

Care of the Neonatal Intensive Care Unit Graduate after Discharge



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KEYWORDS

- Infant, premature • Infant, newborn • Neonatal intensive care • Medical complexity
- Follow-up • Complex care • Pediatric care

KEY POINTS

- Premature and critically ill term infants are often discharged from the NICU with a variety of ongoing medical problems including: chronic lung disease; growth, nutrition, and feeding problems; and neurologic injury.
- At discharge, NICU graduates may be dependent on technology such as supplemental oxygen, tracheostomy, mechanical ventilation, surgically placed feeding tube and feeding pump, and various types of monitors.
- Primary care physicians must have special knowledge and understanding of the medical complications of NICU graduates to coordinate their post-discharge care and provide them with an effective medical home.

INTRODUCTION: POST-DISCHARGE CARE

Every primary care provider (PCP) who follows neonatal intensive care unit (NICU) graduates in their practice must be knowledgeable about the child's neonatal course and understand the various morbidities they have experienced. Providers should be familiar with the treatments for medical problems still present at discharge, be able to troubleshoot the technology that the infant is dependent on, and be able to coordinate the complicated care that they require. This Review will examine the most common post-discharge medical problems that may be present in former premature and critically ill term infants and inform the PCP about expected outcomes and possible new problems that may be encountered.

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Few outpatient clinics provide comprehensive medical follow-up for the myriad of medical problems still present at discharge in NICU graduates. Follow-up clinics for NICU graduates, in general, provide periodic developmental evaluations for high-risk infants and arrange intervention services when needed. A few will offer primary care and/or more specialized medical care (eg, weaning oxygen, adjusting or weaning off medications). Eligibility for NICU follow-up varies by center with respect to gestational age and/or birth weight and/or primary medical problems. However, many NICUs do not have their own follow-up clinic either for medical or developmental care. Instead, multiple subspecialty follow-up appointments are frequently scheduled at discharge (Table 1). It then becomes the responsibility of the PCP to integrate information from all subspecialists and coordinate care for the infant and family.^{1,2}

Expectations of the PCP and Caregivers

Expectations of PCPs who care for medically complex NICU graduates are quite high. These include up-to-date knowledge and understanding of:

1. Neonatal technologies and therapies
2. Drug doses and indications
3. Laboratory tests that need to be followed
4. Indications for special formulas and recipes for adjusting calories
5. Various types of equipment (supplemental oxygen, nasogastric tube, gastrostomy tube [GT], ventriculoperitoneal [VP] shunt, ostomy, pulse oximeter, apnea monitor, tracheostomy, ventilator) and ability to recognize and troubleshoot problems

Parents are expected to understand the complex medical problems and needs of their NICU graduate, which include:

1. Multiple medications with fractional dosing and variable dosing intervals
2. Complicated feeding strategies and schedules, often throughout the day and night
3. Poor state regulation and sensitivity to sensory stimulation
4. Increased susceptibility to infection
5. Multiple subspecialty appointments
6. Multiple intervention services provided in and out of the home
7. Simultaneously, parents are expected to continue with their prior responsibilities (eg, care for siblings, return to work) despite having little or no respite time. They may also be struggling financially because of lost income

To provide optimal care for a medically complex infant, the PCP needs to have complete information about all medical problems and expectations at the time of discharge. PCPs should confirm that the parents are familiar with this content as well. A list of this content is included in Table 2. If information is missing from the discharge summary, the discharging physician should be contacted.

RESPIRATORY PROBLEMS AFTER NEONATAL INTENSIVE CARE UNIT DISCHARGE

Respiratory problems of NICU graduates may be congenital or acquired. Although the etiologies of problems in premature and term infants differ, treatments are similar. The most common respiratory problems are the sequelae of prolonged mechanical ventilation (bronchopulmonary dysplasia [BPD] or chronic lung disease) and congenital anomalies of the lungs and airways (congenital diaphragmatic hernia [CDH], tracheoesophageal fistula [TEF], pulmonary hypoplasia, tracheo- and/or bronchomalacia). Pulmonary hypertension may develop and persist in infants with

Table 1 Subspecialty clinic follow-up for medical problems in NICU graduates	
Specialty Clinic	Medical Problems Followed
Pulmonary	Bronchopulmonary dysplasia Reactive airway disease Home ventilator management Interstitial disease
Cardiology	Patent ductus arteriosus Other congenital heart disease Pulmonary hypertension
Neurology	Seizures Spasticity Neuromuscular disease
Nephrology	Hypertension Renal failure Kidney anomaly
Endocrine	Hypothyroidism Adrenal insufficiency Hypopituitarism
Gastroenterology	Gastro-esophageal reflux Cholestatic jaundice Short gut syndrome Constipation
Infectious diseases	Cytomegalovirus infection Herpes simplex infection Other TORCH infections Perinatal human immunodeficiency virus exposure Perinatal hepatitis C exposure
Pediatric surgery	Congenital diaphragmatic hernia Surgical necrotizing enterocolitis Bowel atresia Nissen fundoplication Gastrostomy tube Hernias Ostomy
Urology	Hydronephrosis Vesico-ureteral reflux Meningomyelocele Other genital-urologic malformation
Otolaryngology	Tracheostomy Stridor Vocal cord dysfunction
Neurosurgery	Hydrocephalus Ventriculoperitoneal shunt Meningomyelocele
Orthopedic surgery	Hip dysplasia Vertebral anomalies Club foot Meningomyelocele Other skeletal dysplasia
Genetics	Suspected or documented chromosomal syndrome Metabolic disorder

(continued on next page)

Table 1 (continued)	
Specialty Clinic	Medical Problems Followed
Ophthalmology	Retinopathy of prematurity Cortical visual impairment Cataract Glaucoma
Audiology	Failed hearing screen Risk of progressive hearing loss
Physical therapy	Abnormal muscle tone (decreased or increased) Torticollis/plagiocephaly
Occupational therapy	Brachial plexus injury Feeding (oral aversion) Other sensory integration problem
Speech/feeding	Feeding problem (dysphagia, swallowing problem) Vocal cord dysfunction Cleft lip and/or palate
Dietician (often in specialty clinic)	Special formulas and/or diets Advancement of gastrostomy tube feeds Failure to thrive

BPD, CDH, pulmonary hypoplasia or meconium aspiration syndrome. The most common reason for readmission in extremely low-birth-weight (ELBW) infants is respiratory problems.

Bronchopulmonary Dysplasia

1. Definition of bronchopulmonary dysplasia (BPD)³

Table 2 Necessary information for PCPs about NICU graduate	
Category	Specifics
Prescribed medications	<ul style="list-style-type: none"> • Explanation of the "indication" for each medication and the problem it is treating • Whether the dose is calculated per kg of weight or is a standard dose • What to do if the infant misses a dose or vomits a dose • Where and when to refill the medication • Whether the medication needs to be adjusted for weight gain and, if so, how often
Feeding	<ul style="list-style-type: none"> • Indications for special formula • Mixing instructions for 2, 3, and 4 ounces of formula • Name of alternate formula (eg, Neocate/Elecare, Neosure/Enfacare, Alimentum/Nutramigen) to prevent substitution error • Local source for special formulas (pharmacy, grocery store) • How long special formula should be continued and what formula to transition to
Subspecialty clinic referrals	<ul style="list-style-type: none"> • Which clinic is for which problem? • What will be done at first visit (if repeat laboratory tests, can PCP order and send results to subspecialists)? • Which clinic to reschedule immediately if missed (eg, ophthalmology clinic for active ROP)

- a. Old versus new BPD
 - i. Old BPD refers to damage caused to lungs and airway by mechanical ventilation and/or oxygen resulting in inflammation and fibrosis. This type of BPD may occur in premature and term infants, and has been greatly reduced by the administration of surfactant and high frequency ventilation.
 - ii. New BPD refers to abnormal or arrest in lung development (fewer and larger alveoli) and decreased microvascular development in ELBW infants.
- b. Premature infants with severe respiratory distress syndrome, pulmonary interstitial emphysema, congenital pneumonia, or pulmonary hypoplasia are most likely to develop BPD.
- c. Criteria for diagnosis in premature infants in the Vermont Oxford Network is the need for supplemental oxygen at 36 weeks post-menstrual age (PMA). Criteria for diagnosis in the NICHD Neonatal Research Network includes supplemental oxygen or any respiratory support at 36 weeks PMA.⁴ Therefore, identification of an infant with BPD may vary from one NICU to another.
- d. Diuretics and inhaled steroids are sometimes used to treat residual lung inflammation or fluid retention.
- e. Full-term infants with meconium aspiration syndrome, CHD, or need for extracorporeal membrane oxygenation (ECMO) for another reason are the most likely to need treatment for BPD after discharge.
- f. All infants with BPD are at increased risk of lower respiratory tract infections and need for rehospitalization during the first year of life.
- g. Reactive airway disease (RAD)
 - i. Infants with BPD have a high risk of developing RAD in infancy, and asthma in later childhood.
 - ii. The most common symptoms are tachypnea either at rest or with exertion.
 - iii. Occult RAD (ie, without wheezing) may be diagnosed based on response to a trial of bronchodilator treatment or results of pulmonary function testing.
- h. Chronic home ventilation after discharge

Infants with severe BPD may require placement of a tracheostomy for prolonged mechanical ventilation at home. Timing of tracheostomy and age of discharge for infants receiving chronic mechanical ventilation varies among NICUs and often depends on the infant's clinical course, health care provider preferences, ability of the family to care for the infant at home, and medical resources (eg, home health nursing) in the community.

Congenital Anomalies of the Lungs and Airways

1. CDH/pulmonary hypoplasia
 - a. CDH occurs when there is a defect in formation of one of the diaphragms, leading to herniation of the abdominal viscera into the pleural cavity on that side. This prevents normal growth and maturation of the lung parenchyma and pulmonary vasculature. This "hypoplasia" of the lungs results in pulmonary hypertension (PHTN) because of thickening of the muscular coat of arterioles, making these vessels more reactive to hypoxemia and acidosis. It is not a reason for premature birth (although it is often diagnosed in utero), so most infants are born at term or near term.
 - b. Infants with CDH may recover completely after initial treatment in the NICU without residual lung problems, but most will develop some degree of chronic lung disease and have persistent PHTN requiring supplemental oxygen and other medications after discharge.

- c. Infants with premature and prolonged rupture of membranes often develop some degree of pulmonary hypoplasia due to oligohydramnios, which prevents normal growth of the lungs in utero. Premature infants born with pulmonary hypoplasia often require prolonged mechanical ventilation, develop significant BPD, and have associated PHTN. They are frequently discharged on supplemental oxygen and other medications.
2. Tracheoesophageal fistula
 - a. TEF is a congenital malformation of the trachea and esophagus.
 - b. There are three types of TEF, the most common being esophageal atresia with a fistula between the trachea and lower esophagus.
 - c. Repair of this defect sometimes results in tracheal stenosis or an area of tracheomalacia (collapse) at the fistula site causing prolonged stridor.
3. Tracheo- and/or bronchomalacia

Malacia or collapse of the proximal (trachea) or distal (bronchial) airways can result in stridor and increased work of breathing. This may be secondary to tracheal repair (as in TEF) or caused by an intrinsic weakness of the airway-supporting structures. Airway malacia almost always improves with growth of the child but may require prolonged ventilatory support (tracheostomy) during infancy and early childhood.

Pulmonary Hypertension

1. Some infants with severe BPD will develop secondary PHTN requiring increased oxygen and treatment with vasodilators (most commonly inhaled nitric oxide acutely followed by sildenafil chronically).
2. PHTN may develop before or after discharge from the NICU.
3. Infants with CDH or other etiology for pulmonary hypoplasia also often have significant PHTN requiring prolonged treatment after discharge.
4. Diagnosis of PHTN is made by evidence of increased pulmonary artery pressure (right ventricular hypertrophy, flattening of the intraventricular septum, tricuspid valve regurgitation) evident by echocardiography or cardiac catheterization.
5. This serious complication of BPD and other respiratory problems in term and preterm infants needs to be followed closely by a pediatric cardiologist and/or pulmonologist. Infants with PHTN will require periodic echocardiograms to determine if medications and oxygen should be weight adjusted or may be weaned.
6. Chronic aspiration (secondary to gastro-esophageal reflux disease [GERD] or swallowing problem) and infection should be prevented because they can exacerbate PHTN.

Follow-up of Infants with Bronchopulmonary Dysplasia

1. Infants with BPD with or without PHTN (ie, home on supplemental oxygen) should be followed in an NICU Graduate Clinic, and/or by a Pediatric Pulmonary Clinic, to determine when supplemental oxygen and medications should be adjusted or weaned.
 - a. Good growth and medical stability should be established before decreasing the treatment.
 - b. Oxygen is often weaned off first during the day and then at night.
 - c. Infants who are unable to wean from oxygen as expected, should be evaluated for PHTN, if not already diagnosed.
2. Respiratory syncytial virus (RSV) prophylaxis with Synagis.³
 - a. Eligibility for RSV prophylaxis changes each year. The most recent criteria are:

- i. Infants born ≤ 28 weeks gestation who are less than 12 months old
 - ii. Infants less than 1 year old with hemodynamically significant congenital heart disease
 - iii. Children less than 2 years old with BPD who continue to require medical intervention (supplemental oxygen, chronic corticosteroid, or diuretic therapy)
 - iv. Children with pulmonary abnormality or neuromuscular disease that impairs the ability to clear secretions from the upper and lower airways in the first year of life
- b. Influenza vaccine—all infants with BPD greater than 6 months of age and their immediate family and other caretakers should receive a flu shot

FEEDING, GROWTH, AND NUTRITION IN THE NEONATAL INTENSIVE CARE UNIT GRADUATE

Feeding problems in the NICU are frequently a barrier for discharge.^{5,6} These difficulties often persist, or even worsen, once the infant has transitioned to the home environment and are among the most common parental stressors post-discharge.⁷ Whether these feeding problems are caused by physiologic immaturity in premature infants, comorbidities of prematurity, or a complication of an underlying diagnosis requiring NICU admission (eg, respiratory, cardiac, neurologic, genetic), they are also a primary reason for readmission.^{8–10} It is important for the PCP to be aware of the different stages of feeding skills and factors that may interfere with their normal progression.

Common Feeding Problems by Age (Age Corrected for Prematurity in Premature Infants)

Birth to 3 months:

1. Oral feeding skills are driven by primitive reflexes. Rooting, sucking, and swallowing are the basic skills newborns possess to breast or bottle feed shortly after birth. Protective reflexes including gagging, coughing, and the laryngeal chemoreflex provide safety measures to allow for successful early feeding.
2. Any disturbance in the autonomic nervous system, as may be seen in extremely premature birth or neurologic injury, may interfere with this involuntary process.
3. Comorbidities such as BPD, necrotizing enterocolitis (NEC), or GERD that may interrupt normal breathing and feeding schedules (eg, nil per os, continuous feedings), may negatively impact the natural progression of early feeding.

3 to 6 months:

1. Feeding becomes a voluntary activity. Primitive reflexes integrate with brain development and the upper aerodigestive tract grows to resemble that of an adult by 5 months of age. With this, along with developing head control, a transition to solid foods is supported.
2. The infant must now coordinate the movement of food from the anterior oral cavity to the posterior pharynx to swallow, a much different eating pattern than sucking liquid from a nipple directly into the pharynx.
3. Oral exploration is abundant (hands, feet, clothing, toys to mouth) and works to desensitize the tongue to accept more textured foods.
4. Delays in head control or gross motor skills, as well as negative oral experiences (eg, orogastric and endotracheal tubes, suctioning, GERD), may disrupt this transition to voluntary feeding and may lead to oral aversion or difficulty in transition to textured foods.

6 to 9 months:

1. Infants begin eating thicker solids and finger foods, further increasing sensory stimulation with visual, auditory, tactile, taste, and smell contributing to the feeding process.
2. A more mature “munching” chewing pattern develops with vertical movement of the mandible and tongue protrusion coordinated with lip closure to retrieve food and keep it in the mouth.
3. Gross and fine motor skills begin to become more important as upright seating becomes the preferred feeding position, and reaching out and holding on to finger foods emerges.

9 to 12 months:

1. Infants begin eating mixed textures, including table foods. Infants also develop a more mature “rotary” chewing pattern required to shred more textured foods.
2. More advanced gross and fine motor skills are necessary for trunk stability, self-feeding, and initiating drinking from a cup.

Breastfeeding in Neonatal Intensive Care Unit Graduates

Problem:

1. Breastfeeding rates post-discharge from the NICU are low.
2. Only about one-fourth of very low-birth-weight infants are still receiving human milk at 6 months of age.
3. Less than one-fourth are actually feeding at the breast at the time of discharge.¹¹

Barriers to maintaining breastfeeding in the home environment:

1. Common concerns of mothers and providers:
 - a. Unknown volume of milk ingested when breastfeeding
 - i. By using a breastfeeding scale to measure pre-/post-breastfeeding weights, mothers and providers can get a sense of how much breast milk the infant takes with each breastfeed, which will guide how much expressed breast milk or formula should be given by bottle or tube.¹²
 - ii. Lactation specialists and skilled nurses should be available during discharge teaching, as well as post-discharge, to help support the mother and teach techniques to maximize efficiency at the breast.
 - iii. Breastfeeding positions that help support the infant’s head, neck, and shoulders will allow for more effective latch and transfer of milk. This will become less necessary as the infant shows increased gross motor strength and endurance.¹³
 - b. Concern that the mother can keep up her milk supply once the infant is home
 - i. A common misconception is that mothers of infants in the NICU only need to use a breast pump because they are separated from their infants, and, once their baby is discharged to home, they will feed their infant on demand and discontinue pumping.
 - ii. Studies have shown that continuing pumping in the home environment actually helps maintain the mother’s supply and allows for the transfer of milk despite a weaker suck in those first few months after going home from the NICU.¹¹
 - c. Whether human milk provides adequate nutrition for a growing premature or high-risk infant
 - i. There is some controversy about whether or not exclusive human milk feedings provide adequate nutrition for premature and sick term infants post-discharge, if they are taking sufficient volumes.

- ii. Because most very premature and high-risk infants sustain poor growth in the NICU and need to establish some catch-up growth post-discharge, breast milk alone usually has insufficient energy, protein, and minerals, such as calcium and phosphorous, to meet their nutritional needs after discharge (**Table 3**).

Growth in the Neonatal Intensive Care Unit Graduate

Poor growth is a common outcome of the NICU hospitalization, with postnatal growth failure the norm, and need for “catch-up growth” post-discharge the expectation.¹⁴

Reasons for growth failure:

1. Difficulty with feeding, food absorption, or tolerance.
2. Increased metabolic demands of conditions such as BPD, congestive heart failure, and hypertonemia requiring increased caloric intake to establish a return to standardized growth curves.

Use of Growth Curves

1. Standardized World Health Organization (0–24 months) and Centers for Disease Control and Prevention (24–36 months) growth charts with weight, length, and head circumference plotted according to corrected age should be recorded at all follow-up visits of premature infants.
2. Weight should continue to be adjusted for degree of prematurity for 24 months, with length and head circumference adjusted closer to 36 months.¹⁵
3. Weight-to-length ratio is also an important growth parameter to monitor in premature infants, because body composition in very premature infants acquiring catch-up growth is a strong predictor for the development of the metabolic syndrome later in life.

Goals for Growth Post-discharge

1. The American Academy of Pediatrics recommends that the goal for growth of premature infants should match fetal growth rate and body composition.¹⁵
2. “Extra-uterine growth restriction” is a well-known entity in premature infants and is usually dealt with by altering calories of expressed breast milk or formula.
3. Post-discharge diet should also meet protein and mineral needs for linear growth, as rapid weight gain without an increase in length leads to increased adiposity and future risks for hypertension, cardiovascular disease, and type II diabetes.^{16,17}

	Energy	Protein	Calcium	Phosphorus
Recommended for premature infants after discharge	120–130 kcal/kg/d	2.5–3.1 g/kg/d	70–140 mg/kg/d	35–90 mg/kg/d
Human milk without fortification	100 kcal/kg	1.5 g/kg	44 mg/kg	14 mg/kg
Term infant formula	100 kcal/kg	2 g/kg	80 mg/kg	42 mg/kg
Post-discharge premature formula	110 kcal/kg	3.1 g/kg	117 mg/kg	69 mg/kg

4. Post-discharge diet should correct for deficiencies of micronutrients (essential fatty acids, iron), as well as calcium and phosphorous, protein and energy.
5. Conditions with increased metabolic demands and increase energy/protein needs include:
 - a. Bronchopulmonary dysplasia
 - b. Congenital heart disease, especially if uncorrected with pulmonary overflow
 - c. Surgical NEC, especially if resulting in short bowel syndrome
 - d. History of intrauterine growth restriction
6. Goals for growth
 - a. Before term corrected age: weight increase of 18 g/kg/d and head circumference growth of 0.9 cm/wk.
 - b. After term corrected age and over 2 kg: 25 to 30 g/d, length to match the weight velocity, and head circumference growth closer to 0.5 cm/wk.

Recommendations for Achieving Energy, Protein, and Mineral Needs

For premature infants receiving human milk:

1. Feed at the breast a couple of times daily and then supplement with either fortified expressed breastmilk by bottle or 2 to 4 feedings of a transitional preterm formula (Enficare or Neosure concentrated to at least 24 cal/oz).
2. The growth chart and bone health indices (calcium, phosphorus, alkaline phosphatase) should be followed monthly until catch-up growth has been established. Simply fortifying the expressed breast milk with formula powder often does not meet the protein and mineral needs for these high-risk infants.
3. If an infant is not demonstrating appropriate linear growth to match weight gain or if bone health becomes a concern (phosphorus <4.2 mg/dL, alkaline phosphatase >400 IU/L), supplementing with 2 to 4 pure formula feedings daily for increased protein is recommended.

For infants receiving infant formula feedings:

1. Infant formulas have standard mixing instructions without regard to specific needs of the NICU graduate.
 - a. Post-discharge premature infant formulas (Enficare, Neosure) mixed to standard dilution are 22 cal/oz. Term infant standard and specialty formulas are 19 and 20 cal/oz. Specific formula recipes are available for increasing caloric density up to 30 cal/oz.
 - b. The post-discharge premature formulas have increased protein and mineral content (especially calcium and phosphorous) intended for former premature infants; however, many NICU graduates are discharged home on special term infant formulas, regardless of gestational age at birth, because of comorbidities (eg, GERD, NEC, short gut) leading to poor linear growth and osteopenia.
 - c. As with the breastfed NICU graduate, all growth parameters need to be followed closely, and caloric density increased as tolerated to establish steady, symmetric catch-up growth.
 - d. When increasing to 27 cal/oz or higher, the high osmolality can lead to intolerance with constipation (especially if on diuretics), malabsorption, or high serum calcium and phosphorous levels. These parameters should be closely monitored.

For infants >1-year adjusted age:

1. Many very premature or chronically sick term infants have not yet established appropriate catch-up growth in the first year of life. These children often have oral feeding difficulties as well.

2. Complete balanced milk-based toddler formulas, as well as specialty toddler formulas, can be used to supplement their age-appropriate diet or as a complete diet for tube-fed children.
 - a. Toddler formulas are available as 30 cal/oz, and sometimes 45 cal/oz, to assist with the continuation of catch-up growth in the second year of life.
3. Older children may also benefit from blended diets of different food groups. A Pediatric Gastroenterology Clinic and/or dietician can help with appropriate food selection.

NEUROLOGIC PROBLEMS IN NEONATAL INTENSIVE CARE UNIT GRADUATES

Term and preterm infants may be born with a variety of malformations of the central nervous system or may develop ischemic damage or bleeding in the brain before birth or in the neonatal period due to prematurity, birth trauma, or severe illness.^{18,19} All suspected or documented brain malformations or injury result in the infant being at increased risk for abnormal neurodevelopment in infancy and early childhood.

Malformations of the Central Nervous System

1. Hydrocephalus, congenital, or acquired

a. Congenital hydrocephalus

i. Aqueductal stenosis

Obstruction of the aqueduct, which connects the third and fourth ventricle, is the most common cause of congenital hydrocephalus. Blockage of the aqueduct causes progressive enlargement of the lateral and third ventricles, which eventually requires either a VP shunt to be placed, or, later in infancy, a third ventriculostomy to be performed. A shunt may be placed in the neonatal period or after initial NICU discharge.

ii. Dandy-Walker malformation

Dandy-Walker malformation is a congenital defect affecting the cerebellum, which can potentially impact a child's movements, behavior, or cognitive ability. A Dandy-Walker malformation can cause obstruction of the normal drainage of cerebrospinal fluid (CSF) from the fourth ventricle, resulting in a build-up of CSF with resultant hydrocephalus.

b. Acquired hydrocephalus

i. Post-hemorrhagic hydrocephalus

Infants with bleeding inside the ventricles (grade 3 or 4 intraventricular hemorrhage [IVH]) in premature infants, or a choroid plexus bleed in term infants, can lead to obstruction of the drainage of CSF out of the ventricles as a result of blockage of the ventricular lining secondary to inflammation (ie, ventriculitis) or from blood obstructing the aqueduct. This post-hemorrhagic hydrocephalus may self-resolve over time or require a VP shunt for permanent drainage of the CSF.

Infants with a diagnosis of hydrocephalus in the newborn period, with or without a shunt, must be followed closely for abnormal growth of the head and signs of increased intracranial pressure (lethargy, irritability, emesis, sun-setting of eyes). Parents must also be educated about these signs as well as the clinical presentation of shunt failure (ie, increased intracranial pressure or swelling around the shunt tubing or entrance site) or shunt infection (same as shunt failure plus fever).

2. Neural tube defect (with or without hydrocephalus)

A neural tube defect (or meningomyelocele) is failure of closure of a portion of the neural tube during development with resultant exposure of the spinal cord. This type of defect is typically repaired in the first days after birth. Infants may have an associated Dandy-Walker malformation. Problems following repair may be progressive hydrocephalus requiring a shunt, wound dehiscence or infection, neurogenic bladder, and urinary tract infection (UTI). Parents are often required to perform a straight catheterization of the bladder one or more times per day to prevent urine retention and UTI. Infants should be followed closely for acceleration of head growth, neurologic deficits, and signs of UTI (fever, blood in or discoloration of urine). Close follow-up with the PCP is integrated with follow-up with other subspecialties such as Pediatric Neurosurgery, Urology, and Orthopedics.

3. Microcephaly

Microcephaly (head circumference below the 3rd percentile) can be caused by intrauterine viral infections such as cytomegalovirus and Zika early in pregnancy, or by other environmental toxins (eg, alcohol). Infants with microcephaly must be watched closely for muscle tone abnormality and developmental delay. Depending on the cause, other problems should be screened for (eg, deafness, visual impairment, congenital heart defects).

Ischemic Brain Injury

Ischemic brain injury may be global or focal. The most common ischemic-type injuries include:

Hypoxic-ischemic encephalopathy

Hypoxic-ischemic encephalopathy (HIE) is a clinical diagnosis when an infant has suffered a period of decreased blood and oxygen to the brain, resulting in depression at birth and an abnormal neurologic exam. HIE is categorized as mild, moderate, or severe using the Sarnat scoring for encephalopathy. Treatment with therapeutic hypothermia (either whole body or head) in the NICU is now standard of care for infants ≥ 36 weeks gestation with moderate or severe HIE. Following cooling and rewarming, the infant will have a brain magnetic resonance imaging (MRI) to determine the presence and extent of brain injury. The history of a normal MRI after cooling carries a good prognosis for normal developmental outcomes. Patterns of brain injury after HIE may be focal or global. Injury in the basal ganglia and/or thalamus or global ischemic injury (diffuse cystic encephalomalacia being the most severe) is associated with a poor neurologic outcome including cerebral palsy (CP). Seizures in the first few days in infants with HIE are not predictive of a poor outcome; however, persistent seizures after rewarming are a poor prognostic sign.

Middle cerebral artery infarct/other focal stroke

Middle cerebral artery (MCA) stroke is the most common focal ischemic injury in full-term infants. It often presents with apnea and/or seizures in the first 24 hours of life. An electroencephalogram may be consistent with a focal lesion but definitive diagnosis will be by MRI. Moderate-to-severe MCA stroke is associated with hemiplegic CP on the opposite side. Small strokes may have no long-term neurologic sequelae. Close follow-up is warranted and physical therapy should be ordered when asymmetry of muscle tone or movement is detected.

Other focal strokes can result from arteriolar emboli. This is most frequently found in infants treated with ECMO, but may be diagnosed in other infants as well (eg, infants with congenital heart disease). These infarcts may not be clinically apparent before

discharge unless detected on an MRI. Affected infants may present with asymmetry of tone and movement in later infancy.

Periventricular leukomalacia

Periventricular leukomalacia (PVL) is the most common ischemic brain injury in premature infants, but is also seen in some term infants after cardiac surgery and prolonged time on cardiac bypass. PVL can be cystic or non-cystic. Cystic PVL most commonly manifests as cysts in the temporoparietal periventricular white matter on postnatal ultrasonography. The cysts are usually bilateral and are associated with the development of CP (diplegia or quadriplegia). Non-cystic PVL may be suspected on head ultrasound by the appearance of mild ventriculomegaly without former IVH. Follow-up MRI will demonstrate thinning of the periventricular white matter, which is also associated with the development of CP. PVL can also be diagnosed in the frontal area and the long-term outcome of this injury is less certain.

Hemorrhagic Brain Injury

Hemorrhage or bleeding can occur in the ventricles or parenchyma of the brain. The most common types of hemorrhages include:

1. Intraventricular hemorrhage (IVH)
 - a. An IVH arises from the germinal matrix in premature infants. The germinal matrix is a very vascular area of the brain during development that disappears by 36 weeks gestation. Hypoperfusion and reperfusion injury in this subependymal area causes rupture of tiny capillaries and bleeding to occur. A grading system (grades I–IV) had previously been used to describe the type of IVH; this has now been replaced with a preference of description of the finding. The mildest IVH is limited to the germinal matrix (formerly grade 1 IVH). A more severe type is blood that extends into the ventricle but does not cause ventricular dilatation (formerly grade II IVH). Infants can also have bleeding that extends into the ventricle resulting in ventricular dilatation (formerly grade III IVH); this can result in post-hemorrhagic hydrocephalus. The most significant IVH occurs when blood is noted in the parenchyma usually adjacent to the ventricle (formerly grade IV IVH), which can lead to post-hemorrhagic hydrocephalus and/or a pencephalic intraparenchymal cyst. This type of hemorrhage may be the result of bleeding into an area of infarction. The PCP needs to closely monitor the head circumference of infants with severe IVH; if a child has not yet received a shunt, head ultrasounds should be repeated until the ventricular dilation resolves (see post-hemorrhagic hydrocephalus section above).
 - b. Choroid plexus bleed

In term infants, a choroid plexus bleed may occur with severe illness or birth trauma resulting in an IVH. This may also result in post-hemorrhagic hydrocephalus. The infant's head circumference should be followed, and ultrasound should be repeated periodically until the blood and ventricular dilatation, if present, resolves.

Other Neurologic Problems

Other neurologic problems that are common in NICU graduates include:

Seizures

- a. Both term and preterm infants can develop seizures secondary to brain injury or infection. Efforts to wean off seizure medication may be unsuccessful before discharge, so many infants will be discharged on continuing seizure medications.

- b. Follow-up with a pediatric neurologist should be scheduled to determine when the medication needs to be weight adjusted or weaned off. Seizure medication should not be stopped abruptly.
- c. Parents should be educated in detecting signs of seizure activity, such as jerking of arms or legs (which is not stopped with restraint), eye deviation, or stiffening of the body. A seizure may be followed by a period of somnolence (post-ictal period).
- d. Infants with brain injury are at risk of developing seizures after discharge, and parents should be aware of the signs and symptoms.
- e. Fever in an infant can lower the seizure threshold so parents should be instructed on proper temperature control during times of illness and after immunizations.

Muscle tone abnormalities

Abnormalities of muscle tone (increased or decreased) are common in premature and sick term infants and may be transient in nature or persist and result in a diagnosis of CP. Some NICU follow-up clinics have physical therapists who will teach home exercise programs. If this is not available, infants with abnormal muscle tone should be referred for physical therapy after hospital discharge.

a. Hypotonia

1. The most common abnormality of muscle tone following discharge in an NICU graduate is hypotonia (low muscle tone), either central (just in the trunk) or generalized (in the trunk and extremities). Sometimes this is secondary to muscle wasting from poor nutrition and other times from weakness secondary to illness.
2. Truncal hypotonia is manifested early on by poor head control and poor prone skills and later by delay in reaching motor milestones (rolling, sitting, and walking). However, low muscle tone usually improves over time as the underlying chronic illness improves. This is particularly true for infants with BPD.
3. Significant generalized hypotonia can also be seen with severe brain injury (eg, HIE, severe IVH, particularly in the early months), cerebellar injury, and various genetic syndromes (eg, Prader-Willi, Trisomy 21).

b. Hypertonia

1. Transiently increased muscle tone, particularly in the lower extremities, is common in premature infants. These infants often have an imbalance in flexion and extension of various muscle groups from lack of movement and exercise. Mild-to-moderate hypertonia may improve over time with exercise and physical therapy.
2. Significant hypertonia in the extremities, particularly when coupled with decreased truncal tone and exaggerated primitive reflexes, may represent early precursors of CP.

Cerebral Palsy (CP)

- a. Definition: NICU graduates who have experienced severe IVH, HIE, or other ischemic brain injury causing damage to the motor cortex or pathways may have persistent abnormalities of muscle tone and motor function known as cerebral palsy. Patterns of increased muscle tone can affect the upper and lower extremity on the same side (hemiplegia), both lower extremities (diplegia) or all 4 extremities (quadriplegia). CP is characterized as mild, moderate, or severe based on degree of functional impairment by the Gross Motor Function Score. Hypotonic CP is associated with ataxia.

- b. Diagnosis and intervention: it is important for infants who have sustained significant brain injury to be followed closely for early signs of CP. This is best accomplished in an NICU follow-up clinic or by a pediatric neurologist. Appropriate early intervention with physical and occupational therapy will help to prevent contractures and maximize functional outcomes.

Sensory impairment

a. Vision problems

Retinopathy of prematurity (ROP)

- Characterized by abnormal growth of the retinal vessels with tortuosity and clumping.
- Occurs in premature infants to varying degrees depending on gestational age and severity of early illness.
- Severe stages of ROP, if not detected and treated, can result in retinal detachment and blindness. Less severe stages of ROP can result in either myopia or hyperopia requiring refraction.
- Because growth of the retinal vessels is not complete until approximately 44 weeks gestation, follow-up visits will often be scheduled for premature infants soon after discharge from the NICU.
- The PCP should be aware of the infant's ROP status and make sure that follow-up with an ophthalmologist is scheduled and attended.

Cortical visual impairment

- Results from injury to the occipital lobe of the brain or generalized ischemic damage to the cerebral cortex.
- Most commonly seen in term infants with HIE, infants born with microcephaly secondary to intrauterine infection or in utero ischemic damage, and kernicterus.
- Cortical visual impairment is not corrected by refraction (ie, glasses). However, visual therapy is usually available from early intervention programs to help infants accommodate to this disability.

b. Hearing problems

- Hearing loss in premature and term infants may be sensorineural, conductive, or mixed.
- Sensorineural hearing loss involves injury to the auditory nerve and can be genetic in origin or secondary to various medications or illnesses (TORCH infections, kernicterus).
- Conductive hearing loss is caused by a problem in conduction of sound through bone and inner ear. Premature infants, in particular, have an increased incidence of Eustachian tube dysfunction resulting in conductive hearing loss. Improvement in hearing can be achieved by inserting myringotomy tubes to drain fluid from the middle and inner ear. Premature infants with repeated otitis should be evaluated by a pediatric otolaryngologist to determine if tubes are indicated.
- Hearing loss in both premature and term infants may improve with hearing aids or cochlear implants. Close follow-up with a pediatric otolaryngologist is essential to maximize hearing before 1 year of age to maximize potential for language development.

Developmental delay

Risk for developmental problems in NICU graduates can be identified at the time of discharge. Infants with conditions associated with moderate to high risk of

neurodevelopmental delay should be followed in an NICU follow-up clinic if available. These include:

1. Prematurity (please see article “[Neurodevelopmental Follow-up of Preterm Infants: What is new?](#)” by Elisabeth McGowan and Betty R. Vohr, in this issue.)
 - a. Extremely low birth weight (<1000 g)
 - b. Extreme prematurity (≤ 26 weeks gestation)
2. Serious neonatal illness/morbidity
 - a. Bronchopulmonary dysplasia
 - b. PHTN treated with nitric oxide
 - c. Respiratory failure treated with ECMO
 - d. Surgical NEC
3. Suspected or documented brain injury
 - a. Severe IVH (grade 3 or 4)
 - b. PVL/other stroke (eg, MCA)
 - c. HIE
 - d. Neonatal seizures
 - e. Hydrocephalus (congenital or acquired)
 - f. Central nervous system malformation
 - g. Meningitis, encephalitis
4. Poor intrauterine environment
 - a. Intrauterine growth restriction
 - b. Neonatal abstinence syndrome
 - c. Intrauterine viral infections

TECHNOLOGY DEPENDENCE IN THE NEONATAL INTENSIVE CARE UNIT GRADUATE

NICU graduates with medical complexity are often discharged with dependence on one or more forms of technology.²⁰ It is important for PCPs to understand why they are being used and know how to troubleshoot common problems.

Oxygen

1. As many as 60% of infants with moderate-severe BPD will be discharged home on oxygen therapy, most being weaned off in the first year of life.
2. Oxygen therapy is a first-line treatment for infants with PHTN.
3. Infants requiring supplemental oxygen should be sent home with an oximeter to measure peripheral oxygen saturations (SpO₂) with a goal of greater than 90% in infants with BPD and greater than 94% with concerns of PHTN. The oximeter is also a valuable tool to be used during room air trials when weaning off oxygen.
4. Administration of supplemental oxygen.
 - a. Supplemental oxygen is provided by nasal cannula in infants without an artificial airway.
 - b. Infants with a tracheostomy who require oxygen: use a trach collar or oxygen is entrained into a home ventilator.
 - c. Most infants will be discharged on ≤ 0.5 L/min. Oxygen gauges are either in decimal (0.1 increments) or fractions of a liter. Oxygen can be delivered from as little as 1/16 L/min (0.03 L/min) to several liters/minute. Patients have small portable oxygen tanks (typically for travel, lasting ~ 4 hr) and a larger tank with a concentrator for home use.
5. Important points:
 - Infants discharged home on oxygen therapy should also have a portable oximeter.

- Humidification should be placed on all condensers for delivery of supplemental oxygen greater than 1.0 L O₂.
- Higher oxygen requirement in the home environment can be due to the length of oxygen tubing going to the condenser.
- If a child is suddenly desaturating at home, caregivers should check for mechanical errors first and attempt to increase oxygen delivery to solve the problem (eg, unplugged tubing or power source, empty oxygen tank)
- Oxygen is generally weaned in step-wise fashion over a period of time (weeks to months) with no consensus statement on standardized protocol.
 - Weaning oxygen therapy first versus diuretics or bronchodilators is clinician dependent, but often oxygen is weaned off first.
 - Daytime oxygen is usually discontinued first, allowing freedom for travel, therapies and developmental playtime, while maintaining oxygen use at night.
 - Continuous overnight pulse oximetry to evaluate nocturnal saturations is generally used to evaluate ability to discontinue overnight oxygen.

Apnea Monitor

Indications

1. Monitoring of infants at increased risk of life-threatening episodes of apnea, bradycardia, and hypoxemia.
 - a. Persistent apnea of prematurity treated with caffeine
 - b. Persistent central or obstructive apnea secondary to neurologic, metabolic, or other disorders
 - c. Severe GERD
 - d. Frequent seizures
 - e. History of apparent life-threatening event post-discharge from NICU
 - f. History of sibling dying from sudden infant death syndrome
2. Important points
 - Discharge settings: low heart rate alarm at 80 bpm (70 bpm if >44 weeks PMA), high heart rate alarm at 220 bpm, and apnea alarm at 20 seconds.
 - Frequent alarms and artifact may occur if electrodes are placed incorrectly or if the chest strap is too loose. Use of stick-on electrodes, as used in the hospital setting, may alleviate the problem.
 - As the infant grows older, low heart rate alarm will need to be decreased from 80 bpm to 70 or 60 bpm to prevent false alarms during deep sleep periods.
 - Apnea monitors should have memory-recording ability; these are generally downloaded by durable medical equipment companies and information outsourced. Apnea monitor use and event occurrences are reported to the PCP in a print out.
 - Parents and other caretakers should be taught infant cardiopulmonary resuscitation before discharge and have an emergency plan for frequent or prolonged alarming or equipment failure.

Tracheostomy and Home Ventilator

1. Indications for tracheostomy:
 - a. Prolonged respiratory failure
 - b. Subglottic stenosis
 - c. Severe tracheo- and/or bronchomalacia

- d. Vocal cord paralysis or dysfunction
 - e. Congenital airway malformations
 - f. Tumors
 - g. Craniofacial anomalies
 - h. Neuromuscular disorders
2. Description:
 - a. Made of either polyvinyl chloride (Shiley) or silicone (Bivona).
 3. Important points:
 - Decimal point and the number zero (no. 4.0) are used to designate a neonatal or pediatric tracheostomy tube. Tracheostomy tubes are identified as either no. 3.5 NEO Shiley or no. 3.5 PED Shiley on the neck plates of the tracheostomy tube.
 - Pre-measured suctioning depth not longer than the trach cannula is essential to prevent epithelial tissue damage.
 - Tracheostomy care should be performed twice daily and more frequently, as needed, to prevent skin breakdown.
 - Clean technique should be used for tracheostomy changes in the home environment. Sterile technique does not decrease infections.
 - Parents and/or caregivers should demonstrate proficiency in tracheostomy tube change, suctioning, and trouble-shooting before discharge. Caregivers should be taught assessment skills and be aware of and know how to implement emergency measures.
 - All patients with a tracheostomy tube should have an emergency supply bag containing a replacement tracheostomy of the same size and one tracheostomy tube one size smaller, flexible suction catheter and suction machine, scissors, spare tracheostomy ties, gloves, water-based lubricant, Ambu bag, and oral endotracheal tube.
 - Ventilated patients and those with thick secretions should always use humidification. Use of the motto “When in doubt, change it out” may be applied to most situations where tracheostomy tubes require action due to the inability to diagnose the problem during patient emergency.

Home Ventilator; Laptop Ventilator

1. Indications: Provide ventilation for infants with chronic respiratory failure due to various disease processes such as BPD, bronchomalacia, congenital and acquired central hypoventilation syndrome, and neuromuscular disease in the home setting.
2. Description: Small, laptop-sized, portable ventilator for home use.
3. Important points:
 - Patients with a home ventilator should always have an Ambu bag readily available in case of ventilator failure.
 - Condensation in ventilator tubing can cause ventilator to auto-cycle and trigger additional ventilator breaths. Troubleshoot by emptying ventilator limbs to remove water.
 - Local emergency services and power company should be notified of the dependent infant’s address in case of future emergency or power outage.

Feeding Tube

1. Indications: for children with dysphagia, aspiration, oral aversion, and/or those who have failure to thrive for other reasons.
2. Description:

- a. The gastrostomy tube (GT) is generally placed in the left upper quadrant to deliver liquid feedings at prescribed volume (“dose”) and rate.
 - b. The feeding tubes can be placed directly in the stomach, jejunum, or passed from the stomach into the jejunum (trans-gastric jejunal or “GJ” tube).
3. Important points:
- Bolus feedings should only be attempted with GT feedings.
 - Continuous feedings only are permitted through a jejunal tube secondary to risk for dumping syndrome, diarrhea, or intestinal injury.
 - Patients who cannot tolerate large daytime bolus feedings may benefit from continuous nighttime feedings at a lower rate for 8 to 10 hours per night with smaller daytime bolus feedings. This is also a strategy for transitioning to oral feedings if unable to take enough by mouth during awake periods.
 - The skin around the tube should be cleansed twice daily with soap and water, and should be assessed daily for leakage, irritation, infection, or granulation tissue.
 - The GT should be rotated a quarter of a turn with every diaper change to prevent skin breakdown, and the water volume (generally 3–7 mL) in the balloon should be assessed weekly (if Mic-Key or AMT Mini ONE)
 - The GT button should be replaced every 3 months and the parents should be comfortable in doing this after the first change, as it is not uncommon for a GT with an established tract to become dislodged.
 - Skin irritation due to leakage or infection may occur. Typically, over-the-counter skin barriers assist with local irritation from gastric leakage. True skin infections around the GT are relatively uncommon but intense redness, tenderness, or systemic signs of fever or malaise may occur. Mild local infections may be treated with topical antibiotics, whereas true cellulitis requires oral or intravenous antibiotics covering typical skin organisms. Rashes may also occur and are typically yeast and may be treated topically.
 - Granulation tissue is excessive reactive tissue around the GT. It is often moist with mucous discharge and bleeds easily. It can lead to leakage around and, sometimes, dislodgement of the GT. It is usually treated by chemically cauterizing with silver nitrate, and, if chronic, may be treated at home with topical steroid ointment.
 - Infants discharged home with gastrostomy, jejunostomy, or nasogastric feeding tubes should be provided with a feeding pump so that feedings can be given at a consistent rate.

Home Nursing Services for Technology-Dependent Infants

- Caring for an NICU graduate with medical complexity, particular one who is technology dependent, can be very expensive financially, and emotionally draining, for parents and siblings.
- Availability of home nursing services varies by location and type of insurance coverage.
- The PCP should investigate what might be available for their patient and family through their established insurance coverage or additional Medicaid waiver services for which they may be eligible.

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