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Approach to Prematurity Part II (Initial Stabilization and Short-Term Complications of Prematurity)

Developed by Jhanahan Sriranjan and Dr. Kristin Inch for PedsCases.com.
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Introduction

Welcome to Approach to Prematurity, Part II – Initial stabilization and Short-Term Complications of Prematurity.

This is the second part of a two-part video made for PedsCases.com. My name is Jhanahan Sriranjan and I am a medical student at the Michael G. DeGroote School of Medicine at McMaster University. This podcast was made in collaboration with Dr. Kristin Inch, a pediatrician practicing at the Special Care Nursery at St. Joseph's Hospital in Hamilton, ON.

Learning Objectives

If you haven't already, please check out part one of this podcast, where we provide an overview of prematurity.

In this podcast, we will be focusing on the initial stabilization of a premature infant, as well as provide the learner with a systems-based approach to managing common short-term complications associated with prematurity.

Back to our cases…

In Part I, we were introduced to 3 expecting mothers. Now, let's welcome to the world the children of Amy, Brintha, and Catherine!

Baby Boy Austin was born at 38 weeks gestation age and has a birth weight of 3.6kg. Baby Boy Austin has been feeding well and sleeping well and passed his meconium 6 hours after delivery.

Baby Girl Balakrishnan was born at 32 weeks gestational age at a birth weight of 1.6kg. She was admitted to the NICU, due to respiratory issues.

Baby Boy and Girl Chang were born at 35 weeks gestation, at birth weights of 2.0 and 2.2kg respectively. Baby Boy Chang has been getting very tired during feeds,

sometimes even struggling to breathe. Baby Girl Chang has been feeding fine but it is noted that she required resuscitation procedures immediately following delivery.

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You recall that Baby Girl Chang required delivery room resuscitation.

What are important considerations to consider in the initial stabilization of a premature infant?

Objective #4 – Initial Stabilization of a Premature Infant

Generally, neonates born prematurely are more likely to require resuscitation!

The Apgar is useful tool in determining if an infant requires resuscitation[1]. An Apgar score assesses a neonate's color, heart rate, reflexes, muscle tone, and respiration a quick assessment of newborn well-being. Apgar scores are reported at 1 minute and 5 minutes postnatally for all infants, then at 5-minute intervals thereafter until 20 minutes for infants with a score <7. Changes between 1 and 5 minutes are useful indications of responses to resuscitation measures.

However, in pre-term infants, the Apgar score is limited, as only muscle tone, reflexes, and respiration correlate well. In brief, there are 3 important questions to ask that can help you determine if resuscitation measures are necessary[2]:

1. *Does the infant appear full-term?
2. *Does the infant have good muscle tone?
3. *Is the infant breathing/crying?

If the answer to all three are YES, then there is no need for resuscitation and the infant should stay skin to skin with their mother. If the answer to one or more of these questions is NO, the child should be assessed by the Neonatal Resuscitation team and managed according to the NRP guidelines.

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There are four important issues to consider when stabilizing a premature infant[2]. The first important aspect of stabilization is assessment of the infant's airway and breathing. Inadequate ventilation is not uncommon in preterm infants. This results from surfactant deficiency and/or an immature respiratory drive, which can lead to apnea and poor respiratory effort. This is best signified by marked chest retractions and increased work of breathing, as blood gas evidence of inadequate ventilation is a late feature. Treatment begins with **supplemental oxygen**, to maintain oxygen at 45-80mmHg and O2 saturation at 90-95%. It is important to avoid hyperoxia, as this increases the risk for Retinopathy of Prematurity – more on that later. Moderate respiratory distress is treated with nasal CPAP, whereas more severe respiratory

distress, as indicated by increasing PaCO2, increasing oxygen requirement, or work of breathing, is treated using mechanical ventilation.
The second is hypothermia. Because of their low subcutaneous fat, large surface area: body size ratio, and thin skin, premature infants are predisposed to hypothermia. These neonates can be supported via Kangaroo Care, which involves holding the premature infant in a manner that involves skin-to-skin contact. The Canadian Pediatric Society endorses Kangaroo Care, as it is associated with improved cardiorespiratory and temperature stability, sleep organization, neurodevelopmental outcomes, and breastfeeding[3]. When the neonates are not with parents, they should be in an isolette depending on gestational age to ensure temperature stability.

Infections are a serious concern as well and may be classified as early onset (occurring within first 7 days of life) or late onset (symptoms begin at >7 days of age)[4]. The primary pathogens implicated in infections include Group B Streptococcus, Streptococcus agalactiae, and E. coli. Most infants with early-onset infections will present within first 12 hours of birth. Late onset infection is more common and is often caused by gram positive organisms. Treatment in both cases involves Empirical antibiotics, which are given to all preterm infants with signs consistent with sepsis, especially if they have specific risk factors such as prolonged rupture of membranes lasting greater than 18 hours.

Finally, premature neonates are vulnerable to certain organ system injuries because of their incomplete development. These will be discussed shortly.

Back to our cases…
Over the next few days, following initial stabilization, our 3 neonates from the NICU are transferred to the nursery. You will be following each of them closely in case any problems arise.

Objective #5 – Develop a Systems-Based Approach to Managing Complications of Prematurity

A systems-based approach may be useful in diagnosing the various short-term complications associated with prematurity. This is because different conditions have different timings of onset – for example respiratory and cardiovascular complications present earlier than gastrointestinal, neurologic, and hematological issues[2]!

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On her first day in the nursery, you notice that Baby Girl Balakrishnan appears irritable. She is making grunting noises, her nose is flaring, and she is starting to appear blue. Her vitals are: RR: 65, HR: 170, Temp (rectal): 37^{o}C, BP 79/43

Respiratory Complications

When it comes to the respiratory system, there are 3 major complications associated with prematurity to look out for.

The first is **Respiratory Distress Syndrome**, or RDS[2,5]. RDS is caused by a lack of surfactant production in utero, which typically occurs in the late 2nd or early 3rd trimester. Without surfactant, the lungs will have low compliance and high surface tension, which can lead to atelectasis. Symptoms include tachypnea, chest retractions, nasal flaring, grunting, and cyanosis. Appropriate imaging includes a CXR, which will reveal low volume lungs with fine granular opacities, commonly referred to as a "ground glass" appearance. Treatment of RDS begins with supplemental oxygen. In some cases, such as if the neonate is less than 35 weeks gestational age, exogenous surfactant replacement may also be indicated. As mentioned earlier in the podcast, antenatal glucocorticoids can be prophylactic for RDS, and are typically administered when the expecting mother is less than 34 weeks pregnant and delivery is likely in the next 7 days.

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The second complication is **Bronchopulmonary Dysplasia[2,5]**. BD is defined as oxygen requirement at 36 weeks corrected GA. It occurs most commonly in EPT infants with surfactant deficiency or immature lungs who require mechanical ventilation. BD can be caused by longer mechanical ventilation times but is generally considered multifactorial. BD is commonly associated with conditions later in life, including pulmonary hypertension, central airway disease, and frequent respiratory infections or asthma-like symptoms. Symptoms include pallor, tachypnea, chest hyper-expansion, chest retractions, crackles and wheezes on auscultation, fluid retention, heart failure, recurrent pneumonia, and failure to grow. Appropriate imaging includes chest x-ray, which reveals generalized opacification of lung fields, lung collapse, fibrosis, cystic changes, and overdistension of the lungs. Treatment of Bronchopulmonary Dysplasia typically involves a low flow nasal cannula, nasal CPAP, or mechanical ventilation to maintain 90-95% SpO2. Pharmacological therapies may be considered, such as inhaled bronchodilators or corticosteroids. The CPS does not recommend routine dexamethasone for all ventilated infants, but rather a short course of low-dose dexamethasone for infants at high risk of, or with severe chronic lung disease.

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Finally, **apnea of maturity**, which is defined as cessation of breathing for >20 seconds (or less when associated with desaturation and/or bradycardia), commonly occurs due to immature central respiratory control and weak respiratory muscles[2,5]. In term infants, this is always considered abnormal! Apnea spells typically occur within 1-2 days postnatally and can be regularly monitored. Most cases resolve by 37 weeks gestational age, but management beyond may include caffeine or theophylline.
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Recall that Baby Boy Chang was struggling with his feeds, sometimes turning blue during breastfeeding. On day 2 of his stay in the nursery, you note that he is blue again, and there are some changes in his vitals. His HR is 180, RR 64, BP 100/28, and Temp 37.4. Physical exam reveals a murmur on auscultation.

Cardiovascular Complications

The main cardiovascular complication of concern is a **Patent Ductus Arteriosus**, or PDA[2,5]. The ductus arteriosus is located between the pulmonary trunk and aorta, which in utero permits fetal circulation to bypass the high-resistance pulmonary vasculature and allow for systemic perfusion. At term, the ductus arteriosus functionally closes in 50% of infants by 24 hours and 100% by 72 hours of life, with anatomic closure occurring in the ensuing 2-3 weeks. However, in preterm infants this is delayed, which results in a left to right shunt, causing systemic hypoperfusion.

Preterm infants with a PDA often have tachycardia, tachypnea, carbon dioxide retention, widened pulse pressures (as signified by bounding pulses), a holosystolic murmur on auscultation, systemic hypotension (signified by low diastolic blood pressure), and may have hepatomegaly. Diagnosis can be established using echocardiography with pulsed color Doppler. Management to induce constriction of a PDA includes indomethacin, ibuprofen, and acetaminophen. Some fluid restriction may also be indicated, although strong diuretics such as furosemide are not recommended in the first one to two weeks of life. Finally, if medical treatment is ineffective, these infants may be candidates for surgical closure.

Gastrointestinal Complications

After her initial stabilization, Baby Girl Chang has been spending some time in the nursery. Her vitals currently are**: RR: 55, HR: 148, BP: 85/45, Temp: 35.9.** While early on she made some sporadic movements, you note that she appears very lethargic currently. Her abdomen appears to be distended and is tender to the touch. One of the nurses tells you she vomited just before you got there, and that there appeared to be a lot of bile in her vomit.

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The most common GI emergency in neonates is **Necrotizing Enterocolitis (NEC),** with significant morbidity and mortality[2,5]. NEC refers to ischemic necrosis of the intestinal mucosa, and is more common in infants, especially those who were oxygen deprived at birth. Although this case involves a 35-week old infant, NEC is generally inversely correlated with gestational age.

Neonates with NEC often have abdominal distension/tenderness, gastric residuals, bilious emesis, diarrhea, hematochezia, temperature instability, apnea, and lethargy. Labs may show thrombocytopenia, metabolic acidosis, hyponatremia, and unconjugated hyperbilirubinemia. Appropriate imaging for NEC includes abdominal X-

Ray, which reveals dilated bowel loops, thickened intestinal walls, inspissated stool, intramural air, and possibly air in the portal venous system. Management of NEC involves ensuring a patent airway and breathing, followed by IV fluids, NPO, nasogastric drainage, and antibiotics. These infants need to be monitored continuously for any further abnormalities, and any indicates of surgery.

Establishing oral feeds is a crucial aspect of recovery from NEC, as it is often the last hurdle premature infants have to overcome to be discharged from nursery.

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Several other systems may have complications associated with prematurity. This includes ophthalmologic complications, neurologic complications, metabolic complications, and hematologic complications

Ophthalmologic Complications

Retinopathy of Prematurity (ROP) is an important ophthalmological concern in neonates[2,5]. ROP may be triggered by hyperoxia (i.e. during initial stabilization), which causes inhibition of VEGF and restricts retinal vascular growth. However, subsequent hypoxia may lead to inappropriate and excessive growth of retinal vessels, as mediated by increased VEGF. This often results in poor visual acuity/blindness and poor neurodevelopmental outcomes later in life. ROP is a concern if birth weight is <1250g or GA is <30+6, and is typically identified at screening and is managed based on severity. In more severe cases, treatment may include laser photocoagulation or intravitreal injection of anti-VEGF to prevent inappropriate growth.

Neurologic Complications

The main neurologic complication of concern is **Germinal Matrix-Intraventricular Hemorrhage (GMH-IVH)[2,5].**

IVH occurs in about 25-30% of very low birth weight infants. Hemorrhaging occurs within the germinal matrix but may extend into the ventricle or parenchyma. The degree of parenchymal extension can be differentiated into three grades of GMH-IVH. GMH-IVH has a complicated, multifactorial pathogenesis, including impaired venous drainage. It should be noted however that the germinal matrix disappears at about 32 weeks gestation. Other risk factors for IVH beside prematurity include neonatal transport, respiratory distress, mechanical ventilation, hypotension, and resuscitation/intubation.

GMH-IVH can have some severe complications, including posthemorrhagic ventricular dilatation in 35% of cases, with possible evolution in about 22% to posthemorrhagic hydrocephalus. Of these infants, 9% may require the placement of a permanent shunt. Most infants with IVH are asymptomatic, but some may require increased ventilatory support or have abnormal neurologic signs such as seizures, apnea, bradycardia, or even shock. Diagnosis of IVH is done via crania ultrasound, which is routine for all

infants born <32 weeks GA. Management should focus on optimizing airway and breathing, maintaining circulation, treating seizures, and correcting any apparent coagulation abnormalities.

Metabolic Complications

The most common metabolic complication of prematurity is **neonatal hypoglycemia**[2,5]. As with hypothermia, premature infants may be predisposed because of their low-fat stores. They additionally have immature gluconeogenesis pathways, higher metabolic demands, and often poor oral intake.

Neonatal hypoglycemia may present with tremors, jitteriness, lethargy, poor feeding, apnea, cyanosis, weak cry, or seizures; however in many cases is asymptomatic. Diagnosis can be established when blood glucose is below 2.6mmol/L for the first 72 hours of life, then <3.3mmol/L beyond. Management focuses on increasing feeds or supplement. IV glucose and glucagon may be considered in severe cases. Some centres may also use a dextrose gel, depending on their specific protocol.

Hematologic Complications

Finally, we have two important complications associated with the hematologic system.

Anemia of Prematurity (AOP) is a common hematologic issue, caused by birth occurring before placental iron transport and fetal erythropoiesis are complete[2,5]. All neonates experience a decline in circulating RBCs during the first few weeks of life. Term infants are typically born with a hemoglobin value of 146-225, with a nadir of 100-120 by 8-12 weeks. Preterm infants have a deeper, faster nadir of 70-80 in 3-12 weeks. Clinical findings vary with the severity of anemia – if mild there may be no signs. In more severe cases, pallor, tachypnea, poor feeding, hypotension, tachycardia, apnea, lethargy, hepatosplenomegaly, and wide pulse pressure may be present. Diagnosis may be determined using CBCs and reticulocyte counts. Management may include transfusion in more severe cases.

Transfusion Thresholds (CPS):

CPS has recommended transfusion thresholds for pRBCs specifically for preterm infants, depending on their age as well as whether they require respiratory support or not[6].

In preterm infants without respiratory support, the recommended threshold for transfusion are hemoglobin levels of 100g/L at one week of life, 85g/L at two weeks of life and 75g/L at three weeks of life.

In preterm infants WITH respiratory support, the recommended thresholds are 115g/L, 100g/L, and 85g/L at one, two, and three weeks of life respectively.

Hematologic Complications

Unconjugated Hyperbilirubinemia and **Jaundice** may also occur because preterm infants have increased RBC breakdown, an immature hepatic system, and increased enterohepatic circulation[2,5]. If left unchecked, this may progress to bilirubin-induced neurologic dysfunction, such as kernicterus.

All infants are screened at 24-48 hours of age. It should be noted that almost all preterm infants <35 weeks GA have elevated total serum/plasma bilirubin. Use of nomograms can help determine if bilirubin levels are elevated. Management is primarily phototherapy, if the neonate is above the threshold based on age and risk factors. Other treatments may include RBC transfusion if hyperbilirubinemia is severe, and IVIG for ABO incompatibility when indicated.

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With that, we have now established a systems-based approach to managing some of the common complications of prematurity!

Learning Objectives

So, by now we have been able to define prematurity, evaluate risk factors for preterm birth, discuss differences between term and preterm infants, outline major issues of stabilization in preterm infants, and have developed a systems-based approach to evaluating some common complications associated with prematurity.

It should be noted that the effects of prematurity last a lifetime in many cases. Preterm infants are more likely to have increased hospitalizations and neurodevelopmental disabilities, especially Cerebral Palsy, impaired growth, hypertension, and CKD. These children and their families are also more likely to face social and emotional issues later in life, so it is extremely important to monitor these infants closely and support them the best you can.

This concludes this PedsCases podcast – Approach to Prematurity. Thank you for listening! If you have any questions or concerns, please feel free to email us at one of the emails listed here.

References

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