

Common Issues in the Care of Sick Neonates

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Newborn infants may be transferred to a special care nursery because of conditions such as prematurity (gestation less than 37 weeks), prolonged resuscitation, respiratory distress, cyanosis, and jaundice, and for evaluation of neonatal sepsis. Newborn infants' core temperature should be kept above 36.4°C (97.5°F). Nutritional requirements are usually 100 to 120 kcal per kg per day to achieve an average weight gain of 150 to 200 g (5 to 7 oz) per week. Standard infant formulas containing 20 kcal per mL and maternal breast milk may be inadequate for premature infants, who require special formulas or fortifiers that provide a higher calorie content (up to 24 kcal per mL). Intravenous fluids should be given when infants are not being fed enterally, such as those with tachypnea greater than 60 breaths per minute. Hypoglycemia can be asymptomatic in large-for-gestational-age infants and infants of mothers who have diabetes. A hyperoxia test can be used to differentiate between pulmonary and cardiac causes of hypoxemia. The potential for neonatal sepsis increases with the presence of risk factors such as prolonged rupture of membranes and maternal colonization with group B streptococcus. Jaundice, especially on the first day of life, should be evaluated and treated. If the infant does not progressively improve in the special care nursery, transfer to a tertiary care unit may be necessary. (Am Fam Physician 2002;66:1685-92. Copyright© 2002 American Academy of Family Physicians.)

Some newborn infants require observation and care that is beyond the scope of a normal newborn nursery. In many hospitals, this level of care is designated intermediate, level II, or special care nursery (SCN).¹ Infants in these nurseries may be managed by family physicians and general pediatricians who later continue their care in the ambulatory setting.

Clinical evaluation in neonatal patients remains inexact in discriminating between sick infants and healthy infants, even with the aid of adjuvant laboratory tests. Care varies depending on standards of acceptable risk and availability of local resources. Physicians should continually refine their clinical criteria for treatment by using low thresholds in cases of uncertainty, achieving consistency in risk assessment, and consulting colleagues when necessary. Physicians should also work with nursery nursing staff, using established protocols (e.g., initiating feeding accord-

ing to birth weight, performing blood glucose monitoring in infants at risk of hypoglycemia).

Transferring Infants to the SCN

Newborn infants may be transferred to the SCN immediately after birth because of prenatal diagnoses, delivery complications, or early postnatal signs of instability (Table 1). Infants who initially undergo a stable transition to extrauterine life may later develop signs suggestive of sepsis or jaundice, or other abnormal findings that require closer observation and treatment.² Infants may be observed in the SCN for self-limited conditions such as transient tachypnea. Patients with risk factors such as significant prematurity (gestation less than 34 weeks) or known fetal abnormalities requiring early intervention should be delivered at a tertiary care center.

Temperature Regulation

Newborn infants are vulnerable to heat loss and should be kept in an environment that protects them from the stress of cold. A core body temperature below 36.4°C (97.5°F) in neonates has been correlated with poor brain and somatic growth, and increased mortality.³ Hyperthermia above 37.0°C (98.6°F) should be avoided. Unstable infants may be observed under the radiant warmer for several hours, with attention to increased fluid losses. The

A newborn infant who requires observation and care beyond the scope of a normal newborn nursery may be placed in what is known as an intermediate, level II, or special care nursery.

TABLE 1
Reasons to Consider Transfer of Neonate to SCN

Immediately after birth

- Prenatal diagnosis warranting special care
- Significant prematurity (less than 34 to 35 weeks' gestation)
- Intrauterine growth restriction
- Twin-to-twin transfusion syndrome
- Clinically significant congenital anomalies
- Rh sensitization
- Maternal conditions (e.g., drug use, diabetes)
- Maternal medications resulting in neonatal depression (e.g., opiates for pain control, magnesium sulfate)
- Risk factors for sepsis (e.g., clinical chorioamnionitis)

Delivery complications

- Asphyxia, low 5-minute Apgar score, prolonged resuscitation
- Placental abruption, placenta previa, vasa previa

Early postnatal period

Cardiorespiratory

- Poor peripheral perfusion (slow capillary refill, low blood pressure)
- Respiratory distress (grunting, tachypnea more than 60 breaths per minute, intercostal retractions)
- Cyanosis (congenital heart disease)
- Apnea and/or cyanotic episodes

Gastrointestinal

- Feeding intolerance
- No meconium passage by 24 hours of age
- Bilious vomiting

Neurologic

- Seizures
- Signs of drug withdrawal
- Poor tone
- Lethargy

Jaundice

- Any visible jaundice at less than 24 hours of age
- Clinically significant, age-specific hyperbilirubinemia
- Rate of rise of bilirubin more than 0.5 mg per dL (8.55 μ mol per L) per hour

Metabolic and others

- Temperature instability (consistently below 36.4°C [97.5°F])
- Low blood glucose level (less than 45 mg per dL [2.5 mmol per L]) or high blood glucose level (more than 180 mg per dL [10.0 mmol per L])
- Petechiae and purpura
- Clinically significant congenital anomalies

SCN = special care nursery.

TABLE 2
Neonatal Monitoring

<i>Parameter</i>	<i>Expected range</i>
Weight gain	20 to 30 g (0.07 to 1.05 oz) per day, 150 to 200 g (5.3 to 7.0 oz) per week
Axillary temperature	36.4°C (97.5°F) to 37.0°C (98.6°F)
Calorie intake	100 to 120 kcal per kg per day
Fluid intake	150 to 200 mL per kg per day
Urine output	At least 6 wet diapers per day
Urine specific gravity	1.005 to 1.015
Hematocrit	45 to 65 percent
Sodium	135 to 145 mEq per L (135 to 145 mmol per L)
Potassium	4.0 to 7.5 mEq per L (4.0 to 7.5 mmol per L)
Calcium	Term infants: 9 to 10.8 mg per dL (2.25 to 2.70 mmol per L) Preterm infants: 6.5 to 9 mg per dL (1.62 to 2.25 mmol per L)
Creatinine	0.3 to 1.0 mg per dL (26 to 88 mmol per L)
Pao ₂	60 to 80 mm Hg
Oxygen saturation	94 to 99 percent

PaO₂ = partial pressure of arterial oxygen.

Information from references 2 and 3.

newborn may be transferred from an incubator isolette to an open crib when consistent weight gain and stable body temperature have been achieved (*Table 2*).^{2,3}

Nutrition

Caloric intake, fluid intake, and vitamin and mineral supplementation should be sufficient for optimal growth without endangering the fragile gut of the newborn. Feeding should start as soon as possible for most newborns, including premature infants, with a preference for breast-milk feeding. Reasons to withhold enteral feeding are listed in *Table 3*. Newborns should be closely and frequently monitored to be sure they achieve optimal growth, to correct delays in growth, and to avoid the risk of excessive intake⁴ (*Table 2*).^{2,3}

Infants who exhibit a difficulty in feeding or who are less than 32 weeks of gestational age may have an immature suck-and-swallow reflex; these infants can be fed using an orogastric or nasogastric tube. The volume and frequency of feedings should be increased gradually to avoid gastrointestinal complications.^{5,6}

Weight and head circumference should be measured daily and weekly, respectively, and the results should be plotted on appropriate growth curves. Breastfed infants

TABLE 3
Reasons to Withhold Enteral Feeding in Neonates

Prolonged asphyxia (hypoxia, metabolic acidosis, hypercapnia), hypotension, and low Apgar score (5 or below) at 5 minutes
Respiratory difficulties (respiratory rate of more than 60 breaths per minute, nasal flaring, grunting, or retractions)*
Significant neurologic depression
Abdominal distension
No stool by 24 hours of age
Signs of severe sepsis

*—Infants may be fed when breathing at 60 to 80 breaths per minute if they are without nasal flaring, grunting, or retractions ("permissive or peaceful tachypnea"), especially in the first four to six hours of life.

should be monitored for frequency of feedings (usually every two to three hours), quality of feedings (judged by the mother), and urine output (minimum of six wet diapers per day).

Standard infant formulas (usually providing 20 kcal per 30 mL) and maternal breast milk may be inadequate for premature neonates, who need a higher concentration of nutrients.⁷ Premature infant formulas provide a higher calorie content (up to 24 kcal per 30 mL), and powdered or liquid fortifiers can be mixed with expressed breast milk to yield concentrations up to 23 to 24 kcal per 30 mL with an improved calcium/phosphate ratio. Dietary supplements and corn syrup solids containing glucose polymers may be added to boost specific nutrient intake, such as medium-chain triglycerides. Care should be taken with concentrated formulas to avoid high osmolar loads by limiting them to no more than 30 kcal per 30 mL.⁷

Neonates generally should not be fed enterally (by

mouth or feeding tube) under certain conditions (*Table 3*). Feedings should be delayed a minimum of 72 hours if the neonate has been depressed (5-minute Apgar score of 5 or less) and has experienced significant asphyxia (hypoxia, metabolic acidosis, hypercapnia) or hypotension, to allow potentially compromised gastrointestinal mucosa to recover. In 95 percent of newborns, meconium is passed by 24 hours of age. If this does not occur, the physician should search for possible causes, including meconium plug syndrome, Hirschsprung's disease, and anatomic anomalies such as gastrointestinal tract stenosis or atresia. Initial work-up includes a thorough physical examination and an abdominal radiograph.⁸

Fluid Balance

Infants who are not receiving adequate enteral feedings should be given intravenous fluids to provide adequate water, electrolytes, and calories. Administration of fluids should be guided by timely assessment of the neonate, initiation of treatment, and close monitoring.⁹

Newborn infants differ from other age groups in their increased basal metabolic rate and water requirement, and limited sodium excretion. A 5 to 10 percent weight loss may occur in the term infant during the first seven days of life. Insensible water losses range from 30 to 60 mL per kg per day in healthy term neonates, and these losses are increased by prematurity, low birth weight, tachypnea, fever, and use of the radiant warmer. These factors are additive and may increase fluid requirements up to three times the basal needs (*Table 4*).¹⁰

TABLE 4
Initial Rates for Neonatal IV Fluid Administration by Weight and Day of Age

Birth weight (g)	Range of water loss* (mL per kg per day)	Day of Age			
		Day 1	Days 2 to 3	Days 4 to 7	Days 8 to 30
<1,250	95 to 280	120	140	150 to 175	120 to 180
1,250 to 1,750	75 to 160	90	110	130 to 140	120 to 180
1,750 to 2,500	70 to 150	80	90	100 to 120	120 to 180
>2,500	—	60	70	100 to 120	120 to 180

IV = intravenous.

*—Total loss from insensible water loss, urine, and stool. Add 20 to 30 mL per kg per day if radiant warmer is used.

Adapted with permission from Merenstein GB, Gardner SL. *Handbook of neonatal intensive care*. 4th ed. St Louis: Mosby, 1998:252.

TABLE 5
Guidelines for the Treatment of Neonatal Hypoglycemia

<i>Plasma glucose (venous sample)</i>	<i>Asymptomatic or mildly symptomatic</i>	<i>Symptomatic</i>
35 to 45 mg per dL (1.94 to 2.50 mmol per L)	Breastfeed or give formula or D5W by nipple/gavage	IV glucose (D5W to D12.5W) at 4 to 6 mg per kg per minute
25 to 34 mg per dL (1.39 to 1.89 mmol per L)	IV glucose (D5W to D12.5W) at 6 to 8 mg per kg per minute	IV glucose (D5W to D12.5W) at 6 to 8 mg per kg per minute
<25 mg per dL	Minibolus of 2 mL per kg (D10W) and continue at a rate that provides 6 to 8 mg per kg per minute	Minibolus of 2 mL per kg (D10W) and continue at a rate that provides 6 to 8 mg per kg per minute

D5W = dextrose (5%) in water; IV = intravenous; D12.5W = dextrose (12.5%) in water; D10W = dextrose (10%) in water.

NOTE: Changes in infusion rate should not exceed 2 mg per kg per minute per change. If blood glucose level is less than 25 mg per dL (1.39 mmol per L) and IV access is not available, give glucagon at a dosage of 0.1 mg per kg per dose (maximum, 1 mg) intramuscularly or subcutaneously every 30 minutes. Not effective in small-for-gestational-age babies.

Adapted with permission from Alexander DC, Robin B. Neonatology. In: Siberry GK, Iannone R, eds. The Harriet Lane Handbook: a manual for pediatric house officers. 15th ed. St Louis: Mosby, 2000:426, and Cornblath M, Ichord R. Hypoglycemia in the neonate. Semin Perinatol 2000;24:136-49.

Because infants do not generally need electrolyte replacement on the first day of life, initial intravenous fluid therapy uses 10 percent dextrose in water (10 to 12.5 percent glucose may be given peripherally) at a rate of 4 to 6 mg per kg per minute.¹⁰ Infants who are small-for-gestational-age, those who are intrauterine growth-restricted, and those whose mothers have diabetes may require glucose administered at a rate of up to 10 to 15 mg per kg per minute to maintain glucose homeostasis.¹⁰

Electrolytes are usually introduced on the second day of life, with sodium administered in a dosage of 1 to 4 mEq per kg per day (usually a one-fourth normal saline solution), and potassium administered in a dosage of 1 to 4 mEq per kg per day (only after establishing urine flow). Serum calcium levels should be measured (*Table 2*),^{2,3} especially in very-low-birth-weight and very sick infants, and calcium should be provided as calcium gluconate at 2 to 3 mEq per kg per day.¹⁰

Parenteral nutrition, including amino acids and lipids, should be considered for infants whose oral intake is less than 50 kcal per kg per day for more than 48 hours.

Hypoglycemia

Hypoglycemia, defined as a whole-blood glucose level of less than 45 mg per dL (2.50 mmol per L), can occur in infants who are small- or large-for-gestational-age, or premature, and in those who have low glycogen stores, hyperinsulinemia, stress, or mothers with gestational diabetes.^{11,12} At-risk infants should be screened with glucose monitoring protocols because many infants remain asymptomatic. When present, signs include abnormal cry,

poor feeding, hypothermia, diaphoresis, tremor, jitteriness, hypotonia, irritability, lethargy, seizures, apnea, and even cardiac arrest. An effective approach is an initial bolus of 10 percent glucose administered at a rate of 2 to 4 mL per kg, followed by an intravenous infusion of 6 to 8 mg per kg per minute, with frequent monitoring of serum levels. Clinical judgment should guide management after initial administration of glucose (*Table 5*),^{13,14} because infants who can feed orally should be given formula to keep a sustained rise in blood glucose. Administration of dextrose water should be avoided because it may lead to rapid rises and subsequent falls in blood glucose levels. Blood glucose levels should be followed closely, especially during weaning to breastfeeding, since oral intake is difficult to assess in these infants.

Cardiorespiratory Problems

Newborn infants with cardiorespiratory problems can present with cyanosis and tachypnea.¹⁵ The delivery of oxygen to tissues depends on several factors, including partial pressure of arterial oxygen (PaO₂), tissue perfusion, and hematocrit¹⁶ (*Table 2*).^{2,3} Therefore, an assessment of oxygenation includes the PaO₂ as well as clinical impression of tissue perfusion, assessed as capillary refill time and mean arterial pressure, which varies with, and roughly coincides with, gestational age in weeks (e.g., a 33-week-gestation newborn should have a mean arterial pressure of at least 33 mm Hg). Rapid deterioration can occur with low blood pressure, which can result from a wide range of causes, including pneumothorax, hypoplastic left heart, coarctation of the aorta, hypoglycemia, and infection.

TABLE 6
Indications for Additional Testing of Sick Neonates

<i>Clinical signs</i>	<i>Commonly used diagnostic aids</i>
No stool for 24 hours	Abdominal radiograph
Cyanosis, tachypnea	Arterial blood gases, chest radiography
Cyanosis (cardiac cause suspected)	Four-limb blood pressure and pulse oximetry, hyperoxia test, electrocardiography
Risk factors for sepsis	Complete blood count with neutrophil differential, blood culture
Jaundice (nonphysiologic)	ABO and D(Rh) blood-type matching (infant and mother), direct Coomb's test, peripheral blood smear

Distinguishing between pulmonary-systemic causes and cardiac causes of hypoxemia is based on prenatal history, newborn examination, and postnatal course (including age at onset of symptoms and laboratory values such as arterial blood gases). A hyperoxia test may be used to differentiate between pulmonary and cardiac causes of hypoxia—the latter will often not improve with high-inspired oxygen tension. Exposing the infant to more than 95 percent inspired oxygen in an oxygen hood for 30 minutes is an acceptable hyperoxia test.¹⁷

In the presence of a cyanotic cardiac lesion, PaO₂ will not rise above 100 mm Hg and is commonly 30 to 60 mm Hg. In most cases of symptomatic, cyanotic congenital heart disease, empiric therapy with intravenous prostaglandin E₁ should be initiated at a dosage of 0.05 to 0.1 mcg per kg per minute.¹⁷ Intubation should be available because prostaglandin infusion may cause apnea.

Four-limb blood pressure measurements and pulse oximetry provide additional information in the work-up of cardiopulmonary signs (Table 6). A margin greater than 10 percentage points in oxygen saturation between

upper and lower extremities suggests shunting across the patent ductus arteriosus, which commonly occurs in pulmonary hypertension. Pulmonary hypertension may be caused by respiratory distress syndrome, meconium aspiration, or pneumonia.

Sepsis

Neonatal sepsis is an infrequent but serious (25 percent mortality) illness that may present with nonspecific signs and can progress rapidly. Early treatment is warranted in infants with risk factors, and a high index of suspicion is helpful, with the understanding that many uninfected infants will be exposed to unnecessary antibiotic therapy. Antenatal risk factors that have been shown to correlate with an increased incidence of neonatal sepsis include prolonged rupture of membranes and chorioamnionitis, maternal colonization with group B streptococcus,¹⁸ prematurity, birth asphyxia, male gender, and maternal urinary tract infection.¹⁹ Asymptomatic neonates with two of these risk factors may be observed closely after a complete blood count is obtained.¹⁹ Neonates with three or more of these risk factors should be given empiric antibiotic therapy, such as ampicillin and gentamicin (Garamycin), for 48 to 72 hours until culture results are obtained¹⁹ (Table 7).²⁰

TABLE 7
Drugs Used in Treatment of Neonatal Sepsis

<i>Drug</i>	<i>Age/birth weight</i>	<i>Dosage*</i>
Ampicillin, IM, IV	< 1 week of age: <2,000 g	50 mg per kg per dose, every 12 hours
	< 1 week of age: >2,000 g	50 mg per kg per dose, every eight hours
	> 1 week of age: <2,000 g	50 mg per kg per dose, every eight hours
	> 1 week of age: >2,000 g	50 mg per kg per dose, every six hours
Gentamicin (Garamycin), † IV, IM	≥ 34 weeks	4 mg per kg per dose, every 24 hours
	28 to 34 weeks	3 mg per kg per dose, every 24 hours
	< 28 weeks	2.5 mg per kg per dose, every 24 hours
Ceftriaxone (Rocephin), ‡ IV, IM	§	50 mg per kg per dose, every 24 hours

IM = intramuscular; IV = intravenous.

*—These dosages are not standard; dosages may vary by institution.

†—Follow peak (5 to 10) and trough (<2) levels.

‡—If no hyperbilirubinemia.

§—Dosage is the same regardless of birth weight.

Information from Young TE, Mangum B. *Neofax: a manual of drugs used in neonatal care*. 13th ed. Raleigh, N.C.: Acorn, 2000.

TABLE 8
Treatment Thresholds for Jaundice in Neonates

Age (hours)	TSB level, mg per dL ($\mu\text{mol per L}$)			
	Consider phototherapy*	Phototherapy	Exchange transfusion if intensive phototherapy fails†	Exchange transfusion and intensive phototherapy
≤ 24 ‡	—	—	—	—
25 to 48	≥ 12 (210)	≥ 15 (260)	≥ 20 (340)	≥ 25 (430)
49 to 72	≥ 15 (260)	≥ 18 (310)	≥ 25 (430)	≥ 30 (510)
> 72	≥ 17 (290)	≥ 20 (340)	≥ 25 (430)	≥ 30 (510)

TSB = total serum bilirubin.

*—Phototherapy at these TSB levels is a clinical option, meaning that the intervention is available and may be used on the basis of individual clinical judgment.

†—Intensive phototherapy should produce a decline in TSB of 1 to 2 mg per dL (17 to 34 $\mu\text{mol per L}$) within four to six hours, and the TSB level should continue to fall and remain below the threshold level for exchange transfusion. If this does not occur, it is considered a failure of phototherapy.

‡—Term infants who are clinically jaundiced at ≤ 24 hours of age are not considered healthy and require further evaluation. Start treatment irrespective of level and initiate work-up for cause.

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Clinical signs of early sepsis include obvious findings such as respiratory distress, shock, fever, apneic or cyanotic episodes, and seizures, and more subtle findings such as poor feeding, lethargy, high or low blood pressure, temperature instability, poor peripheral perfusion, and petechiae. Symptomatic neonates, even those without perinatal risk factors or a positive blood culture, should be treated with a full course (usually 14 to 21 days) of antibiotics (Table 7).²⁰

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Lumbar puncture for cerebrospinal fluid culture should be performed in most cases where sepsis is the primary diagnosis, when the blood culture is positive, and when there are neurologic signs. Urine cultures are not always reliable in neonates. Neutrophil counts have limited sensitivity for sepsis with neutropenia (below 5,000 per mm^3 [5×10^9 per L]) but are more specific than high neutrophil counts.²¹ Normal ranges for neutrophil counts depend on the age (in hours) of the neonate. The ratio between immature and total neutrophil counts (I:T ratio) is a predictor of sepsis when greater than 0.2 to 0.3.²² The I:T ratio is also useful in the presence of a normal-range white blood cell count that has a wide normal range (5,000 to 30,000 cells per mm^3 [5 to 30×10^9 per L]).

Jaundice

The primary reason for treating jaundice in neonates is to prevent neurologic damage. Susceptibility to bilirubin toxicity is important in setting treatment thresholds (Table 8).²³ Risk factors that lower the threshold for treatment include prematurity, low birth weight, sepsis, and jaundice appearing within 24 hours of life.^{24,25}

TABLE 9
Reasons for Transfer from SCN to NICU

Gestational age and examination consistent with age less than 32 to 34 weeks
 Birth weight less than 1,500 to 1,800 g (3 lb, 5 oz to 4 lb)
 Progressive respiratory distress likely to require assisted ventilation
 Severe hemolytic disease of the newborn
 Meningitis
 Circulatory failure
 Perinatal asphyxia with severe symptoms
 Congenital malformations requiring immediate evaluation and/or surgery
 Cardiac disorders requiring immediate evaluation or intensive medical observation
 Seizures
 Infants requiring intensive observation or care for any other reason (e.g., inadequacy of enteral feedings requiring intravenous fluids to maintain hydration and/or normal glucose levels)

SCN = special care nursery; NICU = neonatal intensive care unit.

Discharge from SCN

Neonates whose condition is progressively worsening may have to be transferred to a regional neonatal intensive care unit if they require ventilator support and consultants who are not available in the SCN²⁶ (Table 9). These problems can sometimes be anticipated on the basis of prenatal ultra-

Parenteral nutrition, including amino acids and lipids, should be considered for infants whose oral intake is less than 50 kcal per kg per day for more than 48 hours.

sound scans and premature labor (at less than 34 weeks). A nursery's level of care depends on the availability of resources such as neonatal nursing skills, respiratory therapy, and laboratory support. Consequently, the threshold for transfers varies regionally. Transfers should be preceded by detailed communication between responsible physicians at both hospitals, during which time a decision not to transfer can be made for pre-viable or nonviable infants.

Discharge from an SCN to the home can be a major stressor for the family and should be handled carefully, with multidisciplinary involvement.²⁷ Safe discharge requires that the infant be able to grow adequately at home with available support and follow-up (Table 10).

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TABLE 10
Home Discharge Criteria

Premature neonates

Corrected gestational age more than 34 and one-half weeks
 Able to maintain body temperature (>36.4°C [97.5°F]) in an open crib
 Consistently feeding well by mouth
 Steady growth of 20 to 30 g (0.7 to 1 oz) per day on home feeding regimen
 Weight greater than 1,800 g (4 lb) for a small-for-gestational-age infant and greater than 2,000 g (4 lb, 6 oz) for an appropriate-for-gestational-age infant (may be disregarded if other criteria are met)
 No major changes in care before discharge (such as change in feeding route or medications)
 No major medical or nursing care needs that cannot be managed at home

Information from reference 4.

Term neonates

Resolution of symptoms (e.g., respiratory distress)
 Resolution of jaundice
 Adequate treatment of sepsis (or sepsis ruled out)
 Adequate monitoring (e.g., 48 hours if group B streptococcus infection is involved)

Family readiness, support at home

Adequate follow-up assured
 Social work involvement, as necessary

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