levels measured during

[12] This approach is the one considered in certain regions of France for cases of early postnatal discharge [31].

the first few hours after birth (at the same time as screening tests are performed for metabolic diseases, for example) and the subsequent risk of developing jaundice. This association permits the identification of high-, medium- and low-risk newborns so that the appropriate follow-up can be provided. Although this method involves certain biases [75] and certain aspects still need to be validated, it appears to be very effective in predicting hyperbilirubinemia. In the context of short postnatal stays, the use of predictive screening methods could prove to be very useful, since they pave the way for planning a safe, well-targeted screening strategy.

3.3.2 Screening approaches

In this section, we present the results of the rare published studies on assessing neonatal hyperbilirubinemia outside a clinical setting. A first study, conducted by Brucker and MacMullen in 1987 [21], examined the usefulness of transcutaneous bilirubinometry in screening, in the home, neonates for elevated serum bilirubin levels. In this study, the population consisted of infants of different ethnic origins with an average age of 63 hours and with a low risk of hyperbilirubinemia (in fact, they had undergone a medical evaluation prior to discharge). The coefficient of correlation between the serum bilirubin and transcutaneous bilirubin was 0.69, a value usually lower than what has been observed in a clinical setting (see following section). No false negatives and three false positives were reported in the 20 infants examined. Although the small number of neonates in the study limits its significance, the authors conclude from the results that transcutaneous bilirubinometry can be of assistance to nursing personnel in assessing jaundice during home visits.

In 1996, Ruchala et al [91] conducted a pilot study aimed at determining if the use of transcutaneous bilirubinometry in the home would enable them to validate nurses' visual assessments. A high correlation ($R_s = 0.85$; $p > 0.01$) between the visual assessment and the transcutaneous bilirubin index was reported. Based on the results, the authors were of the opinion that, in addition to enabling experienced nurses to validate their assessments, this device would be useful for preparing less experienced nurses to assess jaundice in infants during their home follow-ups. In fact, as stated in Section 2.5.1, the transcutaneous bilirubinometer can be used to identify cases of significant hyperbilirubinemia requiring a closer follow-up.

Maisels and Kring [73] report that transcutaneous bilirubinometry is useful in ambulatory settings, especially when used on a regular basis by nurses in home follow-up programs and by residents working in outpatient clinics. According to these authors, in the context of early postnatal discharge, the ideal situation would be for each pediatrician's office to be equipped with such a device.

No details or quantitative data are provided on the efficacy of this technology or on the conditions governing its use in these different contexts.

As regards Québec, we note that the use of transcutaneous bilirubinometry both in clinical settings and in the home is well established in the Québec City area. A detailed quality control program for this technology was developed in 1996 and is currently in effect[13]. Based on the preliminary results of their follow-up, which cover slightly more than one year, Béland and Leclerc [8, 63][14] emphasize the usefulness of this technology in screening for cases where a serum bilirubin determination is required.

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[13] See, in this regard "Virage ambulatoire en période postnatale – Région de Québec" [5], "Programme de contrôle de qualité pour les bilirubines cutanées" [8] and "Rapport annuel du programme de contrôle de qualité pour les bilirubines transcutanées à domicile" [7].

[14] Unpublished data or data published in a journal that is not indexed in MEDLINE.

Several published studies demonstrate the efficacy of transcutaneous bilirubinometry in assessing neonatal hyperbilirubinemia in a clinical setting and the benefits associated with its use. In the next sections, we present some of the available information on this subject, then discuss the economic and organizational implications of purchasing transcutaneous bilirubinometers and using them within the framework of home visitation and in hospitals. This information will enable us to better assess the usefulness of providing each region in Québec with these instruments and to identify the indications and requirements for using this technology.

4. EFFICACY AND UTILITY OF TRANSCUTANEOUS BILIRUBINOMETRY

With one exception, all the published articles on the efficacy and utility of transcutaneous bilirubinometry specifically concern the type Minolta/Air Shields Jaundice Meter™. When we started to write this report, it was the only transcutaneous bilirubinometer approved in Canada. It has been on the market since the early 1980s. The first model was the JM-101, which was superseded by the JM-102[15]. The publications still do not specify which model was studied. This is why special attention is given to the more recent studies. The only scientific publication on another type of transcutaneous bilirubinometer concerns the ColorMate™ TLc-BiliTest™, whose use has not been approved by Health Canada[16].

4.1 RELATIONSHIP BETWEEN THE TRANSCUTANEOUS BILIRUBIN INDEX AND THE BLOOD BILIRUBIN LEVEL

Several authors have observed, in populations of healthy term newborns of the same ethnic origin, that the transcutaneous bilirubin measurement (TcB), or transcutaneous bilirubin index, is usually highly correlated with the serum bilirubin level and that there is a usually linear relationship between the TcB and the SB (see Figure 3). In such populations, the coefficient of correlation between the TcB and the SB is generally high, often ranging from 0.90 to 0.95 [46, 49, 70, 96, 113, 115, 120].

However, the relationship between the transcutaneous bilirubin index and the blood bilirubin concentration is affected by several factors. Thus, in newborns, estimates of blood bilirubin concentrations by transcutaneous bilirubinometry are affected by skin colour and the degree of skin pigmentation, phototherapy, exposure to ambient light, gestational age, birthweight, the thickness of the skin, the body site of measurement and other factors [29].

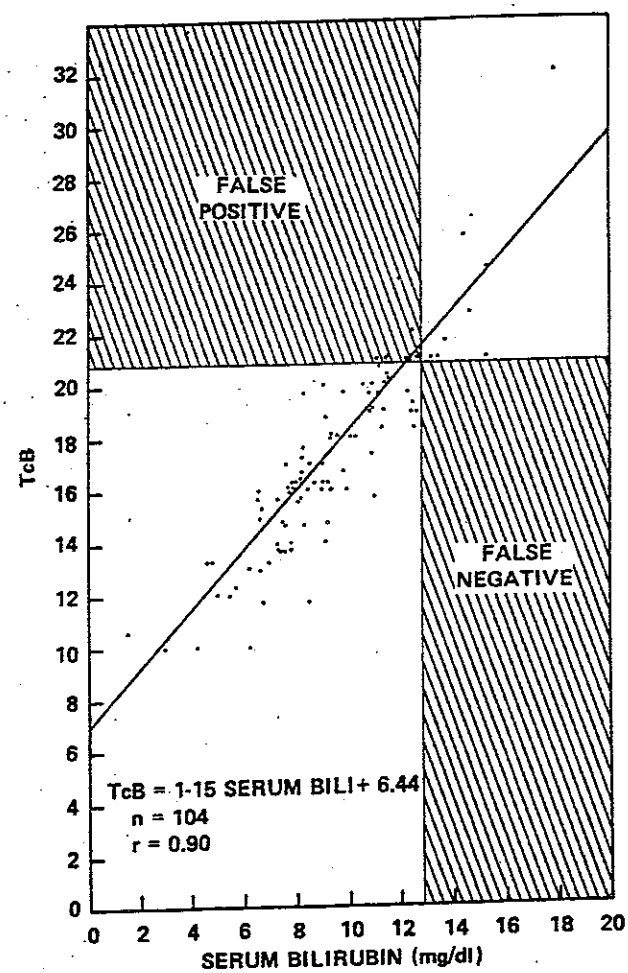
Studies involving term newborns of different ethnic origins and whose skin was not light indicate that this index increases as skin pigmentation increases. Such a situation therefore has few clinical consequences, other than having to perform a larger number of serum bilirubin tests in a multiethnic or predominantly non-Caucasian population compared to the number required when the transcutaneous bilirubin decision level is exceeded [29]. The effect of skin pigmentation on the relationship between the blood bilirubin level and transcutaneous bilirubin level can be taken into account by plotting calibration curves specific to the different ethnic populations of interest or by sequential readings taken in the same newborn and corrected by subtracting an initial reading taken shortly after birth [68][17].

[15] In the new model (JM-102), the battery does not have to be recharged as often (500 vs. 100 measurements with the previous model), the instrument has better precision and it is lighter in weight [29].

[16] Information e-mailed (May 19, 1999) by C. Choquet, head of In Vitro Diagnostic Instruments, Medical Devices Bureau, Health Canada.

[17] According to a systematic review conducted in 1998 by the Centre for Clinical Effectiveness of the Monash Institute of Public Health, in Australia, transcutaneous bilirubinometry is the most suitable technology in a clinical setting for screening for jaundice in term neonates in multiethnic populations. Source: Report entitled "Assessing Neonatal Jaundice in a Multicultural Population", as consulted on the Internet on January 19, 2000 at httw://www.med. monash.edu.au/publichealth/cce/evreports.htm.

Figure 3: Relationship between the transcutaneous bilirubin (TcB) index and the serum bilirubin level (from Smith, 1985 [99])



A strategy for improving the accuracy of transcutaneous bilirubinometry in a multiethnic setting should be evaluated on a case-by-case basis, taking into account the characteristics of the population of interest.

With a few exceptions [46, 61], studies indicate that the relationship between the TcB index and the SB concentration is affected very significantly by subjecting or not subjecting neonates to phototherapy [45, 48, 49, 70, 113, 115, 116, 117]. This can be explained by the rapid change in skin colour. Additionally, when a portion of the skin is covered during phototherapy, the TcB reading is much higher on that portion than on the uncovered portion [48]. However, no study has examined the correlation between the TcB and the SB on unexposed skin during phototherapy. Such a study would make it possible to document the efficacy of transcutaneous bilirubinometry during such treatment. Thus, until such studies are available, TcB measurements cannot be used in infants subjected to phototherapy.

In one study, it was observed that infants close to windows and exposed to sunlight showed a slight decrease in the TcB level compared to that of infants exposed to artificial light [121]. Although statistically significant, this difference is of no clinical consequence [29].

Since prematurity and birthweight seem to affect the relationship between the TcB and the SB [40, 106, 107, 113], the use of this instrument in premature infants is not recommended. In term infants, the relationship between skin colour and the plasma bilirubin concentration remains almost unchanged more than ten days after birth [59, 118].

The relationship between the TcB and the SB is also affected by the body site of the TcB measurement. It was thus necessary to standardize the choice of site, and, after trials on various parts, the forehead and sternum, which yield similar TcB readings, were chosen for the purpose of transcutaneous bilirubin measurements. Using the device on the forehead of a crying infant can yield slightly lower readings, probably because the contact between the skin and instrument is not as good [122].

Table 8: Performance of transcutaneous bilirubinometry with regard to serum bilirubin concentrations[a]

Predicted SB (μmol/L)	TcB decision level	Positive predictive value	Negative predictive value	Sensitivity	Specificity	n	Population	Reference(s)
≥ 175	≥ 15	62	93	96	50	146	White, term	Knudsen, 1990 [55]
	≥ 16	72	87	87	72	114		
≥ 225	≥ 16	25	100	100	52	114		
	≥ 17	27	97	86	63	90		
≥ 170	≥ 16	94	---	100	---	76	White, term	Suckling et al, 1995 [105]
≥ 240	≥ 18	63	---	100	---	76		
≥ 260	≥ 17	27	100	100	68	45	White, term	Dai et al, 1997 [29]
≥ 225	?	30	95	68	80	---	Chinese	Lin et al, 1993 [67]
≥ 225	≥ 15	52	100	100	35	58	White, term	Knudsen et al, 1993 [59]
≥ 225	≥ 16	58	96	97	51	50	Age: 5-14 days	
≥ 214	≥ 21	78	88	74	90	155	Arabs, term	Karrar et al, 1989 [54]
≥ 220	≥ 20	44	99	94	78	106	White, term	Schumacher et al, 1985 [95]
≥ 220	≥ 24	58	100	100	97	157	White, term	Maisels and Conrad, 1982 [70]

[a] From Dai et al, 1997 [29].

Although information on the ColorMate™ TLc-BiliTest™ is limited, it indicates that the transcutaneous bilirubin index is highly correlated with the serum bilirubin concentration. The coefficient of correlation was 0.96 (range of values, 3.2 to 338.1 μmol/L), and 96% of the difference between the two measurements was less than 32.2 μmol/L. This relationship does not seem to be affected by infant race or weight or exposure to phototherapy [108].

4.2 ACCURACY OF THE TRANSCUTANEOUS BILIRUBIN INDEX

The accuracy of a screening tool is defined in terms of sensitivity, specificity and positive or negative predictive value[18]. Most studies on the subject indicate that transcutaneous bilirubinometry is effective in screening for cases where a serum bilirubin test is required. To do this, one must determine a transcutaneous bilirubin reading below which the likelihood that an infant has a blood bilirubin level requiring treatment is, for all practical purposes, nil. In other words, steps are taken to prevent any false negatives.

Table 8 shows results obtained for these screening parameters in a few studies. It should be noted that the studies were almost always conducted in a clinical setting where the infants had been preselected by the physician or nursing staff. Consequently, only those infants with visible jaundice were usually tested with a bilirubinometer.

The studies by Knudsen [55] and Knudsen et al [59] are of particular interest because they showed the impact of an increase in the TcB decision level on sensitivity, specificity and positive and negative predictive values for serum bilirubin values of 175 and 225 μmol/L. Thus, a TcB decision level of 15 or 16 units in

[18] See the definitions of these terms in the glossary.

their population of newborns and infants 5 to 14 days of age yielded a negative predictive value of about 100%. With this decision level, practically no cases with a serum bilirubin concentration greater than 225 μmol/L would be missed.

With this decision level, the positive predictive value ranged from 25 to 58%. This is a judicious approach, since a false negative can have a disastrous effect on a newborn, while a false positive only results in a blood sample being taken. This decision level can be maintained for the first 14 days of life, since the relationship between skin colour and the plasma bilirubin concentration remains practically unchanged during this period [59].

All these considerations bring out the need for a close link between the use of transcutaneous bilirubinometry and the clinical laboratory, for with this link, one could ensure safe use of the instruments, establish the decision level associated with a negative predictive value as close as possible to 100% for the population of interest, and minimize the number of SB tests.

4.3 PRECISION OF THE TRANSCUTANEOUS BILIRUBIN INDEX

Various authors have examined the precision[19] of bilirubinometers of the type Minolta/Air Shields Jaundice Meter™ and have generally shown that they have a high degree of precision. In *in vitro* studies (readings made with the instrument using a glass cuvette rather than on the infants' skin), the reported coefficients of variation range from 3.7% for a TcB index of 12.2 to 1.1% for a TcB index of 39.2 [119]. In an original article published in 1980, Yamanouchi and collaborators reported the results of five readings obtained by the same operator on newborns [113]. The coefficient of variation ranged from 4.9% for a TcB index of 9.2 to 2.6% for a TcB index of 27. There is close agreement between the results of these two studies, even if the study by Yamanouchi and collaborators was based on the use of a prototype directly on newborns.

That the bilirubinometer has good precision was confirmed in subsequent studies comparing successive measurements made in the same subjects and by the same operators. In these conditions, the coefficients of variation ranged from 2.2 to 3.5% for 20 readings taken in six infants in one study [38], whereas in another study they ranged from 1.9 to 3.8% when five readings were taken and from 3.2 to 4.2% for 100 readings [49]. These results seem to indicate that successive readings in a given subject can modify certain conditions in the skin and thus affect their precision.

Yamanouchi et al [113] also studied interoperator precision of the transcutaneous bilirubinometer. They observed a coefficient of variation ranging from 2.1 to 5.0% when four users took five readings.

Brown et al [18, 19] observed considerable variance between the results with two instruments used in their institution (interinstrument precision). Based on this observation, they recommend determining the same decision level for each instrument, not changing instruments and always using the same device for a given infant. Little variability was observed in another study aimed at comparing the use of eight commercially available transcutaneous bilirubinometers on newborns [119].

It should be noted that several studies on measurement precision have been conducted on prototypes and on model JM-101 and that, as a result, their findings might not apply to the devices found on the market (JM-102). Furthermore, and as pointed out by Dai et al [29], despite the fact that there have been a number of studies on interinstrument variability, they did not concern the performance of these instruments used in different locations with various operators and

[19] See the definition of this term in the glossary.

according to various procedures.

According to Tayaba et al [108], the Color-Mate™ TLc-BiliTest™ provides precise results. In newborns tested repeatedly by three different operators over a 30-minute period, the coefficient of variation for the transcutaneous bilirubin measurements was 3.1% around a mean estimate of 135 μmol/L, which is comparable to the results obtained with the first instrument.

4.4 COMPARISON OF TRANSCUTANEOUS BILIRUBINOMETRY WITH OTHER SCREENING METHODS

It has been reported that in clinical settings, transcutaneous bilirubinometry was more effective than a clinical assessment in determining the degree of jaundice in neonates. In 1982, Engel compared the performance of the transcutaneous bilirubinometer in identifying infants (of four different ethnic origins) requiring a serum bilirubin test and the visual assessments by three neonatologists [35]. The coefficient of correlation between the transcutaneous bilirubinometer measurements and the serum bilirubin measurements was 0.86. The coefficients of correlation between the results of the visual assessments by the three neonatologists and the serum bilirubin measurements were lower, ranging from 0.60 to 0.74. More recently, Tayaba et al [108] observed an even greater disparity between the results of visual assessments and those of transcutaneous bilirubinometry. They report a coefficient of correlation of 0.96 between the transcutaneous bilirubin index and the serum bilirubin concentration (1,600 separate measurements in 900 patients). The coefficient of correlation between the results of the visual assessments and the serum bilirubin determinations was lower—0.75 (1,470 separate measurements in 851 patients). Although interesting, the results of these studies are not very useful, since the first one is too brief and the second one concerns a device which has not yet been approved for use in Canada.

Three studies comparing the efficacy of the icterometer with that of the transcutaneous bilirubinometer were identified in the literature: those by Bilgen et al [13], Bhardwaj et al [10] and Schumacher et al [95]. Because of the too small a sample (n = 30) and the study population (three groups of premature infants of Indian origin), which differs too much from the context of the present study, the article by Bhardwaj et al [10] is of limited interest. It will nonetheless be noted that the correlation between the serum bilirubin levels and the bilirubinometer readings was good for the three groups studied (0.84, 0.89 and 0.72). The correlation between the bilirubin levels and the icterometer readings was not as good for the third group (0.84 and 0.82 vs. 0.67), whose gestational age was higher than that of the other two groups.

The studies by Bilgen et al [13] and Schumacher et al [95] both involved a relatively limited number of infants—about one hundred newborns with visible jaundice of Turkish origin in the first case and of Caucasian origin in the second. The results presented in both articles concern the accuracy of the instruments rather than their precision. Although the study by Bilgen et al is relatively recent, the bilirubinometer used in both cases was the JM-101, which was the previous model, whose precision is reported to be lower than that of the JM-102 [29].

Generally, and as can be seen from Table 9, in terms of accuracy, the bilirubinometer's performance is slightly better than that of the icterometer. In the study by Bilgen et al [13], it is seen that 44% of infants tested with a bilirubinometer will be false positives (1 - specificity) compared to 52% for those tested with an icterometer. In both cases, this means that a large number of infants needlessly undergo a serum bilirubin test. Despite this drawback, and based on the small difference between the values of the parameters studied and the cost of each instru-

Table 9: Results obtained with the icterometer and transcutaneous bilirubinometer*

Device	Correlation with SB concentration	Test sensitivity (%)	Test specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Reference
Icterometer[a]	0.78	100	48	29	100	Bilgen et al, 1998 [13]
Bilirubinometer[a]	0.83	100	56	33	100	
Icterometer[b]	0.63	82	74	38	96	Schumacher et al, 1985 [95]
Bilirubinometer[b]	0.74	94	78	44	99	

[a] n = 96.
[b] n =106.
* In these studies, an icterometer reading of 3 or higher was the decision level regarding the need for a serum bilirubin test.

ment, Bilgen et al [13] believe that the use of the icterometer should be promoted, especially in countries with a birth rate and an incidence of hyperbilirubinemia as high as those observed in Turkey.

Schumacher et al [95] conclude that both instruments are useful for screening for hyperbilirubinemia but acknowledge that the bilirubinometer, which provides an objective measurement of the degree of jaundice, may be particularly useful when infants are to be tested by different health-care professionals.

Because of the very limited number of comparative studies (2), their small sample size (about 100), the populations investigated (jaundiced infants, ethnic origin) and the model of bilirubinometer studied (the JM-101 rather than the JM-102), the data are insufficient to come down in favour of either of these approaches (icterometry or transcutaneous bilirubinometry). Furthermore, as indicated in Section 2.5.2, icterometer readings seem to be less reliable because of their subjective nature and lack of precision and are probably of limited usefulness in the context of early postpartum discharge. Should this option be chosen, one would have to check the results of each icterometer used and prepare a calibration curve in each different clinical laboratory rather than rely on published values to describe the relationship between serum bilirubin concentrations and icterometer readings.

4.5 ADVANTAGES ASSOCIATED WITH USING TRANSCUTANEOUS BILIRUBINOMETRY

The transcutaneous bilirubinometer is compact, battery-operated and very easy to use and maintain, and is safe for patients. It provides quick results that can be interpreted immediately, thus avoiding the waiting associated with serum bilirubin tests. The device is therefore handy in clinical settings and in nurseries as well as in the home.

As pointed out by an official at the Ministère de la Santé et des Services sociaux[20], the use of transcutaneous bilirubinometry in the context of early discharge provides nurses reassurance when assessing an infant's health status. They are less afraid of overlooking signs suggestive of jaundice due to a lack of experience or of being challenged over their clinical assessment. The practice of home nursing is more difficult, given that there is no sharing of responsibilities, as there is in institutions. The use of this technology reassures nursing personnel during home follow-up visits by giving them a sense of protection

[20] Note from Paul Boivin (engineer, Department of Biomedical Technologies, Ministère de la Santé et des Services sociaux) sent to Jeannine Auger, September 18, 1998).

against the ever-present possibility of legal action.

Since severe hyperbilirubinemia is a serious and very rare phenomenon, one must, so as not to miss one of these rare cases, monitor and measure the serum bilirubin level in a large number of infants who will never develop this condition. The number of serum bilirubin tests is therefore relatively high in relation to the number of infants who require treatment. Thus, as was mentioned earlier, 5% of term newborns reportedly develop significant hyperbilirubinemia (serum bilirubin > 290 μmol/L). This small proportion means that 95% of the serum bilirubin tests systematically performed in newborns are negative and consequently unnecessary. If serum bilirubin tests are performed only in infants with visible jaundice (about 45 to 60% of healthy term neonates, according to Blackburn and Loper [14]), as is often recommended [10, 90], the total number of tests could be reduced, but nearly 50% could still be avoided. Both of these screening strategies are expensive.

Determining the serum bilirubin concentration requires a blood specimen, which is obtained from the infant's heel. There, the distance between the surface of the plantar skin and the underlying bone is 2 mm. There is therefore a risk of an accidental bone puncture and of osteomyelitis if the procedure is not performed properly. In addition, heel pad punctures involve a risk of infection, in addition to the discomfort and pain involved. This being said, minimizing the number of blood specimens obtained by heel pad puncture is a second major concern for health professionals involved in neonatal care [28, 29].

4.5.1 Impact on the number of serum bilirubin tests

Bourchier et al [15] did not observe a reduction in the number of serum bilirubin (SB) tests after the introduction of transcutaneous bilirubinometry in clinical settings. However, it should be noted that the physicians could order tests as they wished without having to adhere to any protocol.

Maisels and Kring [73] observed that the number of serum bilirubin tests performed in their nursery decreased by 40% after instituting the general use—without any strict protocol—of transcutaneous bilirubinometry. The decrease was attributable only to the fact that the physicians ordered fewer SB tests when bilirubinometers were available. The authors also assessed the economic impact of using a transcutaneous bilirubinometer in their clinic, where there are 5,000 deliveries a year. The net savings associated with the use of a transcutaneous bilirubinometer was estimated at $1,625 US a year.

In a study involving 2,000 infants, Schubiger et al [94] reported that the number of blood specimens had decreased by 79% after the introduction of a bilirubinometer (used in accordance with the recommendations of the Swiss Neonatology Group). Lastly, Dai et al [28] estimated that the use of a bilirubinometer for screening purposes in a clinical setting led to a 43% reduction in the number of heel pad punctures (performed solely for the purpose of SB tests). This figure decreased to 20% when the cases involving infants subjected to phototherapy or a battery of tests, including a serum bilirubin determination, were taken into account.

As pointed out by Dai et al [29], the actual reduction in the number of SB tests or heel pad punctures in institutions depends on the prevalence of hyperbilirubinemia, the practice regarding serum bilirubin tests (i.e. the extent to which such tests are performed, whether they are performed alone or in conjunction with other tests) and whether or not there is a protocol governing the use of transcutaneous bilirubinometry.

4.5.2 Additional advantages of emerging models

Although the information is limited [108], the new models of transcutaneous bilirubinometers,

such as the Bili*Check*™[21] and the ColorMate™ TLc-BiliTest™, reportedly eliminate interference caused by skin colour in the relationship between the transcutaneous bilirubin reading and the blood bilirubin concentration. Such a feature would be an advantage in those regions of Québec where there is significant ethnic diversity.

These models, reportedly have the additional advantage of sustained efficacy even when used during phototherapy. This is of great interest, given the experience with home phototherapy treatment, which has been a practice in the United States for more than 15 years [33, 42, 98]. Furthermore, two Montreal hospitals (Hôpital du Sacré-Coeur and Hôpital Sainte-Justine) are currently conducting tests on a phototherapy system planned for home use. The likely savings that the use of home phototherapy can generate in relation to in-hospital phototherapy and the possibility of maintaining an uninterrupted bonding process between the mother and infant during treatment [42] are two factors that could promote the adoption of this practice in Québec in short or medium term.

[21] Accessed on the Internet on February 2, 1999 at http://www.healthdyne.com/interact…/infant_management/bilicheck1.html

5. IMPLICATIONS OF INSTITUTING TRANSCUTANEOUS BILIRUBINOMETRY IN THE CONTEXT OF EARLY POSTNATAL DISCHARGE

5.1 COST OF HYPERBILIRUBINEMIA SCREENING WITH AND WITHOUT THE USE OF TRANSCUTANEOUS BILIRUBINOMETRY

The purpose of this section is to attempt, for the first time in Quebec, a preliminary assessment of the financial impact of using transcutaneous bilirubinometry to screen for neonatal hyperbilirubinemia. In concrete terms, we compare the costs associated with using this technology with the costs generated by visual assessments and serum bilirubin determinations. To provide a better perspective of the situation, the assessment scenario, which is detailed in Appendix A, covers the costs incurred for hyperbilirubinemia screening in institutions of birth and during follow-up visits in connection with early neonatal discharge. This scenario, which seems the most plausible, is based on the following working hypotheses:

- 53% of healthy infants present with visible jaundice.
- A serum bilirubin test is performed in 50% of jaundiced newborns.
- Two bilirubinometers are purchased and used per institution of birth or CLSC.
- The number of serum bilirubin tests in healthy term neonates decreases by 43%.
- The cost of a serum bilirubin test is calculated to be $19.78, whether it is performed in a clinical setting or elsewhere[22];
- Lastly, the costs are calculated for a period of 10 years [23].

According to the assessment, the costs associated with neonatal hyperbilirubinemia screening by a visual assessment and by a serum bilirubin test in healthy newborns would be $2,288,111 for a 10-year period, or an average of $1,031 per year per institution. The use of transcutaneous bilirubinometry would result in a cost of $7,166,290 over ten years, which works out to an average of $3,228 per year per institution. This cost was discounted at a rate of 5%.

Said differently, the use of transcutaneous bilirubinometry would result in a cost of $8.90 per infant compared to $2.83 per infant when hyperbilirubinemia screening is done by a visual assessment and a serum bilirubin test (cost differential, $6.07). Assuming that a CLSC follows 500 infants a year, the use of transcutaneous bilirubinometry could result in $4,450 in annual costs per CLSC.

Although it gives some indication, this preliminary assessment is marked by uncertainty. Table 10 explains the main sources of uncertainty and their likely impact on the cost estimate. The results of the sensitivity analysis, which are presented in Table 11, show that the number of transcutaneous bilirubinometers per institution is the parameter with the greatest impact on costs. Thus, depending on the number of

[22] The cost of transporting the blood specimens is not included because they are usually obtained during the follow-up visit. No additional travel is therefore required for this sole purpose.

[23] Based on information provided verbally by P. Leclerc, medical biochemist, Hôpital du Saint-Sacrement, Québec City (December 1998) and completed in writing (July 1999), the lifespan of a bilirubinometer is more than ten years.

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Table 10: Main sources of uncertainty associated with the cost estimate for neonatal hyperbilirubinemia screening

Working hypothesis (potential impact on estimate)	Factor/data considered
53% of healthy infants present with visible jaundice	• Between 45 and 60% of healthy term newborns reportedly experience an episode of clinical jaundice during the first few days after birth [14].
A serum bilirubin test is performed in 50% of jaundiced newborns • Because it is more difficult to detect jaundice in the home, it is possible that 1) in order to prevent false negatives, a larger number of serum bilirubin tests would be performed (underestimate of the cost of screening by SB); and 2) jaundice would not detected in a newborn and that an SB test would not be performed (overestimate of the cost of screening by SB). • It is also assumed that each infant undergoes a single SB test, although in a number of cases, more than one test would be required (underestimate of the cost of screening by SB).	• Empirical evaluation based on the fact that some authors recommend a serum bilirubin test in all jaundiced infants [9, 90], whereas others [5, 88] maintain that, after an infant is discharged, jaundice and other factors should be considered when assessing the need for a serum bilirubin test.
Purchase and use of two bilirubinometers per institution of birth or CLSC • In certain outlying regions, a CLSC can have two or three points of service 40 to 50 kilometers apart, a situation which would require that several devices be available (underestimate of the cost of using TB). • A portion of the instruments' purchase cost has already been incurred, since a certain number of institutions have already purchased at least one transcutaneous bilirubinometer (overestimate of the cost of using TB). • The additional costs associated with quality control for this use and with user training were not taken into account (underestimate of the cost of using TB).	• There are no data available on the actual need (in terms of numbers) for transcutaneous bilirubinometers at each institution.
43% decrease in the number of serum bilirubin tests performed in healthy term neonates • In the home, the decrease in the number of SB tests could be larger (overestimate of the cost of using TB). • In certain regions, the population may be very diverse in terms of ethnic origin, hence the need to perform more SB tests (underestimate of the cost of using TB).	• According to published data, in a clinical setting, the use of a bilirubinometer for screening purposes could reduce the number of serum bilirubin tests by between 0 [15] and 79% [94]. An intermediate figure of 43% was used as a basic estimate, since, in Manitoba, Dai et al [28] observed that the use of a bilirubinometer for screening purposes can reduce, by up to 43%, the number of serum bilirubin tests performed in healthy term neonates with no prior exposure to phototherapy (clinical setting).
The cost of a serum bilirubin test is $19.78, whether it is performed in a clinical setting or elsewhere (overestimate of the cost of screening by SB).	• A serum bilirubin test costs $1.38, obtaining the blood specimen $18.40[24] [80], for total of $19.78.

[24] The starting point for calculating these figures was the price lists posted by seven institutions in the health and social services system. Care was taken to eliminate the extreme values, which could distort the results. These figures should be used as a guide only, since the actual cost of performing these procedures in a given laboratory varies according to the volume of work, the level of automation and the staff's experience [80].

Table 11: Results of the sensitivity analysis concerning the cost of neonatal hyperbilirubinemia screening with and without the use of transcutaneous bilirubinometry (TB)

Parameter	Basic estimate and range (minimum - maximum)	Cost range without the use of TB Base = $2,288,111 (over 10 years)	Cost range with the use of TB Base = $7,166,290 (over 10 years)	Additional cost of using BT Base = $4,878,179 (over 10 years)
Number of devices per institution	2 (1 - 4)	Min.: $2,288,111 Max.: $2,288,111	Min.: $3,776,052 Max: $13,946,766	Min.: $1,487,941 Max.: $11,658,655
Prevalence of jaundice	53% (45% - 60%)	Min.: $1,942,735 Max.: $2,590,314	Min.: $7,117,937 Max.: $7,208,598	Min.: $5,175,202 Max.: $4,618,284
Proportion of newborns who undergo an SB test	50% (20% - 100%)	Min.: $915,244 Max.: $4,576,221	Min.: $6,974,088 Max.: $7,486,625	Min.: $6,058,844 Max.: $2,910,404
Decrease in the number of SB tests when BT is used	43% (23% - 63%)	Min.: $2,288,111 Max.: $2,288,111	Min.: $8,081,534 Max.: $6,251,045	Min.: $5,793,423 Max.: $3,962,934

instruments used at each institution, the use of transcutaneous bilirubinometry could result in an additional cost of $1.5 to $11.7 million over a 10-year period in relation to a strategy based solely on visual assessments and serum bilirubin tests. This works out to a cost differential of $1.86 to $14.47 per infant.

These estimates can be considered a starting point for a more accurate determination of the amounts to be allocated for the use of transcutaneous bilirubinometry in the context of neonatal hyperbilirubinemia screening. Screening using this technology has advantages which, although difficult to quantify, could offset some or all of the cost differential that it entails. These advantages are discussed in detail in the next section.

5.2 ADVANTAGES OF SCREENING FOR HYPERBILIRUBINEMIA USING TRANSCUTANEOUS BILIRUBINOMETRY

As mentioned earlier, over the past few years, there have been isolated cases of nuclear jaundice in term or near-term infants following early postnatal discharge [23], although this condition had practically disappeared in North America[25]. Furthermore, a significant increase was reported in the number of readmissions for hyperbilirubinemia during the first week of life following early discharge, which was associated with increased severity of hyperbilirubinemia in the infants who were readmitted [65]. These two phenomena are particularly worrisome. Even if the link between early postnatal discharge and an increase in mortality or in severe and irreversible morbidity has not been demonstrated, it cannot be ruled out, especially since these phenomena are rare and therefore difficult to prove.

Nor has it been shown that the follow-up examination by a health-care professional in the first few days after discharge can reveal every case requiring a more thorough assessment or intervention for hyperbilirubinemia. The data pub-

[25] In Québec, data in the MED-ÉCHO system indicate that, for the period 1989-1999, there was one case of readmission for nuclear jaundice not due to isoimmunization in infants aged 10 days and younger in 1992-1993 (before early discharge) and one case in 1998-1999 (after early discharge)

lished by Lee et al [65] indicate, however, that the optimal postnatal age for detecting early problems is three days. At that age, 98% of severe cases of jaundice or dehydration can accordingly be detected.

Since the prevalence of hyperbilirubinemia depends mainly on the ethnic composition of the population and the prevalence of breast-feeding, the use of transcutaneous bilirubinometry should not have an impact on the prevalence of or readmission rate for hyperbilirubinemia. However, although quite limited, certain published data gathered in clinical settings point to the superiority of transcutaneous bilirubinometry in detecting jaundice compared to the visual assessment [35, 108]. Given that it is more difficult to make a visual assessment of jaundice in the home [21] and that, with adequate quality control, almost all cases of hyperbilirubinemia requiring treatment can be identified with transcutaneous bilirubinometry, the use of this technology in the context of early postnatal discharge offers undeniable advantages.

Although this has not been proven either, the use of a transcutaneous bilirubinometer during the follow-up visit a few days after birth could help detect significant jaundice earlier. This advantage could translate into lower hyperbilirubinemia upon readmission of jaundiced infants and consequently into a smaller number of infants having to undergo an exchange transfusion[26].

The use of transcutaneous bilirubinometers also offers the advantage of reducing the number of blood specimens obtained for serum bilirubin tests, thus reducing the risks (risk of an accidental bone puncture and of osteomyelitis when the procedure is performed improperly, risk of infection) and the discomfort and pain associated with obtaining blood specimens, in addition to the costs associated with serum bilirubin tests. However, there are no quantitative data concerning the incidence of the complications associated with heel pad punctures. Also, the use of TB permits validation of the assessment of jaundice by nurses and ensures that they do not miss any cases of jaundice, in addition to creating a sense of security against possible legal action.

5.3 ORGANIZATION OF CARE, SERVICES AND FOLLOW-UP

The Ministère de la Santé et des Services sociaux [82] recommends that the practice of early postnatal discharge be governed by a program ensuring the continuity of services after such discharge. The conditions deemed essential for organizing an early discharge program are listed in Table 12. This information is provided as a guide for better determining the implications of instituting such a program.

One of the services that should be available in this program consists of postdischarge follow-up measures. They have been proposed for the purpose of monitoring the risk of hyperbilirubinemia that might be associated with early discharge and to minimize the consequences in terms of health and resource utilization. The establishment of formal ties between the CLSCs and community breast-feeding support organizations, among others, has been proposed as well [82]. It should be noted that already in 1996 and 1997, partnership between the CLSCs and different community organizations in the area of perinatality was a frequent phenomenon [79].

[26] Data in the MED-ÉCHO system show a decrease in the number of exchange transfusions in infants readmitted when they are 10 days of age or younger, starting in 1995-1996. This could, however, be attributable to factors other than early postnatal discharge (e.g. changes in the decision levels, with regard to serum bilirubin concentrations, for initiating treatment).

Table 12: Essential conditions for organizing an early discharge program[a]

- The existence of a protocol or partnership agreement between the institution of birth and the CLSC for ensuring continuity of care in accordance with the minimum guidelines set out in Part 2 of the MSSS report [90].
- The offer, by the CLSCs, of a range of prenatal and postnatal services and guaranteed free and universal access to these services.
- Adequate budgetary reallocation between the various partners to allow the offer of services to come to fruition.
- Access, on a local basis, to prenatal and postnatal meetings.
- The reorganization of nursing care both in hospitals and at CLSCs.
- The existence of a liaison mechanism with physicians in charge of postnatal follow-ups.
- The existence of a protocol or partnership agreement between the CLSC and community organizations for family support services.
- Participation of physicians working in the area of perinatality in the pre- and postnatal follow-up programs for mothers and infants.
- The guarantee of direct readmission to hospital during the first week of the infant's life, if necessary. Accessibility to a service promoting the mother's physical proximity to the infant, in particular, if she is breast-feeding.
- Accessibility to an Info-Santé-type telephone service 24 hours a day, seven days a week, ideally, to an Info-Perinatality service.
- The rapid exchange of information between the partners after authorization is given to exchange such information.
- Adequate preparation of the staff who provide primary and secondary services. Providing training in the regions in order to promote the development of a common language between the health-care professionals in the various areas would be important[b].

[a] From MSSS, 1999 [82].

[b] Potential training needs regarding jaundice would be skills in performing heel pad punctures for obtaining blood specimens, if necessary, in clinically assessing jaundice in newborns, and in providing breast-feeding support.

This report does not concern the institution of neonatal hyperbilirubinemia screening as part of a perinatal program. However, we are of the opinion that the use of transcutaneous bilirubinometry must necessarily be part of such a program. Its use would permit an objective assessment of the degree of jaundice, in addition to minimizing the number of blood specimens to be taken for bilirubin tests. There should be a quality control program for the use of these instruments in order to ensure their quality, the quality of their use and the interpretation of the results made by the different users[27].

In fact, the conditions governing the use of transcutaneous bilirubinometry should include drafting written operating, maintenance and quality control procedures for these instruments. The people who would be using the instruments should be trained, among other things, on the methods for using them, on interpreting results and on the course of action in light of the results. The training should be complemented with clear and realistic protocols. New instruments should be tested in nurseries and compared to an instrument whose reliability has been checked.

[27] Quality control programs for the use of transcutaneous bilirubinometers should be the responsibility of clinical laboratories. In an outpatient setting, special steps would need to be taken so that the laboratories could provide the necessary technical support for the application of these programs.

Table 13: Examples of quality control measures for the use of transcutaneous bilirubinometers[a]

- Developing a transcutaneous bilirubinometer quality control program for use in nurseries and adapted for use in CLSCs. The program would be supervised by a committee specifically designated for this purpose. The program's objectives would be:
  - To obtain reliable results with the bilirubinometers by validating them with laboratory serum bilirubin test results.
  - To establish procedures for when results do not correlate with the laboratory results.
  - To institute quality control methods, including instrument evaluation, checking readings with laboratory results, and user technique.
- In nurseries, as in each CLSC, designating a nurse to apply the quality control program. She would be responsible for the tasks concerning the instrument's performance and for supervising the different stages of the program.
- Quality controls run by the nurses using the instrument and/or the nurse responsible for the program's application.
- Sending the quality control results once a month and on the same day to the program coordinator, who would compile them.
- Analysis and interpretation of the quality control results by the medical biochemist (in the clinical laboratory).
- Sending a report to each nurse involved in the application of the program, for the purpose of discussing the results.
- Sending a summary report to the members of the committee every three months for discussion purposes during their meetings.

[a] Inspired by Béland and Leclerc, 1997 [7], and Béland et al, 1996 [8].

Also, in the nursery, readings obtained with new instruments and the results of blood bilirubin tests should be compared in order to determine the bilirubinometer reading at or above which a serum bilirubin test is indicated for the population in question. These recommendations are essentially based on experience with the use of transcutaneous bilirubinometers in the Québec City area (See [7, 8, and 63]). The published data generally confirm their relevance. Table 13 lists, as a guide, the quality control measures in place in the Québec City area for the use of transcutaneous bilirubinometry in the context of early postnatal discharge.

Also, special measures should be instituted if transcutaneous bilirubinometers (of the type Minolta/Air Shields Jaundice Meter™) are used in a non-Caucasian or multiethnic population. Lastly, different mechanisms should be put in place to assess the long-term efficacy of using transcutaneous bilirubinometry.

6. CONCLUSION

The practice of early postnatal discharge increases the risk of not detecting cases of significant neonatal hyperbilirubinemia, since the bilirubin level peaks after the infant is discharged. To counter any risk associated with the practice of early postnatal discharge, the Ministère de la Santé et des Services sociaux presently recommends that this practice be part of a perinatal program, which should include early (no later than the third day after discharge from hospital), systematic home visitation. The presence of jaundice in newborns is one of the items to be checked during the visit. The implementation of such a perinatal program with early, systematic follow-up is essential for ensuring the mother's and infant's safety within the context of early postnatal discharge.

Our assessment brings out the benefits of using transcutaneous bilirubinometry for screening for hyperbilirubinemia during this follow-up if such use is included in a well-established perinatal program. However, a wide-scale program for the systematic purchase of transcutaneous bilirubinometers cannot, on the basis of the published data on this technology, be recommended. It is therefore up to each regional or local authority to assess the usefulness of this technology, based on the following considerations:

- In healthy term newborns, transcutaneous bilirubinometry is an effective technology for screening for cases where a serum bilirubin determination is required. Transcutaneous bilirubinometry provides an objective measurement of the degree of jaundice, unlike a visual assessment or an icterometer. This constitutes a major advantage, especially for out-of-hospital use.

- This technology is extremely practical, both in clinical settings and nurseries and in the home. The device is compact, battery-operated and very quick and easy use, and provides an instant readout.

- Transcutaneous bilirubinometry is ineffective when used in infants subjected to phototherapy or who have undergone an exchange transfusion and is of limited efficacy in highly multiethnic populations. Based on preliminary published data, these limitations have been corrected in recent models of transcutaneous bilirubinometers, which have still not been approved by Health Canada. Furthermore, it seems that home phototherapy might, in the short or medium term, be introduced as a practice in Quebec. This being said, the possibility of using transcutaneous bilirubinometry during phototherapy is of particular interest. It would therefore be important for the policymakers concerned to weigh the benefits of the existing models against their limitations before purchasing any transcutaneous bilirubinometers.

- The use of transcutaneous bilirubinometry necessarily requires close ties with a clinical laboratory in order to ensure optimal and safe utilization (e.g. determining a decision level that would prevent practically all potential false negatives and reduce as much as possible the number of serum bilirubin tests). Also required are strict quality control measures, adequate user training and an assessment of the long-term efficacy of the use of this technology. The mechanics of instituting transcutaneous bilirubinometry in the context of early postnatal discharge could be inspired by those presently in place in the Québec City area, where this technology has been in use since 1996.

Conclusion

The use of transcutaneous bilirubinometry in the context of early postnatal discharge could result in an increase in direct costs to the health-care system (additional cost of about $6 per infant). The actual gain associated with the use of this technology cannot, from the available data, be determined. However, the increase in cost over that presently incurred for screening for neonatal hyperbilirubinemia could be offset or justified by different benefits, such as:

- The near-guarantee of detecting all cases of excessive hyperbilirubinemia and therefore of preventing the risk of bilirubin encephalopathy or nuclear jaundice.
- Earlier detection of hyperbilirubinemia, which could result in lower blood bilirubin levels in cases of neonatal readmission for jaundice.
- A decrease in the number of serum bilirubin tests with the concomitant reduction of the risks, discomfort and pain associated with obtaining blood specimens.
- The validation of the assessment of jaundice by nursing personnel, which gives them assurance of not missing any cases, in addition to a sense of security against potential legal action.

APPENDIX A: DETAILED TABLES ON THE ESTIMATE OF THE COSTS ASSOCIATED WITH THE USE OF TRANSCUTANEOUS BILIRUBINOMETRY

Table 14: Cost of serum bilirubin tests compared to the cost of transcutaneous bilirubinometry in healthy newborns based on birth projections in Québec, 2000-2010 (most plausible scenario)

	Years											Total
	2 000	2 001	2 002	2 003	2 004	2 005	2 006	2 007	2 008	2 009	2 010	
Number of births (Québec)[1]	75 090	74 412	73 932	73 606	73 397	73 257	73 146	73 050	72 966	72 886	72 798	808 540
Estimated number of cases of jaundice[2,3]	27 062	26 818	26 645	26 528	26 452	26 402	26 362	26 327	26 297	26 268	26 236	291 398
Neonatal hyperbilirubinemia screening without the use of transcutaneous bilirubinometry												
Estimated % of SB tests if jaundice [4]	50	50	50	50	50	50	50	50	50	50	50	
Estimated number of SB tests[4]	13 531	13 409	13 323	13 264	13 226	13 201	13 181	13 164	13 148	13 134	13 118	145 699
Total cost for SB tests ($)[5]	267 647	265 231	263 520	262 358	261 613	261 114	260 718	260 376	260 077	259 792	259 478	2 881 924
Discounted total cost of SB tests ($)[6]	267 647	252 601	239 020	226 635	215 230	204 590	194 552	185 045	176 030	167 464	159 297	2 288 111
Neonatal hyperbilirubinemia screening with the use of transcutaneous bilirubinometry												
Number of TcB measurements	51 061	50 600	50 274	50 052	49 910	49 815	49 739	49 674	49 617	49 562	49 503	549 807
2 bilirubinometers/inst. (n = 222*2)[7]	2 546 340	548 340	548 340	548 340	546 340	548 340	548 340	548 340	548 340	548 340	548 340	8 029 740
Cost/device + maintenance ($)[8]	49,87	10,84	10,91	10,96	10,99	11,01	11,02	11,04	11,05	11,06	11,08	
Cost/TcB measurement ($)[9]	50,02	10,99	11,06	11,11	11,14	11,16	11,17	11,19	11,20	11,21	11,23	
Total cost of TB ($)	2 553 999	555 930	555 881	555 848	555 826	555 812	555 801	555 791	555 783	555 774	555 765	8 112 211
Discounted total cost of TB ($)[6]	2 553 999	529 457	504 201	480 162	457 280	435 493	414 747	394 990	376 175	358 257	341 192	6 845 954
Discounted total cost of TB ($)[6]												
Number of SB tests after TB	7 713	7 643	7 594	7 560	7 539	7 525	7 513	7 503	7 495	7 486	7 477	83 048
Total cost of SB tests after TB ($)	152 559	151 182	150 206	149 544	149 119	148 835	148 609	148 414	148 244	148 081	147 902	1 642 697
Discounted total cost of SB after TB ($)[6]	152 559	143 982	136 242	129 182	122 681	116 616	110 895	105 475	100 337	95 454	90 799	1 304 223
Decrease in the no. of SB tests if TB (%)[10]	43	43	43	43	43	43	43	43	43	43	43	
Number of SB tests avoided if TB[10]	5 818	5 766	5 729	5 703	5 687	5 676	5 668	5 660	5 654	5 648	5 641	62 651
Cost avoided for SB tests ($)	115 088	114 049	113 314	112 814	112 494	112 279	112 109	111 962	111 833	111 710	111 576	1 239 227
A) Discounted cost avoided for SB tests ($	115 088	108 618	102 779	97 453	92 549	87 974	83 657	79 569	75 693	72 010	68 498	983 888
B) Discounted costs of SB + TB ($)[6]	2 706 558	673 440	640 442	609 344	579 961	552 110	525 642	500 466	476 513	453 712	431 991	8 150 177
Discounted costs of [(A) - (B)] ($)[6]	2 591 470	564 821	537 663	511 891	487 412	464 136	441 984	420 897	400 820	381 702	363 493	7 166 290

N.B.: The shaded lines concern considered variables in the sensitivity analysis.

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Table 14 (suite): Cost of serum bilirubin tests compared to the cost of transcutaneous bilirubinometry in healthy newborns based on birth projections in Québec, 2000-2010 (most plausible scenario)

Notes for Table 14

[1] Data from the Institut de la statistique du Québec, 1999 [50].
[2] Based on the use of an estimated proportion of 68%. This figure was derived from the ratio of the number of normal newborns (code 678.1: infants born in hospital with a weight of at least 2,500 grams and no significant problems) (DRG database, according to data available at the Ministère de la Santé et des Services sociaux [MSSS], 1999). to the number of births in 1997-1998 (data from the MED-ECHO APR-DRG system, available at the MSSS, 1999). It was assumed that the resulting proportion applies to the years 2000 to 2010. Estimate corroborated with data from previous years, where the calculated ratios were 69% in 1996-1997 and 70% in 1995-1996.
[3] Calculations based on the midpoint (53%) in the range of values (45 to 60%) reported by Blackburn and Loper [14].
[4] Some authors recommend a serum bilirubin determination in all jaundiced infants [9, 90], whereas others [5, 88] maintain that, after an infant is discharged, jaundice and other factors should be considered when assessing the need for a serum bilirubin determination. Based on this information, it was assumed that a serum bilirubin test is performed in 50% of jaundiced newborns.
[5] Based on a cost of $19.78 per test, or the cost of a serum bilirubin test ($1.38) and the cost of obtaining the blood specimen ($18.40) [80].
[6] Based on a discount rate of 5%.
[7] The cost of a transcutaneous bilirubinometer is $5,000.
[8] Calculated the first year from the purchase cost ($5,000/instrument) plus the cost of the accessories divided by the number of TcB measurements. The other years, this figure was calculated from the cost of the accessories and maintenance divided, once again, by the number of TcB measurements (see following page for the detailed calculation).
[9] The cost of the instrument + cost of maintenance (preceding line) and the cost of a transcutaneous bilirubin measurement. This cost is based on the following information. Maisels and Kring [73] assessed the economic impact of using a transcutaneous bilirubinometer in their clinic, taking into consideration the manpower costs (nursing personnel) for taking TcB measurements and the time it took to do this. They calculated that, on average, it takes a nurse 27 seconds (range, 10 to 40 seconds) to do a transcutaneous bilirubin measurement. In Quebec, the midpoint on the 1998 wage scale for nursing personnel was an hourly rate of $19.67 (minimum, $16.04; maximum, $23.30) [81]. Based on these data, the cost of a serum bilirubin measurement would work out to $0.15.
[10] The use of a bilirubinometer reduces the number of serum bilirubin tests by between 0 [15] and 79% [94]. In Manitoba, Dai et al [28] observed that the use of a bilirubinometer for screening purposes could reduce, by up to 43%, the number of serum bilirubin tests performed in healthy term neonates with no prior exposure to phototherapy (clinical setting). This value was the one chosen for the purposes of the most plausible scenario.

Table 15: Cost of purchasing and using a transcutaneous bilirubinometer[a]

Variable	Cost
Purchase cost of a bilirubinometer	$5,000
Use: service contract, years 2 to 10 = $500/year Accessories (e.g. batteries) = $735/year	Year 1[b]: $735 Years 2 to 10: $1,235/year ($735 + $500)
Working Hypotheses ❖ Transcutaneous bilirubinometers apparently have a very long lifespan[c]. The annual operating costs are therefore considered for years 1 to 10. ❖ The price of each instrument varies between $5,000 and $7,000, depending on the number purchased. Here, it is assumed that the purchase price could be negotiated at $5,000/instrument. ❖ The annual operating costs are based on 770 tests being performed per year. ❖ According to the ECRI, the accessories cost 14.7% of an instrument's purchase price. ❖ The ECRI estimates that the cost of a service contract is usually about 10% of an instrument's purchase price.	

[a] From the ECRI (1997) [34].

[b] Since the instrument is under warranty during the first year, there are no maintenance fees.

[c] Information provided verbally by L. Leclerc, medical biochemist, Hôpital du Saint-Sacrement, Québec City (December 1998) and completed in writing (July 1999). According to him, one or two bilirubinometers were purchased in the early 1980s at this hospital and are still working.

Cost of purchasing and using transcutaneous bilirubinometers

There are 147 CLSCs and health centres[28] and 75 institutions of birth[29] in Québec. Assuming that each of these 222 institutions acquired just one bilirubinometer, this would involve an outlay of $1,110,000 the first year. There would then be the cost of maintaining the bilirubinometers, which was calculated using a method similar to that used by the ECRI [34]. The first year, we estimate that, in addition to the purchase cost, there would be a cost of $163,170 in accessories (222 x $735), for a total of $1,273,170. From year 2 to year 10, the costs associated with the bilirubinometers would be the cost of the accessories (222 x $735 = $163,170) and of the maintenance (222 x $500 = $111,000), or $274,170. This figure does not include the costs associated with quality control for the use of these instruments.

[28] Information provided in writing by L. Rocheleau, senior consultant, Association des CLSC et des CHSLD du Québec, July 9, 1999.

[29] Information found on the Internet on September 8, 1999 at http://www.msss.gouv.qc.ca./fr/statisti/indexaccounais.htm.

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Annexe