NCC Pediatrics Continuity Clinic Curriculum: NICU Follow-up

Goals & Objectives:

• Know how to manage long term complications of prematurity
• Develop a nutrition plan for a former premature infant
• Counsel parents on what to expect as premature infants get older

Pre-Meeting Preparation:

• NICU Follow-Up: Medical and Developmental Management Age 0 to 3 Years (NeoReviews, 2014)
• NICU Follow-Up Care: The Developmental and Advocacy Perspectives (NeoReviews, 2014)

Conference Agenda:

• Review NICU Follow-up Quiz
• Complete NICU Follow-up Mega-Case

Extra-Credit:

• 2014 AAP Policy Statement: Synagis with 2018-2019 chart
• HealthyChildren: Premature Infants (parent reference)

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NICU Follow-up: Medical and Developmental Management
Age 0 to 3 Years

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Educational Gaps
1. Despite understanding the problems associated with the progression of a variety of diseases in the neonatal intensive care unit (NICU), less is known about the course of common NICU diseases after discharge.
2. The management of NICU graduates requires complicated social, medical, and subspecialty coordination.

Abstract
Over the last several decades, the number of infants graduating neonatal intensive care units (NICUs) continues to increase despite advances in obstetrical practice. Many of these NICU graduates have complex medical, social, developmental, and medicinal needs that require a physician dedicated to providing a NICU follow-up medical home. The object of the present review is to address the epidemiology and management of common problems that occur in the at-risk NICU graduate.

Objectives After completing this article, readers should be able to:
1. Appreciate the epidemiology of common neonatal intensive care unit (NICU) diseases in the outpatient setting.
2. Describe the management and progression of common problems that affect the NICU graduate.
3. Understand the complexity and pitfalls of care of the NICU graduate.

Introduction
There are ~4 million live births in the United States each year, ~400,000 of which are premature. (1) Over the last few decades, there has continued to be both an increase in preterm births and a decrease in preterm mortality, (2) which has led to the growth of academic and community neonatal intensive care unit (NICU) programs dedicated to medical and developmental follow-up of these infants.

These successes are associated with complex medical and developmental outcomes. Post-NICU care has a unique and complex set of social, cultural, geographic, and economic interactions. NICU follow-up experts, general pediatricians, family practitioners, and an array of subspecialists now care for former NICU patients in a myriad of settings.

The goal of the present article was to guide practitioners in approaches to common NICU-related medical and developmental management according to body system and subspecialty. Within each medical approach, particular attention is paid to long-term disease prevention and cost savings for the benefit of both patients and clinicians.

Abbreviations
AAP: American Academy of Pediatrics
BPD: bronchopulmonary dysplasia
CT: computed tomographic
ECMO: extracorporeal membrane oxygenation
GERD: gastroesophageal reflux disease
IVH: intraventricular hemorrhage
PPV: positive pressure ventilation
PVL: periventricular leukomalacia
ROP: retinopathy of prematurity
RVH: right ventricular hypertrophy
VP: ventriculoperitoneal

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Home Oxygen Use

The most common lung disease related to prematurity is bronchopulmonary dysplasia (BPD), which occurs in ~42% of former 22- to 28-week gestation infants who survive to 36 weeks’ postmenstrual age. (3) Both the rate and severity of BPD increase with decreasing gestational age. BPD is currently defined as the use of oxygen or supplemental positive pressure at 36 weeks’ adjusted age. (4)

Further classification of BPD severity can be assessed by using the scale of Jobe and Bancalari that includes detailed assessment of positive pressure and oxygen use in the NICU. (4) Infants born <32 weeks’ gestation who required less than 3 weeks of supplemental oxygen and less than 8 days of ventilation (mild BPD) are considered lowest risk for post-discharge complications of BPD. Those who required up to 4 to 6 weeks of ventilation/continuous positive airway pressure/high-flow nasal cannula and 6 to 10 weeks of supplemental oxygen have moderate BPD. Any child who requires more than 90 days of ventilation is considered to have severe BPD and to be at high risk for readmission and for increased morbidity and mortality from BPD.

In infants with severe BPD, typical home oxygen use is 0.1 to 0.5 L/min of oxygen to maintain oxygen saturation levels of ≥95 to 98%. Any former premature infant who requires more than 0.5 L/min of oxygen or who takes a vasoactive medication such as sildenafil or bosentan is considered to be at high risk for right ventricular heart dysfunction and poor improvement from pulmonary disease. Home oxygen use of more than 0.5 L/min also creates logistic difficulties for families due to the inability to transport sufficient oxygen to perform daily activities of life. Infants who have BPD are also more likely than their peers to be rehospitalized in general and with a respiratory illness specifically. (5)

Postdischarge diuretic use varies substantially across practices. For a child discharged from the hospital with diuretics, correct dosing should be reviewed with the parent at the first visit to the clinic. If a child remains on twice-daily dosing of any diuretic for 1 month after discharge, a complete metabolic panel is recommended at the end of the first month or earlier if there is a concern regarding other electrolyte abnormalities.

Typical strategies for BPD management include a stepwise weaning of diuretic therapy and oxygen therapy. Diuretics are initially weaned to once-daily dosing and then discontinued. Daytime oxygen therapy is weaned by 0.1 L/min per month until it is discontinued. Nighttime weaning of oxygen therapy then occurs in a similar fashion. Continuous pulse oximetry is used before any weaning occurs and can be modified to spot-checks during the daytime when weaning day oxygen and discontinuing night pulse oximetry when night oxygen is discontinued.

Tracheostomy and Positive Pressure Ventilation

Tracheostomies and the need for positive pressure ventilation (PPV) are uncommon in the NICU population, with one study reporting that ~2% of preterm infants required tracheostomy (7) while another showed an increasing rate of 4.77 per 100,000 live births needed PPV. (8) Infants who have congenital airway abnormalities have a greater need for tracheostomy, with that need ranging from 10% to 14%. (7) Almost all infants (97%) discharged from the hospital needing PPV are weaned off PPV by their fifth birthday; the median time of weaning off PPV is 2 years. (8)

Due to the high rate of readmission and death in former NICU patients who have tracheostomies, (8) home nursing staff and family members should be taught the replacement of tracheostomy tubes and to observe for signs of obstruction, displacement, and infection. Any signs of distress within this patient population should trigger evaluation with the physicians in the emergency department or subspecialists involved in the patients’ care while offering stabilization procedures such as the placement of an intravenous catheter, supplemental oxygen therapy, and respiratory flow as well as routine blood and imaging evaluations.

Genetic syndromes and craniofacial abnormalities may also necessitate the need for home oxygen therapy,
tracheostomy, and home ventilation. In obstructive and central sleep apnea syndromes, sleep pulmonologists often guide early therapy. In simple obstructive sleep apnea cases in the older child, first-line medical therapy with montelukast (9) and/or fluticasone can be offered before surgical management.

Apnea

There are practice variations for the use of apnea monitors at discharge of premature infants. (10) When apnea monitors are used, they can be discontinued any time after 44 weeks’ corrected age because preterm infants with apnea are at the same risk as other infants at this age. (11) After an apneic event, the readings of apnea monitors are not as helpful as a full evaluation in the emergency department, urgent care, or primary care office. (12) True apnea can be related to a consequence of immaturity, poor neurologic function, seizures, feeding/gastroesophageal reflux disease (GERD), or control of secretions. Both typical apnea and complicated apnea should be treated seriously, (13) and a cause should be sought. One method of avoiding the uncertainty regarding apnea of prematurity is to develop a protocol in which premature patients are weaned from caffeine citrate at least 3 to 5 days before discharge, allowing for an observation period off caffeine based on gestational age. (14)

Immunizations

A common pitfall when treating NICU graduates is delaying or withholding vital immunizations in a population particularly vulnerable to respiratory diseases. The American Academy of Pediatrics (AAP) guidelines provide guidance on immunization practice for preterm and low birth weight infants, with full doses of diphtheria and tetanus toxoids with acellular pertussis vaccine (DTaP), *Haemophilus influenzae* type b, hepatitis B, poliovirus, and pneumococcal conjugate vaccines given at the chronological age equivalent to that recommended for term infants. (15) Influenza prophylaxis should be offered to all NICU infants at 6 months of age and their caregivers before or during the influenza season.

The need for palivizumab (Synagis®, MedImmune, LLC, Gaithersburg, MD) should be evaluated in all patients with lung pathology related to prematurity (≤36 weeks) and other at-risk NICU graduates. The AAP guidelines also provide guidance on the number of treatments (3 vs 5); the annual start date is based on geographic location and eligibility. (16) Home-based services, streamlined ordering, and delivery procedures are often available to families.

Anemia of Prematurity and Anemia of Chronic or Complex Disease

Anemia of prematurity is common in the NICU but is less common in the outpatient setting because the most severe cases are treated with blood transfusion or erythropoietin before NICU discharge. Counterintuitively, many infants born at 29 to 34 weeks’ gestation may go on to have persistent anemia because they did not undergo transfusion in the NICU, were subject to phlebotomy, did not receive adequate iron supplementation after discharge, and have reduced fetal blood cell life span. (17)

Many centers are comfortable discharging from the hospital a patient who has a hemoglobin level ≥8.0 g/dL and a reticulocyte count ≥3% to 4%. Our practice is to have children who are discharged with a hemoglobin level ≤9.5 g/dL have a repeat complete blood count in the outpatient setting 2 weeks after discharge and 1 to 2 months later, as long as the blood counts are increasing.

Anemia is also common in infants who have complex congenital syndromes who require multiple surgeries. The neonatal follow-up physician can help coordinate ongoing surgical interventions by ensuring normal blood counts before surgery.

Iron therapy is typically adequate for asymptomatic anemia related to NICU care. The appropriate dose range is 2 to 6 mg/kg per day of elemental iron. For almost all infants discharged weighing less than 3.5 kg, 1 mL of a polyvitamin with iron, which contains 10 mg of elemental iron, is sufficient and is simple enough to ensure good compliance. Infants fed human milk should receive additional iron and vitamin D supplementation.

Seizures in the Newborn

Seizures occur in ~0.1% of all newborns (18) but are common in the NICU. As many as 10% of infants who have intraventricular hemorrhage (IVH), (19) ~18% of infants who have periventricular leukomalacia (PVL), (20) and 29% to 35% of infants who have moderate or severe hypoxic-ischemic encephalopathy (21) will have seizures. Many congenital anomalies are also associated with brain malformations and dysfunction leading to seizure.

The most important aspect of seizure management for the generalist is a complete understanding of the plan at the time of discharge. Many infants who require anticonvulsant therapy in the NICU have conditions that improve (22) and where subsequent weaning is planned with no planned escalation of dose or therapy. Other seizure disorders are known to be complex or persistent in nature, and the clinician should be alert for new clinical manifestations.
Currently, phenobarbital is the first-line treatment for maintenance therapy of seizures in newborns. Complex or persistent phenotypes can be managed with levetiracetam, fosphenytoin, or divalproex and the assistance of a pediatric neurologist. Withdrawal of antiepileptic therapy should be guided by the neurology team with the goal of limiting maintenance therapy to weeks or months if possible. If a level needs to be maintained for any of the anticonvulsants, the blood levels should be drawn within a month of discharge and an arrangement should be made with the neurologist regarding subsequent blood draws and the transfer of results between clinicians.

Neuroimaging in the form of an electroencephalogram, computed tomographic (CT) scan, and magnetic resonance imaging can be an important aspect of ongoing seizure care. Before discharge, the primary care physician should assess the need and frequency for this imaging and determine a plan for referral or ordering of these tests. Oftentimes, a prolonged electroencephalogram for 24 hours requires a specialized hospital facility, and magnetic resonance imaging or a CT scan might require sedation and a sedation team or service. These ancillary services can require intensive planning for the general physician.

Intraventricular Hemorrhage, Periventricular Leukomalacia, and Ischemic and Hemorrhagic Stroke

Very preterm infants known to have IVH or PVL have a higher rate of cerebral palsy: Infants who have bilateral cystic PVL have cerebral palsy rates as high as 75% but even with a normal head ultrasound, ~4% of infants less than 32 weeks’ gestational age develop cerebral palsy. Every NICU team should have a plan for developmental follow-up for its high-risk graduates.

Approximately 16% of infants with severe IVH (grade III and IV) require permanent ventriculoperitoneal (VP) shunts with about one-third of those infants requiring a VP shunt after discharge from the NICU. The follow-up team should involve the primary care physician and the neurosurgical teams. Monitoring head circumference is very important; lack of head growth is equally as worrisome as increased growth. The caregivers of infants who have VP shunts should be taught to evaluate for shunt malfunction, obstruction, and signs of increased intracranial pressure, infection, and the need for urgent physician evaluation if concerned.

Ischemic and hemorrhagic strokes occur as vascular accidents related to hypoxic-ischemic encephalopathy, complications of ECMO, clotting disorders, or tumors. An initial evaluation, often occurring in the NICU, consists of laboratory draws for proteins C and S, factor V Leiden, homocysteine deficiency, and antithrombin III deficiency. Some of these levels are difficult to interpret during illness and during the newborn period. These patients are often referred to subspecialty hematology after discharge for a repeat of these studies.

Retinopathy of Prematurity, Myopia, Amblyopia, and Esotropia/Exotropia

The incidence of retinopathy of prematurity (ROP) increases as gestational age and birthweight decrease. Recent studies estimate the rate of severe ROP at 20% to 30% in those infants born at ≤24 weeks’ gestation. Overall, the incidence of severe ROP for 24- to 28-weeks’-gestation premature infants is ~7%. Despite the incidence, the need for invasive therapy is relatively low. In a recent analysis, only 7.7% of those infants diagnosed with ROP required laser surgery and 0.25% required scleral buckle or pars plana vitrectomy.

In the outpatient setting, the most important aspect of ongoing care is an understanding of the urgency of the first ROP follow-up appointment, especially when the state of the retina is uncertain or the infant has received ROP treatment. In cases in which timely follow-up is needed, there are retinal clinics that file with the state Department of Children and Family Services when families fail to make these appointments. However, if the first follow-up examination is less urgent (generally 3–6 months after discharge), assisting the families with timely reminders and referrals continues to be important.

Premature infants without ROP are still at risk for other ophthalmologic issues such as loss of visual acuity, errors of refraction, and strabismus. After 12 months’ adjusted age, every infant born at ≤32 weeks’ gestational age is sent for a formal ophthalmology examination with a general ophthalmologist. They can help determine the need for patching, glasses, and corrective muscle surgery.

For children who have complex vision problems (including partial blindness, severe myopia, and nystagmus), the child should be evaluated by a vision therapist and referred for vision therapy, both of which can help in the developmental rehabilitation of the infant. Many community organizations such as Lighthouse International can help with locating providers and services.

Hearing Loss

Hearing loss occurs in 0.7 to 1.5% of NICU graduates for reasons related to long-term ventilation, amino-glycoside use, ECMO, hyperbilirubinemia, central nervous system complications, and postnatal complications related to prematurity. It is imperative that these infants undergo audiometric testing by the NICU staff during the infant’s NICU stay.

The incidence of otitis media requiring treatment in the NICU is less than 3% for infants born at >32 weeks’ gestation. Very preterm infants known to have IVH or PVL have a higher rate of cerebral palsy. Infants who have bilateral cystic PVL have cerebral palsy rates as high as 75%.
Although thickened feedings are common practice, the consideration in healthy infants corrected past their due date. A screening automated brainstem response test or an otoacoustic emissions test should be performed at NICU discharge because infants who receive therapy have improved language skills, school performance, and occupational performance. Any referred infant should be sent (through the state universal hearing referral system) to a pediatric otolaryngologist. Attentive follow-up is necessary for any infant who fails hearing screening examinations. Many of these children will require sedated screening testing, temporal bone CT studies, tympanostomy tubes, and amplified hearing assistance. Profound deafness is uncommon, but when it is identified, cochlear implantation is a possibility, and early referral is important.

Among high-risk infants, even when a normal hearing screen is obtained at the time of discharge, common practice is to rescreen high-risk infants every 6 months until the age of 3 years. Factors associated with high risk include: very low birth weight, NICU hospitalization for more than 5 days, ECMO course, mechanical ventilation, exposure to ototoxic medications (ie, loop diuretics, aminoglycosides), hyperbilirubinemia that required exchange transfusion, TORCH (toxoplasmosis, other infections, rubella, cytomegalovirus infection, and herpes simplex) infections, craniofacial anomalies around the ear, congenital syndromes associated with hearing loss (eg, Usher, Alport, Pendred, Hunter, Stickler), and culture-positive meningitis. (27)

Gastroesophageal Reflux Disease and Dysphagia

About one-half of all infants have at least 1 episode of regurgitation per day reported in the first 3 months after birth. (28) Preterm NICU graduates and infants who have neurologic impairment, BPD, or esophageal atresia are at higher risk for GERD. (29) Treatment should be considered when a child continues to have spitting up, back arching, and tight shoulder posture that impedes feeding volumes, making weight gain difficult or increasing irritability.

Recent AAP guidelines emphasize lifestyle modification as the starting point for GERD management. (30) Because milk protein allergy can mimic GERD, switching to a hydrolyzed protein formula or having breastfeeding mothers exclude milk and egg from their diet can be a good starting point. Thickening feeds with 1 tablespoon of rice cereal per ounce of formula can also be considered in healthy infants corrected past their due date. Although thickened feedings are common practice, the generalist should be aware that in preterm infants, there has been concern regarding an association between thickened feeds and necrotizing enterocolitis. (31) Families should be reminded that prone or side-lying positioning is not recommended in sleeping or unobserved infants. (30)

Medical therapy for GERD should be approached cautiously on both an inpatient and outpatient basis for premature infants. Neonatologists are growing cautious with inpatient treatment of reflux-related events. Outpatient practitioners can evaluate the risks and benefits of treatment in conjunction with consultation with gastrointestinal specialists.

Dysphagia is prominent among patients with complex conditions. In addition to ongoing feeding supports through speech therapy, patients often have supplemental nasogastric tube or gastrostomy tube feeding. The timing and removal of gastrostomy tubes is complicated. A stepwise approach is needed and starts with a feeding specialist’s evaluation which indicates that the infant is ready to try oral feeding. An oral-pharyngeal motility test is then used to determine if the infant is aspirating liquid. If results of the test indicate that it is safe, feeds are then slowly advanced.

Parent comfort, understanding, and compliance are key elements in the arena of dysphagia and gastrostomy tube management. Education is needed to teach parents about granulomas, the need to change the gastrostomy tube about every 3 months, gastrostomy tube leaks, and what to do when the gastrostomy tube is accidently dislodged.

Parenteral Nutrition–Associated Liver Disease

Parenteral nutrition–associated liver disease is defined as an elevated conjugated bilirubinemia level (≥2.0 mg/dL) that reflects liver dysfunction related to parenteral nutrition. Infants at the highest risk for this disease are those less than 750 g birthweight and those who have gastroschisis or jejunal atresia. (33) Once parenteral nutrition is stopped, both the conjugated bilirubin and alanine aminotransferase levels will slowly normalize. If the infant was discharged from the hospital on ursodiol, it is discontinued with the normalization of these laboratory values, typically within 2 to 3 months.

Osteopenia

Osteopenia of prematurity is related to both low gestational age and prolonged need for intravenous nutrition. Some studies report pathologic fractures in ~ 30% of preterm infants with osteopenia. (34) These infants have many risk factors, including nonweight-bearing, long-term ventilation and exposure to furosemide, postnatal...
steroids, and antibiotics. Typical preterm NICU graduates have elevated alkaline phosphatase levels, with a range of 400 to 600 IU/L, and require vitamin D supplementation. The AAP recommends that all breastfed, partially breastfed, or formula-fed infants taking less than 1,000 mL of vitamin D–fortified milk per day should take 400 IU of vitamin D daily. (35) Some sources recommend up to 1,000 IU for preterm infants. In addition, for non-breastfed infants, the use of a preterm formula provides additional calcium and phosphorus compared with standard formula.

Atypical elevations (alkaline phosphatase more than 650 IU/L) require the aforementioned supplementation plus oral calcium and phosphorus supplementation. Goals for calcium supplementation range from 60 to 90 mg/kg per day; however, most infants need 100 to 160 mg/kg to reach adequate bioavailability. The goal of phosphate supplementation is 60 to 90 mg/kg per day. (34) These regimens are difficult in terms of preparation, in part because of precipitation of supplements when added directly to feedings. Assisting families with the schedule, preparation, and refilling of these prescriptions is important for compliance.

Another group of high-risk patients are those who have prolonged anticonvulsant use. The ongoing need for bone mineralization and maintenance can be overlooked when treating refractory or ongoing seizures. However, these patients may have the most ongoing difficulties with osteopenia. Referral to endocrinology specialists and awareness from the neurology team often helps prevent pathologic fractures.

Nutrition and Growth
Growth in the NICU and follow-up period is a critical factor in determining long-term outcomes. Poor growth noticed during follow-up visits should generate suspicion that medical, social, or economic factors may be affecting the infant’s health. The window for catch-up growth is critical in the first year of age; in particular, poor gains in head circumference in the first 8 months after birth indicate poor long-term outcomes. (36)

Both the National Health and Nutrition Examination Survey and the World Health Organization growth charts are reasonable to use for US infants. For premature infants, height, weight, and head circumference are adjusted for prematurity until the infant reaches a chronological age of 24 months.

For typically developing former premature infants born ≤28 weeks, premature fortified human milk or preterm infant formula (22 kcal/oz) can be used until 12 months’ adjusted age. Most commonly, a 22-calorie formula or human milk fortified to 22 kcal/oz by using preterm infant formula is used, but other caloric densities may be needed. One common strategy to fortify human milk is to use powered preterm formula. In uncomplicated cases, at 6 to 9 months’ adjusted age and with good growth, infants are sometimes transitioned to term formula, especially if cost and/or availability are issues. Regular parental education regarding the mixing of specialized formulas is important for compliance and safety.

Premature formula will provide additional protein, calcium, phosphorus, zinc, vitamins, and trace elements with the goal of providing additional growth. A 2012 Cochrane collaboration demonstrated that feeding “preterm formula” (≥80 kcal/100 mL and protein enriched 2.0 to 2.4 g/100 mL) was associated with increased weight, length, and head circumference at 12 to 18 months. It is unclear if these gains persist into later life or if neurodevelopment is positively affected. (37)

Hydrolyzed formulas can be difficult to obtain commercially. For any surgical or allergy-related complex protein intolerance, it is important to have nutritional and subspecialty supports for switching to hydrolyzed substitutes. Approximately 50% to 75% of infants who are on a hydrolyzed formula at NICU discharge can be transitioned to a term formula at 12 to 24 months of age. Between 25% and 50% of these infants require a specialized formula until 2 to 3 years of age.

Neurodevelopment
Any high-risk neonate should be referred to early intervention or the State 0-3 developmental program at the time of discharge. All NICUs should have a plan for following up and aiding an infant’s neurodevelopmental course.

Many screening tools can be used in the clinic for ongoing assessment. One simple screening tool is the Ages and Stages Questionnaire screening tool used to interview parents about development related to chronologic age. The Test of Infant Motor Performance and the Alberta Infant Motor Scale are often administered by physical therapists in the clinic to assess motor skills. The Bayley examination is used to assess motor, cognitive, and communication skills and can be administered over a 60-minute period by a trained practitioner. The Bayley Screening Tool is a modified shorter version of the same tool that can be administered by many different clinicians. The most important aspect of NICU follow-up care related to development is having a consistent system that can identify suspected delays and trigger referrals for a higher level of developmental service.
When developmental therapy is needed, equipment is also often needed. Finding appropriate referral sites for plagiocephaly helmets, ankle-foot orthotics, splinting devices, bath chairs, standers, and wheelchairs should be investigated when taking care of patients with complex conditions.

**Home Visits and Home Nursing**

Several studies have shown the benefits of home visits to NICU graduates. Meta-analysis indicates that families receiving home visits had an increase in motor disability index and improved interaction between parents and their infant. (38) Many agencies, such as the Adverse Pregnancy Outcomes Reporting System, Early Intervention, and the Division of Specialized Care for Children, offer home visits, case management, social work, and nursing supports to NICU graduates.

**American Board of Pediatrics Neonatal–Perinatal Content Specifications**

- Know the management of apnea of prematurity.
- Know the management of bronchopulmonary dysplasia/chronic lung disease.
- Know the immunizations recommended by the American Academy of Pediatrics and the appropriate schedules for immunizing preterm and term infants.
- Understand the management and prognosis of neonatal seizures.
- Know the approximate risk of cerebral palsy in very low birthweight, moderately low birthweight, and normal birthweight infants.
- Know the prenatal, perinatal, and neonatal risk factors for the development of cerebral palsy.
- Know the types of visual impairments other than retinopathy of prematurity associated with prematurity.
- Know the incidence of bilateral moderate or severe sensorineural hearing impairment in high-risk infants, including those who have hypoxic–ischemic encephalopathy, persistent pulmonary hypertension, or congenital infections.
- Know the prenatal, perinatal, and neonatal risk factors (causes) associated with the development of hearing impairment.
- Know the indications for, the complications of, and surgical management of tracheostomies.

**References**

8. Cristea AI, Carroll AE, Davis SD, Swigonski NL, Ackerman VL. Outcomes of children with severe bronchopulmonary dysplasia who were ventilator dependent at home. Pediatrics. 2013;132(3):e727–e734


Educational Gaps

1. The extent and complexity of prematurity is creating a larger landscape of medical and developmental needs from birth to age 18.
2. Developmental trajectories for former premature infants are increasingly known and modifiable.
3. Social and legal supports for families with premature infants can change developmental trajectories.

Abstract

The responsibility for the medical and developmental care of the premature infant falls to the neonatologist, the general practitioner, subspecialists, and therapists, as well as the family and available community resources. This article reviews the landscape of developmental delays among former premature infants and offers a framework for screening and addressing these delays in infancy and early childhood. A holistic approach to developmental delays, especially with regard to public benefits, can mobilize resources early to assist families and shape the environment for the child both at home and at school. The medical and developmental team working together can improve the developmental trajectory of a child.

Objectives

After completing this article, readers should be able to:

1. Understand the multifaceted nature of developmental, physical, and learning delays associated with preterm birth.
2. Discuss the types and frequency of delays that occur.
3. Offer strategies rooted in developmental advocacy to improve outcomes of infant(s) after hospitalization.

Background

Worldwide there are 15 million preterm births per year. (1) In the United States, 480,000 infants are born at less than 37 weeks and 80,000 are born at 32 weeks’ gestation. (2) A collaboration including the World Health Organization recently published “The Global Action Report on Preterm Birth,”* which stresses careful attention and early identification of impairment and other follow-up issues. (1) This mirrors the American Academy of Pediatrics’ (AAP) policy statement regarding the discharge of high-risk neonates (3) despite the different challenges facing premature infants at the local, national, and global levels.

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Beyond the medical issues that permeate the care of the former premature infant, the long-term neurodevelopmental concerns are often far reaching. The rates of impairment in premature infants have been documented by four major international studies: EPICure (4) from Great Britain and Ireland for infants born in 1995, the Australian Cohort study for infants born in 1997, (5) the NICHD study of infants born from 1998 to 2001, (6) and the EPIPAGE study of French infants born in 1997. (7) Others have chronicled the persistent effects of prematurity on adolescence and young adulthood. (8) It is these survivors of NICU care that account for 40% of children who have cerebral palsy (CP), (9) 25% of children with hearing impairment, (10) and 35% of those with vision impairment. (11)

Infants born at the border of viability (between 22 and 25 weeks’ gestation) seem to have similar rates of impairment and degree of impairment among survivors, (4) (12) but predicting long-term outcomes for the current cohort of preterm infants remains difficult. Continued changes in neonatal intensive care unit (NICU) care mean that impacts can be only anticipated but are not fully known until 15 to 20 years later. Child, adolescent, and adult functioning is difficult to map to a specific individual based on a cohort of individuals. Protective factors, such as maternal education and higher socioeconomic position, also modify risk for some premature infants.

Motor Function
Overall, 7% of surviving infants born at less than 1,500 gms birthweight have CP. As gestational age decreases, the risk of CP increases. Substantial intellectual disability (IQ < 50–55) occurs in less than 5% of very low birthweight (VLBW) infants and is most often associated with quadriplegic CP. Although CP is a well-known developmental outcome of prematurity, many parents and practitioners are not aware that the diagnosis of CP only accounts for a portion of those with delays. The Table (13) (14) (15) (16) describes the outcome risk of CP and developmental delay by birthweight.

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<th>Birthweight, g</th>
<th>Risk for Cerebral Palsy, %</th>
<th>Risk for Developmental Delay, %</th>
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</table>

Motor delays are the earliest objective measure of an infant’s overall condition. (17) Two well-established motor tests are the Test of Infant Motor Performance, (18) used for infants 82 weeks’ corrected gestational age to 4 months and the Alberta Infant Motor Scale (19) used to detect delayed motor performance at adjusted age 6, 9, and 12 months. The Test of Infant Motor Performance shows 80% diagnostic agreement with the Alberta Infant Motor Scale. (20)

The General Movement (Fidgety) assessment is a new tool that aids providers in the detection of early normal and abnormal infant movement patterns. (21) Infants are videotaped and their typical movements are analyzed using the General Movement Toolbox software or a trained practitioner. The toolbox software uses variables derived from a calculation of pixel displacement from frame to frame. Generalized movements, described as either writhing (33 weeks to 7 weeks post-term) and fidgety movements (8–17 weeks post-term), are characterized as normal or abnormal. Those infants with generalized movement patterns devoid of complexity and variation are most at risk for CP.

At adjusted age 4 months, the Bayley Scales of Infant Development (22) (BSID) can be used to detect cognitive, motor, and speech/communication delays. The test has been widely used and has two versions: the BSID II and III. The BSID III expands the psychomotor component (or Psychomotor Developmental Index [PDI]) to include gross and fine motor components and separates the cognitive (or Mental Developmental Index [MDI]) from the expressive/receptive language components. The BSID III classifies fewer children above and below two SDs of the mean than the BSID II. (23) (24) The BSID is typically used at adjusted age 4, 12, 18, and 24 months to evaluate for delays.

Neuroimaging
Objective measures of preterm neurodevelopment can include head ultrasound (HUS), computed tomography, and magnetic resonance imaging (MRI), and the choice of modality varies among centers. Very preterm and VLBW infants have an overall reduction in brain volume. (25) HUS sensitivity for predicting long-term developmental outcomes is poor; however, specificity is good and it is an inexpensive, well-tolerated modality. A normal HUS is only 60% predictive of normal neurodevelopment, yet an abnormal HUS, grade III/IV intraventricular hemorrhage or periventricular leukomalacia, is 90% predictive.
of some neurodevelopmental delay. (26)(27) Using MRI, mild, moderate, and severe white matter changes correlated with cognitive delays in 15%, 30%, and 50% of patients who have severe cognitive delay. Those with moderate to severe white matter lesions had a 9.5 to 10.5 times increased risk of severe psychomotor delay or CP. (28) Diffuse white matter injury seen on MRI is predictive of CP in preterm infants. (29)

Cognitive Delays
As children grow older, different domains can be tested by using standardized measures, such as the Wechsler Preschool Scale of Intelligence (30) or Wechsler Intelligence Scale for Children (31) Standardized Behavior and adaptive questionnaires, as well as screening tools for autism, including the Modified Checklist for Autism in Toddlers (32). In addition, assessments of gross motor, manipulative, communicative, and adolescent functioning include the Gross Motor Classification System, (33) the Manual Ability Classification System, (34) the Communication Function Classification System, (35) and the Child Health and Illness Profile Adolescent Edition, (36) as well as evaluations for psychological functioning, attention, behavior, and conduct. When parents find that a child is not functioning well in a specific domain, the goal of the clinician is to recognize the concern, evaluate it, and establish resources to meet the needs of the child.

The pathway to this solution can involve many different types of assessments and interventions. The AAP recommends (37) that for former premature infants between ages 0 and 3 years, a formal developmental evaluation be performed at least once between 9 and 18 months corrected age and within 2 months of a suspect or abnormal developmental screening test. Often when formal developmental testing is performed, a battery of tests are done to fully represent the strengths and weakness of the child.

School readiness is a construct used to understand how a preschool child entering kindergarten is functioning in relation to the goals of the learning classroom. Domains that are included in school readiness include health, physical development, emotional well-being, social competence, approaches to learning, communication skills, cognitive skills, and general knowledge. (38) In a group of preterm infants from Melbourne, Australia, the standard scores in all domains of school readiness were 0.5 to 1.0 full SD below those of term infants. (39)

Behavioral Delays
In a large meta-analysis of studies from 1980 to 2001, premature infants had cognitive and behavior outcomes evaluated after their fifth birthday. Both cognitive and neuro-behavioral outcomes are correlated with decreasing gestational age. Preterm infants were found to have an increase in externalizing (ie, impulsivity, hyperactivity, oppositional behavior) or internalizing (ie, depression, anxiety) behaviors. (40) A second later meta-analysis echoed these findings and showed that both birthweight and gestational age were correlated with internalizing and externalizing behavioral disorders, poor academic performance, and worse executive function (ie, verbal fluency, working memory, and cognitive flexibility). (41) In the Manual Ability Classification System-5 study, evaluating the impact of antenatal corticosteroids, 1615 infants had a 5-year follow-up that showed a 13% incidence of neurocognitive or neurodevelopmental disability that was defined as more than 1.5 SD from the normal values. (42) A recent meta-analysis found verbal fluency, working memory, and cognitive flexibility were significantly poorer in children born very preterm. (41)

In a study of 261 infants whose birthweight was less than 1,000 g when evaluated at 8 years of age, Hack et al (43) found that, compared with controls, preterm infants had an increased risk of generalized anxiety, autistic disorder, Asperger disorders, and specific phobias. Seven infants in this group fulfilled the criteria for either autistic or Asperger disorder; one child was diagnosed with pervasive developmental disorder. Fifteen percent of infants who did not fulfill full criteria were reported to have symptoms coding for autistic or Asperger disorder “often” or “very often.” A retrospective review of almost 200,000 infants born in Northern California showed that the prevalence of autism spectrum disorders was higher in all preterm infants (1.78%) compared with term infants (1.22%). Infants born before 27 weeks were also found to be three times more likely to have a diagnosis of autism spectrum disorder compared with term infants. (44) An upcoming challenge will be to convert research done by using Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria to the new Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, which now uses the umbrella term “autism spectrum disorder” and is then further divided into different severity levels. (45)

A Swedish study looked at former 23- to 25-weeks gestation infant’s behavior and social developments at age 11 years. The authors found that parents and teachers reported increased internalization and social problems. The authors also reported an increase trend in self-reported feelings of depression. (46)

Several meta-analyses have shown an increased risk of attention deficit/hyperactivity disorder in preterm infants.
Hearing Impairment

Early detection of hearing impairment is vital to maximizing future linguistic and literacy potential in children. Speech delay can often be the first indication that there is a deficit in hearing. Key milestones to note include the absence of babbling by 9 to 12 months or lack of speech by 12 months. According to the AAP policy, all infants should have their hearing screened by the age of 1 month, and if they fail, are entitled to more extensive hearing assessments. It is recommended that this reevaluation occur by no later than age 3 months, with a comprehensive evaluation of both ears by an audiologist. Once hearing loss is confirmed, intervention is recommended by no later than age 6 months. For infants born at less than or equal to 32 weeks, audiology assessments every 6 months is used for surveillance until age 3 years. For those without risk factors, regular surveillance at well-child visits with their primary care physician is advised.

Vision Impairment

Vision impairment is common among preterm infants: 25% go on to have strabismus. After the initial retinopathy of prematurity (ROP) period is stable, infants with any ROP should have a vision screening yearly starting at adjusted age 9 to 12 months. Myopia is more often identified in infants who had a history of an active stage of ROP when laser or bevacizumab treatment was required. Two-thirds of patients who had prethreshold ROP are myopic in the preschool and early school years. At age 10 years, preterm infants were four times as likely to have significant refractive errors compared with full-term controls. For those infants who did not have laser-treated ROP or regressed or no documented ROP, a verbal vision screening (verbal identification of symbols, pictures, or letters) at 3 to 4 years is appropriate.

Feeding Delays

Feeding delays often prolong NICU hospitalization for both preterm and term infants with either congenital anomalies or intensive physiologic illness. Some children will go home using a gastrostomy or nasogastric tube for a portion of their feedings. In addition, human milk or formulas are often enhanced in calories or thickness when some of the feedings are by mouth. Connections to outpatient swallowing therapy with the availability of fluoroscopy evaluation (oropharyngeal motility studies) are important in the discharge of a neonate with early dysphagia.

Developmental Supports

Infant and toddler developmental assessment resources are through hospitals, pediatric practices, state 0- to 3-year-old developmental programs (Early Intervention [EI]), and Head Start programs. The AAP policy statement on NICU discharge advocates for appropriate neurodevelopmental, subspecialty, home nursing, and parental support and that appropriate referrals have been made. Individual states often have laws that support this policy statement.

Nationally, all 50 states participated in federally funded EI programs, Part C of the Individuals with Disabilities Act, and in 2012, 333,982 eligible infants and toddlers (0–3 years) received services. Each state individually determines eligibility for preterm infants. Referrals for EI services also can be made at any time a delay is detected or a medical condition that typically results in delay is diagnosed. Once a referral is made to an EI program, a multidisciplinary team assessment is made. EI evaluators determine the extent of delays in a number of domains: physical, gross and fine motor, hearing and vision, cognitive, social emotional, speech/feeding, nutrition, adaptive skills, and social circumstances.

Resources for eligible families are provided mostly in the form of direct and consultative therapies. In the United States, approximately 87% receive services in their homes, 7% are community based, and 6% are in other settings.

The Figure is a diagram indicating how participation in EI services directly benefits families’ access to other benefits and community supports.

The ideal setting for EI services is the child’s home. However, once a child turns 3, the developmental home of the preschooler becomes the local school, and outpatient services are adjunctive. As the provision of services shifts from concrete functions, such as sitting, walking, and talking to the complex arena of creating young learners, the child is typically transitioned to a learning environment with special educational services and support. It is important for the NICU follow-up team and EI to assist with this important and often daunting transition for children and families. It is intervention during the 2 preschool years that paves the way for school readiness in kindergarten and grade school.

The US Department of Education protects students with disabilities under Part B of the Individuals with
Disabilities Education of the Rehabilitation Act of 1973. The law requires a school district to offer a “free and appropriate public education” to each student with a disability. A school will often create an individualized educational plan or program recognizing a child’s needs for special education. This can be done from preschool at age 3 to young adulthood based on the IDEA provision in the law.

Physiatry

Modifiable aspects of development are best improved by continuous and intermittent intensity therapies and supports. Orthosis for plagiocephaly has a window of 6 to 18 months corrected gestational age. Plagiocephaly is more common among those with developmental delays, multiple gestation, and prematurity. It often coincides with torticollis. Treatment uses both helmeting and physical therapy, overall positioning, and engagement. (53)

Ankle-foot orthotics and superior malleolar orthotics support the stretching of the heel cord and the ankle alignment to promote relaxed motion through the calf, ankle, and foot for stable and easy gait. Children with spastic diplegia often start with this type of positioning and can progress to the need for serial casting or botulinum toxin therapy.

Preterm birth impairs the infant’s stress response due to interruption of autonomic nervous system development. Premature infants demonstrate prolonged and aberrant sympathetic response to stressors. Autonomic nervous system development may be promoted by close skin-to-skin care with a caregiver, as in kangaroo care, (54) and massage can improve the infant stress response (55) and improve weight gain. (56)

For those with sensory and communication delays, occupational therapists can teach parents and modify attention by using pressure manipulations and stimulation systems to improve cognitive attention. These approaches can be used across a spectrum of delays, from modest to severe. In the most formal of approaches, the Applied Behavioral Analysis, therapists are intensely involved with children with autism working toward ideal learning and social behaviors.

Advocacy and Public Benefits

Public benefits are often a lifeline for former premature infants. In the United States, low-income families that qualify for Supplemental Security Income (SSI) benefits can receive up to $721 per month in 2014. Families also may access additional specialized Medicaid programs, such as state home- and community-based waiver programs that are designed to keep children who have severe disabilities out of institutional care. These waiver programs can be used for additional supports, such as home ventilators, home dialysis, and other nursing and equipment needs. Often the parents of former premature infants need to interface with the Department of Health and Human Services, Social Security Administration (SSI), durable medical equipment companies, compounding or specialized pharmacies, and public human services programs to provide income and other supports, such as the Supplemental Nutrition Assistance Program, Temporary Assistance for Needy Families, and Women, Infants, and Children. The provision of all necessary services for a former premature infant can allow the parents to work outside the home, provide housing, developmental, and educational supports to their children and to pursue the goals they had before giving birth to a medically complex child.

Medical Legal Partnerships (MLPs) have strong roots in pediatrics with the first Medical-Legal Partnership for Children (MLPC) born at Boston Medical Center in the 1990s. The first comprehensive MLP research study “Project Access: A Medical, Legal, and Case Management Collaboration” was implemented in Chicago. Project Access followed VLBW NICU graduates for 12 months post-NICU, providing direct legal advocacy and case management and concluded that most families had between three and five unmet legal and case coordination needs, regardless of income. (57)
MLPs provide legal advice and advocacy at both the individual and systemic level. Individual advocacy includes appealing the denial of public benefits, tenant’s rights, access to SSI, support for specialized equipment, lead abatement, implementation of EI services, and advocacy in the school system for special education. Legal advocacy is increasingly available in NICU follow-up clinics: MLPs provide legal care in 119 hospitals and 112 health centers in the United States (www.medical-legalpartnerships.org). Systemic advocacy typically emerges through legislative action to change infrastructure and implement improved and timely services for vulnerable children.

Conclusion

The discharge and developmental follow-up care of former premature infants should be coordinated and comprehensive. The scope of the care of these infants is broad, ranging from medical intervention to implementation of special education to serve the varied spectrum of typical and atypical delays that are seen in this population. Increasingly, unique systems, such as legal advocacy, may help patients obtain the necessary supports they need to thrive.

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American Board of Pediatrics Neonatal-Perinatal Content Specifications

• Know the approximate risk of cerebral palsy in very low birthweight (VLBW), moderately low birthweight, and normal birthweight infants.
• Know the incidence and range of severity of cognitive impairment in the general population and in high-risk groups, including infants with extreme prematurity, or intrauterine growth restriction.
• Know the pattern of development delays that suggest hearing loss in infants and understand the consequences of hearing impairment on development.
• Know the value and limitations of the Bayley Scales of Infant Development (BSID) and other tests of psychomotor development.
• Know the rationale for early intervention programs for infants at risk for cognitive and behavioral problems.

References

52. Technical Assistance and Dissemination Network. Number of infants and toddlers ages birth through 2 and 3 and older, and percentage of population, receiving early intervention services under IDEA, Part C, by age and state: http://ectacenter.org/partc/partcdata.asp. Accessed April 22, 2014
53. Xia JJ, Kennedy KA, Teichgraeber JF, Wu KQ, Baumgartner JB, Gateno J. Nonsurgical treatment of deformational plagiocephaly:


Parent Resources From the AAP at HealthyChildren.org

- English: http://www.healthychildren.org/English/ages-stages/baby/preemie/Pages/Watching-for-Complications.aspx
- Spanish: http://www.healthychildren.org/English/ages-stages/baby/preemie/Pages/Watching-for-Complications.aspx
- English: http://www.healthychildren.org/English/ages-stages/baby/preemie/Pages/Preemie-Milestones.aspx
NICU Follow-up Care: The Developmental and Advocacy Perspectives
Bree Andrews, Patrick Myers, Paula Osterhout, Matthew Pellerite, Amy Zimmerman and Michael Msall
NeoReviews 2014;15:e336
DOI: 10.1542/neo.15-8-e336

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NICU Follow-up Quiz

1. **Define the following terms:**
   a) Premature Infant:
   b) Late Preterm:
   c) Low Birth Weight (LBW):
   d) Very Low Birth Weight (VLBW):
   e) Extremely Low Birth Weight (ELBW):
   f) Chronologic or Post-natal age:
   g) Corrected Age:

2. Most cases of **bronchopulmonary dysplasia** occur in infants with birth weights __________ and who are born at a gestational age _____________.

3. List **pulmonary complications** associated with BPD:
   a) 
   b) 
   c) 
   d) 

4. For infants with **BPD**, maintaining O2 saturations of _________ may have beneficial effects such as promoting growth, reducing the frequency of central apnea, and reducing the transient elevations in pulmonary artery pressures associated with intermittent hypoxemia.

5. All premature infants should be immunized based on their ________________ age, regardless of their weights and gestational age at birth.

6. **Bonus Question (requires independent research):**
   Fill in the blanks regarding the **nutritional content** of 1 liter (=33.8 oz) of each of the following:
   **Term Human Milk** (estimates)
   _____ kcal   _____ g protein   _____ g fat   _____ mg Ca   _____ mg P   _____ mg Fe

   **Enfamil Lipil**
   _____ kcal   _____ g protein   _____ g fat   _____ mg Ca   _____ mg P   _____ mg Fe

   **Neosure**
   _____ kcal   _____ g protein   _____ g fat   _____ mg Ca   _____ mg P   _____ mg Fe
NICU Follow-up Mega-Case

You are seeing Michael, a 6 month-old former 24 wk EGA preemie, whose family recently PCS’d from Hawaii. Per his AHLTA record, his NICU course was significant for intubation for over 6 weeks, bilateral grade III IVH, and bilateral stage III ROP that was treated with Avastin. He was 600g at birth. His mother brings him in for his 6-month well visit and to establish a PCM. Only parental concern today is wheezing and nasal congestion that he has had for the last 24 hours. Per his mom, she has not seen any increased work of breathing and denies any fevers.

What other questions would you ask regarding Michael’s history?

According to his mother he was discharged at 3.5 months of age on 0.5L of NC O2, diuretics, and a monitor. Two weeks ago prior to leaving Hawaii, he was taken off of supplemental oxygen by his previous PCM after one month of a slow wean and lack of significant events on his monitor. He received his first dose of Synagis 1 month ago for RSV prophylaxis. Mom reports that he was fed primarily fortified breastmilk after NICU discharge, but that she ran out of the fortifier packets that she had been provided with, and so now is feeding exclusive, non-fortified breastmilk. On exam today, he has diffuse wheezing on auscultation but no increased work of breathing, and his pulse oximetry shows that his SpO2 is consistently around 98% on room air.

Given his history of chronic lung disease, what would you do for his respiratory symptoms today? Are any referrals needed?

Review the indications for use of Synagis (Palivizumab) for RSV prophylaxis:

- See 2018-2019 Guidelines in Extra Credit Materials (note there is a 2019-2020 version, but guidelines are unchanged)

After giving him a trial of Albuterol in clinic you notice that he has improved air movement and decreased work of breathing on exam. You place a pulmonology consultation and decide to send him home with an Albuterol MDI after spacer teaching.

You then move on to plot his growth curve. **Which growth curve(s) should you use?**
Having selected the appropriate growth curve, **what is Michael’s gestation-adjusted age?**

![Growth Curve](image)

Michael’s weight today is 3.4kg. After plotting his growth curve (*see above*), you notice that his weight gain has started to plateau since discharge from the NICU. His length and head circumference are tracking appropriately. Per his mother he is breastfed 3 times daily, mostly at night. (She estimates that he receives 4oz of milk when he nurses) and takes 4, 4oz bottles of expressed breast milk via a bottle during the day. Michael has not been started on solid foods yet.

Estimate Michael’s average daily fluid (ml/kg/day) and caloric (kcal/kg) intake.

What may be contributing to his decreased growth velocity? What can you do to increase his caloric intake and nutritional status?

What further recommendations would you provide for his ROP and his development?
1. You are discussing infants who have low birthweights on rounds with your residents. You remind them that some low-birthweight infants (<2,500 g) are born at term, after completing 37 weeks’ gestation, and are considered small for gestational age (SGA). Other LBW infants are born preterm, and their LBW status simply reflects this.

Of the following, the MOST likely outcome for term SGA infants is
A. head growth at 6 months postnatal age that lags behind weight and linear growth
B. linear growth that reaches the 50th percentile at 6 months postnatal age
C. more common neurodevelopmental impairment at 2 years postnatal age than seen in preterm IUGR infants
D. neurodevelopmental outcomes at 2yrs postnatal age compare favorably with term infants
E. prediction of school performance is better at age 5 years than 2 years

2. A term infant is delivered by emergency cesarean section following the acute onset of maternal vaginal bleeding and profound fetal bradycardia on electronic fetal heart rate monitoring. The Apgar scores are 1, 2, and 3 at 1, 5, and 10 minutes, respectively. Resuscitation includes intubation and assisted ventilation, chest compressions, and intravenous epinephrine. The infant is admitted to the neonatal intensive care unit and has seizures at 6 hours of age.

Of the following, a TRUE statement about infants who have seizures following perinatal asphyxia is that most
A. develop epilepsy
B. develop microcephaly
C. do not have severe long-term neurodevelopmental delay
D. experience hearing loss
E. require multiple anticonvulsant medications

3. A term infant is delivered by emergency cesarean section following the acute onset of maternal vaginal bleeding and profound fetal bradycardia. The Apgar scores are 1, 2, and 3 at 1, 5, and 10 minutes, respectively. Resuscitation includes intubation and assisted ventilation, chest compressions, and intravenous epinephrine. The infant is admitted to the neonatal intensive care unit and has seizures 6 hours after birth.

Of the following, a TRUE statement about other organ-system injury that may occur in the infant is that
A. cardiovascular injury is uncommon
B. hypoxic-ischemic encephalopathy usually is an isolated condition
C. liver injury may result in a coagulopathy
D. most infants who have seizures develop cerebral palsy
E. necrotizing enterocolitis does not occur in term infants

4. You are following a 3-month-old infant who was born at 30 weeks’ gestation, underwent a distal ileal resection for necrotizing enterocolitis at 2 weeks of age, and subsequently was placed on parenteral nutrition for 2 months. The baby has residual cholestasis from the parenteral nutrition (total bilirubin, 5.0 mg/dL [85.5 mcmol/L]; direct bilirubin, 3.0 mg/dL [51.3 mcmol/L]). Currently, she is receiving a cow milk protein hydrolysate formula concentrated to 24 kcal/oz (0.8 kcal/mL). You are considering adding a supplement to increase the caloric density.

Of the following, the supplement that is the MOST likely to be tolerated and cause less diarrhea is
A. flaxseed oil
B. medium-chain triglyceride oil
C. olive oil
D. omega-3 polyunsaturated fatty acid (fish oil)
E. soybean oil

5. An infant born at 34 weeks’ gestation comes in for her 1-month-old evaluation. Her neonatal course was uncomplicated. Her parents ask if she will have delayed development due to her prematurity.

Of the following, the MOST appropriate response is that healthy preterm infants
A. have age-appropriate language skills by the time they are 12 months of age
B. have an increased risk of mild motor impairment
C. born at 32 to 36 weeks’ gestation have a fourfold increase in intellectual disabilities
D. should have their developmental age corrected for the degree of prematurity until 4 yrs of age
E. show hand preference at an earlier age than term infants