The Decompensated Neonate in the First Week of Life

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Financial Disclosure Statement

The authors have no financial relationships relevant to this article to disclose.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

Abstract

The first week of life can be a critical time period in which previously subclinical disorders may manifest causing significant illness. Newborn infants also have different baseline vitals and laboratory parameters, which complicates the initial evaluation of infants. Rapid identification of sick neonates, stabilization, and directed evaluation are key to minimizing long-term morbidity and mortality. This review targets five conditions that present in the first week of life: neonatal sepsis, critical congenital heart disease, inborn errors of metabolism, congenital adrenal hyperplasia, and hemorrhagic disease of the newborn. The primary focus is on key findings, initial evaluation, and immediate treatment in the emergency department where these infants often present after discharge from the nursery.

Keywords: neonate, shock, early-onset sepsis, late-onset sepsis, congenital heart disease, cyanosis, inborn errors of metabolism, congenital adrenal hyperplasia, hemorrhagic disease of the newborn, Vitamin K deficient bleeding

Many critical and potentially fatal illnesses can arise in the first week of life, making rapid and efficient evaluation and stabilization paramount in this population. Neonates often present with nonspecific findings and may decompensate quickly. It is vital that caregivers are able to recognize at-risk neonates, maintain a broad differential, and approach evaluation and management simultaneously and methodically. Diagnostic priority should be placed on ruling out immediately life-threatening etiologies such as sepsis, critical congenital heart disease, inborn errors of metabolism, endocrine crises, and hematologic emergencies.

RECOGNIZING THE CRITICALLY-ILL NEONATE

The evaluation and identification of at-risk neonates often occurs in triage before a physician sees the patient. The ability to identify abnormal initial history, appearance, and vital signs is key to appropriate triage and timely care. A change of behavior, noted by the family, is often the initial clue to impending decompensation.

A typical neonate sleeps approximately 15-18 hours per day,[1] awakening spontaneously every two to four hours for feeding. Parents should report 8 to 12 feedings of either formula or breast milk, with the infant taking at least two ounces or nursing for 10-15 min at the breast.[2-4] The infant should also have a minimum of 6-8 wet diapers in a 24-hour period.[4] Normal stooling patterns are variable; however, soft, seedy, yellow-to-green stools should be accepted as normal and any stools with blood, mucus, or that are clay-colored must be considered abnormal. Frequent spitting-up is a common complaint in this age group, as 2/3 of normal,

healthy infants have gastroesophageal reflux (GER). GER can be associated with vomiting of gastric contents, typically described as partially-digested breast milk or formula; however, reports of green-colored (bilious) or forceful (projectile) emesis requires further evaluation.[5]

Visual inspection of the infant can be quick and telling regarding the status of the neonate. A healthy neonate should appear comfortable, with a normal respiratory effort. Infants with significant respiratory distress will sometimes develop head bobbing. The infant should have flexed extremities with spontaneous movements. The infant's color should be pink to indicate adequate perfusion, although some infants may become mottled when unwrapped in cold environments. Mucous membranes, as well as palms and soles can be evaluated for color in darkly pigmented infants. The infant may not be vigorous if sleeping, but when presented with stressful stimuli, such as blood pressure measurement, should show signs of arousal.

Abnormal vital signs may be the key to identifying a baby in shock. Over the first days and weeks of life, infants' vital signs change dramatically and need to be understood based on referenced norms (Table 1). A rectal temperature is the preferred method of recording and should be between 36.5° to 38° C, or 97.7° to 100.4° F.[6] The normal respiratory rate of an infant is between 30 and 60 breaths per minute. Heart rate can vary depending on the neonate's sleep-wake status and activity level. Typically, a heart rate (HR) of 85-205 beats per minute (bpm) when awake and 80-160 bpm when sleeping is considered appropriate.[7] Blood pressure measurement may not be standard in initial emergency department triage of neonates, but is important in this population to determine hemodynamic stability. A systolic

blood pressure of 65-85 mmHg and a diastolic blood pressure of 45-55 mmHg is considered adequate for age.[8] A mean blood pressure that approximates the corrected gestational age of the infant can be used as a quick assessment of adequacy. After the initial transition period at birth, the normal oxygen saturation regardless of probe placement should be greater than 94%. Values outside the parameters listed in Table 1 should alert the caregiver that the infant requires immediate attention.

Initial labs and imaging can be obtained to support the evaluation of the sick neonate.

Preliminary labs can include a complete blood count, blood culture, blood gas, lactate, and complete metabolic panel. Chest and abdominal plain radiographs can be obtained for infants exhibiting signs concerning for respiratory or gastrointestinal disorders. Seizing infants or those with suspected intracranial processes should undergo neuroimaging including head computed tomography (CT) or magnetic resonance imaging (MRI). The utility of these studies are discussed further in this article.

NEONATAL SEPSIS

Infection can be a devastating and unfortunately common disorder in the first week of life, occurring in 1-5 neonates per 1000 live births.[9] Neonatal sepsis is divided into early-onset, occurring prior to 72 hours of life, and late-onset, occurring after 72 hours of life. Although the common bacterial, viral, and fungal pathogens vary depending on timing of presentation, Group B streptococcus (GBS), *Escherichia coli*, and herpes simplex virus (HSV) can be causative in both early and late-onset sepsis syndromes. Particular attention to risk factors for infection present

at birth may place infection higher or lower on the differential diagnosis. Risk factors include: maternal GBS colonization, history of chorioamnionitis during labor, prolonged rupture of membranes (greater than 18 hours), history of premature rupture of membranes, or maternal history of HSV.[10,11]

Presenting history and symptoms may be quite variable. Common presenting complaints include difficulty waking (lethargy), inconsolability, fever, hypothermia, poor feeding, poor tone, and signs of respiratory distress. Infants have the potential to progress from symptomatic to decompensated septic shock quickly so the workup should progress rapidly. When sepsis is suspected, a complete blood count (CBC) and blood culture must be obtained, and empiric treatment should be initiated without delay. Important indices on the CBC include the total white blood cell count, the mature (or segmented) neutrophil count, the immature (or band) neutrophil count, and the platelet count. Values outside the normal range for age for any of these indices may indicate the presence of an infection. Additionally, an immature-to-total neutrophil ratio > 0.20 can be a sensitive measure of infection, with a negative predictive value of 99%.[10] In addition to blood, urine should be obtained for analysis and culture. The remainder of the sepsis evaluation can be directed by history and the decision to perform a lumbar puncture can be based on clinical stability, as well as historical and clinical likelihood of meningitis.

If viral sepsis from HSV is suspected, the infant should have serum and cerebrospinal fluid samples sent for polymerase chain reaction assays. Many infants who acquire HSV at birth are

born to women who acquire genital HSV infection during pregnancy but are either asymptomatic or have nonspecific symptoms.[12] Additionally, HSV viral surface cultures from the conjunctiva, mouth, nasopharynx, and rectum should be obtained.

Timely empiric treatment with broad spectrum antibiotics is top priority in infants with suspected sepsis (Table 2). Routinely, ampicillin in combination with gentamicin or a 3rd generation cephalosporin, such as cefotaxime, are used for their synergy against the common pathogens in neonatal sepsis. Any infant suspected of HSV infection and who undergoes viral culturing should also receive empiric acyclovir.

CRITICAL CONGENITAL HEART DISEASE

Congenital heart disease (CHD) occurs in approximately 1% of live births.[9] Although many lesions will present in the immediate postnatal period before discharge from the newborn nursery, there is a subset of lesions that remain subclinical due to compensation from an open ductus arteriosus. In these cardiac defects, systemic or pulmonary blood flow is dependent on the open ductus arteriosus resulting in infants who present with shock or cyanosis, respectively, with ductal closure.

The gold standard for diagnosis of CHD is the echocardiogram; however, this may not be readily available in the emergency department and several other quick diagnostic evaluations can and should be performed during initial assessment. Pulse oximetry can be used as an assessment of

oxygenation. A thorough evaluation includes both pre-ductal (right upper extremity) and post-ductal (either lower extremity) pulse oximetry measurements, which can be nearly 100% sensitive and 100% specific for detecting cyanotic heart disease.[14] Four-extremity blood pressures should be obtained to look for differences between the upper and lower extremities, as well as overall adequacy of the blood pressure. An arterial blood gas is key to determining the presence of acidosis (pH, HCO_3 , base deficit), as well as inadequate oxygenation (pO_2). A serum lactate will also provide information about tissue perfusion and oxygenation, and can usually be obtained with the blood gas. Chest radiography can be performed to look for the presence of cardiomegaly or abnormal pulmonary vascular markings which may also be suggestive of CHD. An electrocardiogram (ECG) can be obtained but can be difficult to interpret in the first week of life due to characteristic ECG findings that are usually abnormal in other patient populations. As previously discussed, the normal heart rate of an infant is higher at baseline, which may be misinterpreted as tachycardia on the ECG if the appropriate age parameters are not set. Right-axis deviation and right ventricular predominance (or hypertrophy) are also normal findings, secondary to ongoing transition from fetal circulation. T-wave inversion in lead V_1 is seen in infants greater than 48 hours old and persists through young childhood.[15]

Suspected ductal-dependent CHD should be treated with a continuous, intravenous infusion of prostaglandin E1 (PGE). The infusion may be started at 0.1 mcg/kg/min, and then slowly weaned to 0.01 mcg/kg/min once the infant has been stabilized (Table 3). Caution should be

exercised when starting PGE, as side effects including apnea and hypotension can result with initial doses.

INBORN ERRORS OF METABOLISM

Metabolic disorders should be considered whenever a critical neonate is being evaluated in the emergency department, as incidence can be as high as greater than 1 in 500 live births.[9]

Although hospital-born infants are universally screened prior to discharge, results may not be available for weeks. During this time, unidentified neonates may begin to manifest symptoms of their disordered metabolic processes as a result of exposure to a particular catabolic insult. Infants that were normal in the regular newborn nursery and then suffered an acute change in status after feeding at home should be carefully evaluated for an inborn error of metabolism.

Details of each metabolic disorder and its sequelae fall outside the scope of this discussion; however, disorders can be roughly categorized as amino acid disorders, urea cycle disorders, organic acidemias, fatty acid oxidation defects, disorders of carbohydrate metabolism, and miscellaneous. Manifestations are characteristic of the disordered process; however, certain findings such as strange odor, feeding difficulties, vomiting, hepatomegaly, profound lethargy, and seizures should prompt the evaluation for an inborn error of metabolism.

The evaluation for inborn errors of metabolism is primarily laboratory driven. A blood gas should be obtained to look for the presence of metabolic acidosis, respiratory alkalosis and an increased anion gap. Blood should be sent to evaluate ammonia, lactate, pyruvate, and quantification of amino acids. A complete metabolic panel should be ordered to assess

electrolytes, glucose, as well as renal and liver function. Ketones, reducing substances, and organic acids can be evaluated in the urine.

The goals of treatment in the evaluation of inborn errors of metabolism should focus on hydration, correction of acid-base imbalance, nutrition, and elimination of offending metabolites. Infants are allowed nothing by mouth and placed on age-appropriate parenteral fluids containing dextrose and electrolytes to prevent a catabolic state. Parenteral nutrition fluids containing protein are held until a specific disorder is identified. Co-morbid issues such as sepsis or seizures should also be attended to. Many infants will require ongoing supportive care until definitive treatment can be provided with the identification of their specific inborn error of metabolism.

CONGENITAL ADRENAL HYPERPLASIA

The most common endocrine disorder that manifests in the first week of life is congenital adrenal hyperplasia (CAH). CAH results from one of five enzyme defects that lead to impaired cortisol production and increased adrenocorticotrophic hormone (ACTH) production.

Manifestations are characteristic to the enzyme defect; however, adrenal crisis secondary to salt-wasting in 21-hydroxylase and 3 β -hydroxylase deficiencies and severe hypertension secondary to salt-retention in 11 β -hydroxylase deficiency are of particular interest, as approximately half of infants with untreated salt-losing CAH present in crisis between 6 and 14 days of age.[16] Female infants will often have abnormal genitalia with some amount of

virilization while male infants often have normal genitalia. Infants often present with dehydration, vomiting and shock like symptoms.

CAH may be detected on the newborn screen; however, results may not be available within the first week of life. Serum quantification of 17-hydroxyprogesterone (17-OHP), 11-deoxycortisol, 17-hydroxypregnenolone, and cortisol may be helpful in diagnosing these disorders. These results may not be available immediately in the emergency department, but should be sent as the patient is being stabilized. Electrolytes should also be obtained to identify abnormalities with the most common type of CAH presenting with hyponatremia, hyperkalemia and metabolic acidosis. Management should focus on correction of hypotension, dehydration, and electrolyte abnormalities. Identified cortisol deficiency should be corrected as well with stress-dose hydrocortisone as shown in Table 4. Inpatient management is encouraged until the specific disorder is diagnosed and ongoing medical management is established.

HEMORRHAGIC DISEASE OF THE NEWBORN

Hemorrhagic disease of the newborn (HDN) or Vitamin K deficient bleeding, as it is also known, typically occurs in three distinct time periods. Early disease, characterized by serious and catastrophic bleeding, occurs within the first 24 hours of life. Classic disease, which may be associated with cutaneous, gastrointestinal, circumcision, or intracranial bleeding, occurs up to one week of life in 1.7% of infants without Vitamin K prophylaxis. Late disease can occur any time after the 1st week of life and may be associated with similar bleeding seen in classic disease, but with a notably higher rate of intracranial hemorrhages. A recent increase in late-

onset disease has been noted in the United States due to the increasing refusal of Vitamin K at birth.[17,18]

Active or serious bleeding should be managed promptly. A hemoglobin, hematocrit, and platelet count should be obtained to evaluate the need for blood product replacement.

Coagulopathy labs including prothrombin time (PT), partial thromboplastin time (PTT), and fibrinogen should be obtained as well. HDN is characterized by a prolonged PT, normal fibrinogen level, and normal platelet count. Unless another bleeding disorder is suspected, specific factor or coagulation assays are not necessary. Treatment with an appropriate dose of Vitamin K, approximately 1 to 10 mg IV via slow push, should resolve coagulation concerns.[13]

Unless associated with inadequate absorption of fat-soluble vitamins due to chronic disease, ongoing treatment should not be necessary.

SUMMARY

The critically ill neonate presents a challenge to caregivers and should be managed rapidly and methodically. Although this review discusses the diagnosis and initial management of these life-threatening neonatal conditions, primary focus should be placed on ensuring the neonate's stability. Ensuring a patent airway, adequate ventilation and oxygenation, and sufficient circulatory perfusion must take priority over diagnostic measures. Once stabilized and initial evaluation and treatment has been completed, these infants should be admitted for ongoing inpatient management.

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Table 1. Normal newborn vital signs.

Temperature	36.5° to 38° C
Respiratory Rate	30 to 60 breaths per minute
Heart Rate	85-205 beats per minute (awake) 80-160 beats per minute (asleep)
Blood Pressure	Systolic 65-85 mmHg Diastolic 45-55 mmHg
Oxygen Saturation	>94%

Table 2. Empiric antibiotics and antivirals for suspected sepsis.[13]

Ampicillin	100 mg/kg/dose IV or IM every 12 hours
Gentamicin	4 mg/kg/dose IV or IM every 24 hours
Cefotaxime	50 mg/kg/dose IV or IM every 8 hours
Acyclovir	20 mg/kg/dose IV only every 8 hours

Table 3. Prostaglandin E₁ (PGE) dosing for ductal patency.[13]

Initial	0.05 to 0.1 mcg/kg/min continuous IV infusion
Maintenance	0.01 mcg/kg/min continuous IV infusion

Table 4. Stress-Dose Hydrocortisone Dosing.[13]

Weight-Based (kg)	1 mg/kg/dose IV every 8 hours
Body-Surface-Area (m ²)	20 to 30 mg/m ² IV divided every 8 to 12 hours
BSA Calculation	$(0.05 \times \text{kg}) + 0.05$