

# Outpatient Care of the Premature Infant

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An increasing number of infants in the United States are born prematurely, with current statistics estimating about 13 percent of all births. Although survival rates and outcomes for premature infants have dramatically improved in recent decades, morbidity and mortality are still significant. Infants born prematurely are at increased risk of growth problems, developmental delays, and complex medical problems. To account for prematurity, growth and development monitoring should be done according to adjusted age (age in months from term due date). Premature infants should gain 20 to 30 g (0.71 to 1.06 oz) per day after discharge from the hospital. Growth parameters may be improved in the short term with the use of enriched preterm formula or breast milk fortifier. Each well-child examination should include developmental surveillance so that early intervention can be initiated if a developmental delay is diagnosed. Routine vaccination should proceed according to chronologic age with minor exceptions, and respiratory syncytial virus immune globulin is indicated in preterm infants who meet the criteria. (*Am Fam Physician* 2007;76:1159-64, 1165-6. Copyright © 2007 American Academy of Family Physicians.)

► **Patient information:** A handout on medical care of the premature infant, written by the authors, is provided on p. 1165.

Infants born before 37 weeks' gestation are considered to be premature.<sup>1</sup> Two percent of all premature infants are believed to be very premature (born before 32 weeks' gestation).<sup>2</sup> Prematurity is the second leading cause of infant mortality after congenital anomalies. The complex biologic interplay responsible for premature birth is not well understood, and interventions have not been successful. However, the use of antenatal steroids and surfactant therapy, and improved use of neonatal intensive care technology have radically improved outcomes. Despite extensive public health and private prevention initiatives, premature birth rates continue to increase.

## Family Support

The transition from the neonatal intensive care unit (NICU) to home can be stressful. The American Academy of Pediatrics (AAP) recommends that planning for discharge from the NICU should include the following six critical components: (1) parental education; (2) implementation of primary care; (3) evaluation of unresolved medical problems; (4) development of the home care plan; (5) identification and mobilization of surveillance and support services; and (6) determination and designation of follow-up care.<sup>3</sup>

Early and active family involvement is paramount to success of the premature infant. At least two family members should demonstrate ability to appropriately feed

and provide necessary care for an infant before discharge. Because of risk of respiratory compromise while restrained, the AAP recommends that infants at risk of respiratory problems be formally tested in a car seat before transport home. Travel for infants at risk of respiratory compromise should be minimized, and infants who cannot tolerate a semi-upright position should use a prone or supine safety device.<sup>4</sup> Physicians should provide families with an accurate and comprehensive summary of the neonatal course with specific written instructions for all necessary follow-up.

## Medical Complications

Infants who have been in the NICU often have complex medical problems and may require prolonged comprehensive or subspecialty follow-up care. Review of the neonatal course will help identify risks. Bronchopulmonary dysplasia or chronic lung disease, apnea and bradycardia, cryptorchidism, gastroesophageal reflux, sudden infant death syndrome (SIDS), ventriculomegaly, and hernias are more common among premature infants than full-term infants.

### BRONCHOPULMONARY DYSPLASIA

The risk of bronchopulmonary dysplasia increases with decreasing birth weight and lower gestational age. Fifty to 80 percent of infants born weighing less than 900 g (31.75 oz) develop bronchopulmonary dysplasia.<sup>5</sup>

## SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Vaccination for premature infants should proceed according to chronologic age with the exception of hepatitis B in infants weighing less than 2,000 g (70.55 oz)	C	10
Respiratory syncytial virus immune globulin should be given to premature infants.	C	11
Fortification of human breast milk will increase short-term growth in premature infants after discharge from the NICU.	C	19, 20
Enriched preterm formula after discharge from the NICU may increase length in premature infants.	C	16
Developmental surveillance should be performed at each well-child visit, and early intervention should be initiated when delay is detected.	C	24

NICU = neonatal intensive care unit.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 1095 or <http://www.aafp.org/afpsort.xml>.

These infants are more susceptible to pulmonary infections and suffer from episodes of respiratory distress and wheezing, which can be indistinguishable from a respiratory infection. Treatment may include bronchodilators, diuretics, oxygen, and antibiotics when appropriate.<sup>5</sup> Premature infants may also require a higher caloric intake to account for increased work of breathing. Children with bronchopulmonary dysplasia continue to show poor lung function until adolescence, which is when lung function typically becomes normal.<sup>5</sup>

### APNEA OF PREMATURITY

Apnea of prematurity is defined as a respiratory pause for at least 20 seconds, or a pause associated with bradycardia, change in tone, abnormal movements, or oxygen desaturation, in an infant born before 37 weeks' gestation. This condition typically resolves after maturation, usually at 42 to 44 weeks after conception. An infant with apnea of prematurity may be given methylxanthines and an apnea monitor upon discharge from the NICU. If infants are event free, discontinuation of pharmacologic therapy should be considered at 40 weeks' adjusted age.<sup>5</sup> Home monitoring is continued until the infant is 43 weeks' adjusted age and free of extreme episodes.<sup>6</sup> A neonatologist or pulmonologist should be readily available to assist in the decision to stop treatment.<sup>5</sup>

### GASTROESOPHAGEAL REFLUX

Premature infants develop gastroesophageal reflux more often than full-term infants because of lower esophageal sphincter hypotonia, delayed emptying, and decreased gastric compliance. Symptoms include postprandial vomiting and, when severe, irritability, respiratory problems, apnea, bradycardia, and feeding difficulties. One management option is to change the feeding regimen, usually by thickening the milk with infant cereal or concentrating the milk for volume reduction. Postprandial prone positioning, while awake and under

observation, may improve symptoms. If conservative measures fail, histamine H<sub>2</sub> blockers, proton pump inhibitors, or prokinetic agents can be tried. Surgery should be considered in some infants with severe symptoms despite treatment.

### INTRAVENTRICULAR HEMORRHAGE AND PERIVENTRICULAR LEUKOMALACIA

Screening cranial ultrasonography is recommended for all infants with a gestational age of less than 30 weeks; screening should take place at seven to 10 days of age and at 36 to 40 weeks' postmenstrual age.<sup>7</sup>

### Vaccination

Vaccination for premature infants remains a critical component of preventive care and should be delivered according to chronologic (not adjusted) age. Routine immunization for diphtheria, tetanus, pertussis, *Haemophilus influenzae* type b, poliomyelitis, and pneumococcal disease remains unchanged.<sup>8-10</sup> There are theoretical risks of increased adverse reactions in very low birth weight premature infants because of lower maternal antibody to rotavirus. The Advisory Committee on Immunization Practices supports rotavirus vaccination of premature infants if they are at least six weeks of age, discharged from the NICU, and clinically stable.<sup>8</sup>

### HEPATITIS B

For infants born weighing less than 2,000 g (70.55 oz), immunization against hepatitis B is dependent on maternal hepatitis B status.<sup>10</sup> *Table 1* outlines the hepatitis B vaccine schedule for all infants.<sup>10</sup>

### RSV

Respiratory syncytial virus (RSV) is the most common cause of bronchiolitis and pneumonia in infants.<sup>11</sup> Prematurity and underlying lung disease, especially bronchopulmonary dysplasia, are factors that increase the

**Table 1. Hepatitis B Vaccination Schedule for Infants**

Maternal HBsAg status	Infant weighing $\geq 2,000$ g (70.55 oz)	Infant weighing $< 2,000$ g
Positive	HB vaccine ( $\leq 12$ hours of birth); HBIG ( $\leq 12$ hours of birth) Three vaccine doses at zero, one, and six months of age Check HBsAb and HBsAg at nine to 15 months of age	HB vaccine ( $\leq 12$ hours of birth); HBIG ( $\leq 12$ hours of birth) Four vaccine doses at zero, one, two, and six months of age Check HBsAb and HBsAg at nine to 15 months of age
Unknown	HB vaccine ( $\leq 12$ hours of birth) Test mother HBIG ( $\leq 7$ days) if mother tests positive Vaccine series based on mother's status	HB vaccine ( $\leq 12$ hours of birth) HBIG ( $\leq 12$ hours of birth) Test mother Vaccine series based on mother's status
Negative	HB vaccine ( $\leq 12$ hours of birth) Three vaccine doses (usual intervals) Combination vaccine allowed at six to eight weeks of age	Delay HB vaccine until one month of age Three vaccine doses (usual intervals) Combination vaccine allowed at six to eight weeks of age

HBsAg = hepatitis B surface antigen; HB = hepatitis B; HBIG = hepatitis B immune globulin; HBsAb = hepatitis B surface antibody

Information from reference 10.

risk of severe RSV infection. Palivizumab (Synagis) is a humanized mouse monoclonal antibody that has been licensed to prevent RSV infection. Palivizumab is an intramuscular injection administered once per month for five months beginning in early November and ending at the beginning of March. The five doses should provide adequate coverage for the RSV season. Passive immunization results in a 45 to 55 percent decrease in hospitalization attributable to RSV.<sup>11</sup> Educating caregivers remains a critical aspect of RSV prevention. Decreasing exposure to contagious settings, proper hand hygiene, and avoidance of tobacco exposure should be emphasized. A documented RSV infection should not alter the vaccine schedule because various strains may circulate. *Table 2* provides indications for RSV vaccination.<sup>11</sup>

#### INFLUENZA

Influenza vaccine is strongly encouraged for infants at least six months of age. It is imperative that all family members and close contacts of infants younger than six months be advised to get the influenza vaccine.<sup>12</sup>

#### Nutrition and Growth

Premature birth is a major disruption at a time when the fetus should be growing rapidly, with all body systems maturing and the brain developing at its fastest rate.<sup>13</sup> Premature infants are often subjected to additional metabolic stressors and have higher energy and nutrient requirements than full-term infants. The purpose of providing continued nutritional care after discharge from the NICU is to support optimal growth, development, and nutritional status.<sup>14</sup> There is considerable evidence that nutrient reserves in premature infants are suboptimal after discharge.<sup>15</sup> Poor postnatal growth, especially of the head, is associated with an increased risk of neurodevelopmental impairment and poorer cognitive outcomes.<sup>16</sup>

Anthropometric measurements, including height, weight, and head circumference, are integral to the nutritional care of newborns. Because of a divergence in growth patterns for premature infants compared with term infants, some experts prefer to use preterm growth charts made specifically for infants born weighing less than 1,500 g (52.91 oz) or for infants who are lower than the third percentile on standard growth curves. Premature growth charts based on the Infant Health and Development Program are available for two ranges of birth weights: 1,500 g or less and 1,501 to 2,500 g (52.95 to 88.18 oz).

Growth patterns among premature infants also differ depending on gestational age, sex, weight, genetics, and

**Table 2. Respiratory Syncytial Virus (RSV) Vaccine Indications**

Infants born before 28 weeks' gestation; vaccine should be given during their first RSV season
Infants born at 29 to 32 weeks' gestation who are younger than six months at beginning of RSV season
Children younger than two years with chronic lung disease requiring medical therapy within six months of the beginning of RSV season
Children younger than two years with hemodynamically significant cyanotic and acyanotic congenital heart disease
Consider infants born at 32 to 35 weeks' gestation with at least two of following risk factors:
Child care attendance
School-age siblings
Exposure to environmental air pollutants
Congenital abnormalities of the airways
Severe neuromuscular disease
Consider infants with severe immunodeficiency

Information from reference 11.

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coexisting morbidities. Definitions of “catch-up” growth vary, but it is generally considered to be achieved when the infant reaches between the fifth and 10th percentile on a standard growth chart.<sup>17</sup> Premature infants with a history of intrauterine growth restriction and those who are small for gestational age tend to demonstrate less catch-up growth and higher rates of poor growth than infants born at appropriate weight for gestational age.<sup>15</sup> Otherwise healthy premature infants typically demonstrate catch-up growth first in head circumference and then in weight and length. After two years of age, a standard growth chart may be used.

Human breast milk remains the recommended source of nutrition for all infants, including those born prematurely. Benefits of breastfeeding include lower risk of infection, ease of digestibility, enhancement of cognitive development, and promotion of mother-child attachment.<sup>18</sup> Despite evidence supporting numerous advantages of breast milk, the nutrient needs of some premature infants still may not be met, especially those weighing less than 1,500 g. Breast milk fortification can be accomplished by adding commercially available liquid or powdered fortifiers that contain additional calories, macronutrients, vitamins, calcium, and phosphorus.

Nutrient deficiencies can potentially result in clinical manifestations of osteopenia, kwashiorkor, hyponatremia, and zinc deficiency.<sup>14</sup> Fortification of human milk minimizes these risks. Multicomponent fortifiers and protein supplementation of human milk lead to short-term increases in head and linear growth and weight gain.<sup>19,20</sup> Data thus far are insufficient to evaluate long-term growth and neurodevelopmental outcomes. Some generally accepted guidelines for breastfeeding after NICU discharge are outlined in *Table 3*.<sup>14,15,18,21</sup>

Formula will be a major source of nutrition for many premature infants after discharge from the NICU. Preterm formulas have higher caloric density, as well as higher levels of protein, minerals, vitamins, and trace elements. The 24 kcal per ounce formula is generally reserved for NICU use and for selected premature infants until term weight is achieved. Following discharge from the NICU, formulas specifically designed for premature infants should be used. These preterm formulas provide 22 kcal per ounce and are enriched with additional protein, minerals, vitamins, and trace elements. Standard formulas contain only 20 kcal per ounce.

Early studies have demonstrated improved short-term growth parameters in premature infants who are fed enriched formula<sup>22</sup>; however, subsequent studies have shown conflicting results in growth and bone mineral mass. A Cochrane meta-analysis found a statistically sig-

**Table 3. Guidelines for Breastfeeding Premature Infants**

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Feed on demand every one hour and one half to three hours  
Supplement some feedings with milk fortifier or enriched formula until catch-up growth is achieved and daily weight gain is adequate (20 to 30 g [0.71 to 1.06 oz] per day)  
Supplement feedings with 0.5 to 1.0 mL of standard multivitamins per day until the infant reaches a weight of 11 lb (5 kg)  
Supplement feedings with 2 to 4 mg per kg of iron per day (maximal dose of 15 mg per day)  
If exclusively breastfeeding, supplement feedings with 200 to 400 IU of vitamin D per day starting at two months of age

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*Information from references 14, 15, 18, and 21.*

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**Table 4. Guidelines for Formula Feeding Premature Infants**

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Use 24 kcal per ounce preterm formula until infant weighs 1,800 to 3,500 g (63.49 to 123.46 oz); usually inpatient only  
Use 22 kcal per ounce preterm enriched formula until catch-up growth obtained or one year adjusted age  
Continue 20 kcal per ounce standard formula once catch-up growth achieved until one year adjusted age  
Formula can be concentrated if needed to increase caloric intake  
Formulas providing 2 mg per kg of iron per day may need to be supplemented with an additional 2 mg per kg per day (maximal dose of 15 mg per day) depending on degree of prematurity  
Vitamin supplements not necessary if formula meeting needs for growth

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*Information from references 15, 16, and 21.*

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nificant increased length in infants fed enriched formula but failed to show any change in weight, head circumference, bone mineralization, or neurodevelopment.<sup>16</sup> Another recent study failed to show any difference in growth or bone mineralization with enriched formula.<sup>23</sup> Some generally accepted guidelines for formula feeding are outlined in *Table 4*.<sup>15,16,21</sup>

After NICU discharge, most premature infants require 100 to 120 kcal per kg per day to grow. Infants should gain at least 20 to 30 g (0.71 to 1.06 oz) per day, and caloric intake should be monitored and adjusted to achieve this goal. Formula can be concentrated and breast milk can be fortified to help increase caloric intake. Once catch-up growth is achieved, the higher-calorie formula should be discontinued to prevent hypervitaminosis and obesity.

Premature infants require iron supplementation through the first year of life. Standard and preterm formulas provide 2 mg per kg of iron per day. An additional 2 mg per kg per day (maximal dose of 15 mg per day) may be necessary depending on the degree of prematurity. For premature infants who are breastfed in the

first year, 2 to 4 mg per kg per day is needed as supplementation.<sup>21</sup> Solid foods should be introduced based on oral-motor readiness, which is usually achieved at an adjusted age of four to six months. Cow's milk should be delayed until 12 months' adjusted age.

### Development

Prematurity puts infants at risk of a variety of neurodevelopmental disabilities resulting from malformation or insult to the developing brain. Disabilities range from cerebral palsy and mental retardation to sensory impairments and more subtle disorders. More subtle problems of higher cortical functioning that have a higher incidence in preterm infants include impaired visual-motor integration and neuromotor and cognitive functions, as well as problems with behavior and temperament.<sup>15</sup> Infant development is a dynamic process encompassing gross motor skills, fine motor skills, language ability, cognitive performance, and adaptive behavior. Emphasis on early identification of a developmental delay creates the opportunity to provide the benefits of early intervention. For the first two years of life, development must be assessed according to adjusted age.

Developmental surveillance is a continuous process of skilled observation, eliciting and attending to parental concerns, obtaining a relevant history, and sharing opinions and concerns with other professionals.<sup>24</sup> The Denver Prescreening Developmental Questionnaire II or the more detailed Denver Development Screening Test II are among a number of acceptable office screening tools.<sup>25</sup> Use of a standardized screening test is essential for consistency and can identify children who need a more comprehensive developmental evaluation. Because of the inherent imperfections of office screening tests, parent or physician concern about development may warrant a referral for formal testing with a subspecialist or multidisciplinary center. Once a delay is diagnosed or detected, referral for early intervention services is recommended. Federally funded state programs are generally available for children younger than three years.

A detailed neurologic examination is a vital component of routine care in premature infants. Assessment should include evaluation of alertness, posture, muscle tone, reflexes, postural reactions, and functional abilities. Abnormalities may include weakness; asymmetries; hyperreflexia; generalized or focal hypertonia; or, more commonly, hypotonia.<sup>26</sup>

The discontinuation of outreach and tertiary follow-up services at two or three years of age is a reflection of limited resources. Infants born prematurely continue to face significant challenges into childhood. It is clear that

educational, psychological, and behavioral problems are of concern during the school years.<sup>27</sup> Consistent deficits in performance on intelligence measures have been observed in premature infants born weighing less than 2,500 g compared with normal weight, full-term infants.<sup>13</sup> Higher rates of school failure and greater need for educational support have been found in children born prematurely, but patterns vary among studies. There is also an increased relative risk of attention-deficit/hyperactivity disorder in children born prematurely. In addition to conventional academics, parents and educators should advocate for comprehensive assessments for struggling children, including visual-motor and visual-perceptive abilities, complex language performance, and attention skills.<sup>27</sup>

### Screening Guidelines

Routine testing for all infants includes state-sponsored screening for metabolic disorders. At times, results may be abnormal because of prematurity, and the test may need to be repeated after discharge from the NICU. Because premature infants are deficient in iron stores, there is a high risk of anemia. Laboratory screening for anemia is recommended at six months and again at two years. Routine lead screening should be performed at nine to 12 months' adjusted age.<sup>28</sup>

### VISION

Prematurity puts infants at risk of visual disturbances including retinopathy, strabismus, and significant refractive error.<sup>29</sup> Retinopathy of prematurity develops when the normal pattern of progressive blood vessel growth within the retina is disrupted, which leads to vascular proliferation, hemorrhage, and retinal detachment. Retinopathy of prematurity is primarily found in infants born before 28 weeks' gestation, in those weighing less than 1,500 g, or those with an unstable clinical course.<sup>30</sup> The AAP recommends that any infant at risk should have an initial screening by an experienced ophthalmologist at a postmenstrual age of 31 weeks, with subsequent screenings based on the results of the examination.<sup>30</sup> Treatment with laser therapy, when indicated, has been shown to have a 41 percent decrease in retinal detachments and a 19 to 24 percent decrease in blindness.<sup>30</sup> Screening and initial treatment take place in the NICU, and follow-up examinations are based on the findings at the first examination. Physicians should have a lower threshold for referral if there is suspicion of visual abnormality.

### HEARING

Premature infants are at risk of sensorineural hearing loss. Universal newborn hearing screening is offered in most

states, and this screening should be done in all premature infants before discharge from the NICU. Because hearing deficits may present later, another evaluation may be warranted, especially if there are concerns about speech or hearing. Early recognition of hearing impairment, appropriate intervention with hearing aids, and communication therapy are critical for optimal language development.

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