# 1 Post-resuscitation Care of the Depressed Newborn

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## Introduction

Newborns who are depressed at birth present a challenge to the practicing physician. A neonate may respond to resuscitation and seem to be improving at 5 or 10 min of age. However, it is often difficult to determine if there has been intrapartum asphyxia or other causes such as sepsis to account for the neonatal depression. Therefore, triage of the newborn to the appropriate nursery may be problematic. If the newborn is admitted to a NICU, multiple tests will be done, and maternal newborn bonding and perhaps breastfeeding will be affected. However, delay in diagnosis of a truly ill newborn may have significant consequences since potential therapies may be delayed. This is especially true for therapeutic hypothermia (TH), which has been shown to be most effective if initiated within the first 6 h of life [1, 2]. If this window of opportunity is missed, the newborn with intrapartum asphyxia may not benefit from the potential positive effects of this treatment.

This chapter will review the approach to the depressed newborn who is successfully resuscitated. It will guide the practicing physician in determining which newborns need more testing and treatment. The reader will be presented three cases, led through the appropriate physical evaluation and queried regarding which tests to order, how to evaluate those tests, and why they may be misleading. The determination of need for further evaluation, treatment, and possibly even transfer to a higher level of care will be discussed.

## Case Presentation

A 40 and 5/7 weeks gestation male is born by emergency cesarean section for non-reassuring fetal status to a 22-year-old primigravida female. Upon rupture of membranes 4 h prior to delivery, meconium-stained amniotic fluid was noted. Fetal heart monitoring revealed multiple variable and late decelerations which led to the operative delivery under general anesthesia. The baby is born limp with a heart rate of 60 beats per minute (bpm). He is suctioned and intubated in the delivery room. No meconium is retrieved from below the vocal cords. Chest compressions are given for only 30 seconds, and his heart rate quickly increases to over 100 bpm. Over the next several minutes, he begins to have gasping respirations which become regular at 6 min of age and he is extubated. Pulse oximetry increases to 90% by 10 min of age, and oxygen is gradually weaned off to room air. Apgar scores of 1, 5, and 7 are assigned at 1, 5, and 10 min of age.

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At this time you:

1. Allow baby to remain skin-to-skin with the mother.
2. Request umbilical cord gases from the obstetrical team.
3. Obtain arterial blood gas on baby.

The American Congress of Obstetricians and Gynecologists (ACOG) currently recommends umbilical cord blood analysis for high-risk deliveries (i.e., low 5-min Apgar score, severe intrauterine growth restriction, maternal thyroid disease, fetal heart rate tracing abnormalities, intrapartum fever, multiple gestation pregnancies, and cesarean deliveries for fetal distress) [3, 4]. As a physician involved in newborn care, it is important to be able to interpret umbilical cord gases correctly. The arterial cord gas can be a valuable representation of the fetal state prior to delivery [5–7]. A low arterial cord pH has been associated with adverse neurologic sequelae [8]. Using both the arterial and venous cord values, the clinician may be able to determine the intrapartum events leading to neonatal depression [4, 5, 9] (Table 1.1).

**Answer: 2**

**Table 1.1** Normal arterial and venous cord blood gas values

| | Venous cord blood normal range (Mean ± 2SD) | Arterial cord blood normal range (Mean ± 2SD) |
|---|---|---|
| pH | 7.25–7.45 | 7.18–7.38 |
| pCO2 (mmHg) | 26.8–49.2 | 32.2–65.8 |
| pO2 (mmHg) | 17.2–40.8 | 5.6–30.8 |
| $HCO3^-$ | 15.8–24.2 | 17–27 |
| Base excess (BE) | 0 to −8 | 0 to −8 |

From Pomerance [10]
Data are mean values ± 2 standard deviations (SD)
Note: "Normal" is arbitrarily defined as the mean ± two times the standard deviation (approximately 95.4% of a normally distributed population)
[a]Base excess, estimated from data
[b]1 kPa = 7.50 mmHg; 1 mmHg = 0.133 kPa

In order to be able to correctly interpret umbilical cord blood gases, one must understand the physiology of fetal-placental gas exchange. Oxygenated blood leaves the placenta and courses through the *umbilical vein* to deliver oxygen to the fetal tissues. Deoxygenated blood containing higher carbon dioxide and increased acids leaves the fetus through the two *umbilical arteries*. Carbon dioxide easily diffuses across the placenta, but acids (such as lactic acid) leave more slowly [4, 7].

Since it carries the oxygenated blood resulting from gas exchange with the maternal circulation, the umbilical venous gas represents both fetal and maternal acid/base status. Conversely, the umbilical artery transports deoxygenated blood from the fetal tissues back to the placenta and therefore is reflective of both the uteroplacental status and the fetal acid/base state [10]. Based on this physiology, the venous umbilical cord gas should have a higher pH and a lower pCO2 than the umbilical arterial cord gas [4–6, 10]. This is the opposite of what one would expect of venous and arterial gases in a newborn who has transitioned to the postpartum circulation (an obvious exception being transposition of the great arteries). Cord gases are an important window into the fetal state while in utero [4, 5, 7]. However, results can be misleading if only a venous sample is obtained, the blood samples are mishandled, or there has been obstruction to cord blood flow in the last several minutes prior to birth [5, 10].

The lab reports the cord blood gas revealing a pH of 7.14, pCO2 of 54, pO2 of 36, and base excess of −11.

At this time you:

1. Are reassured by the cord gas and allow the baby to breastfeed.
2. Request the obstetrical team or respiratory therapist to repeat sampling, obtaining both arterial and venous cord blood gases.
3. Obtain an arterial blood gas on the baby.

In the ideal situation, both arterial and venous umbilical cord blood will be sampled for blood gas analysis [4]. The umbilical artery pH should be at least 0.02 units lower than the vein [6, 11].

The normal umbilical arterial pCO2 is usually more than 4 mmHg greater than the vein [6, 11]. Therefore, if two cord gases are reported and the A-V difference is 0.02 units or less in the pH and <4 mmHg in the pCO2, then the two results are likely from the same vessel [6, 11]. Even if an arterial cord gas is not reported, one can usually estimate the extent of acidemia based on the venous pH. The venous pH is usually >0.02 to <0.10 higher than the arterial pH. For a venous pH of 7.06 or less, there is a greater than 50% probability of significant arterial acidemia (defined as a pH less than 7.0). For a venous pH of ≥7.14 to <7.17 there is an estimated 10% probability of significant arterial acidemia. Finally, for a venous pH of ≥7.17 to <7.23, there is an estimated 5% probability of significant arterial cord acidemia [12].

If only one cord blood gas is reported, it may be from the umbilical vein, as this vessel is larger and more easily sampled [4, 6, 10]. One clue that a single gas sample is of venous origin is the PaO2 value. If the reported PaO2 is >31 mmHg, it is highly likely to be a venous sample [10].

Umbilical cord gases can be drawn from a doubly clamped cord kept at room temperature up to 60 min after delivery with little change in pH or pCO2 [3–5]. However, cord gases are unreliable for lactate beyond 20 min after birth [5, 13]. If too much heparin is added to the specimen to prevent clotting, the acid/base results can be affected due to the acidotic properties of the compound [5]. Therefore, most cord blood-gas samples are collected in pre-heparinized syringes. Air bubbles in the specimen may also affect the results by erroneously increasing the pH and the pO2 and by decreasing the pCO2; however, with most modern blood-gas analyzers, results will not be reported when an air bubble is detected [10].

Delayed cord clamping is currently recommended for *vigorous* newborns [14, 15]. If blood gas analysis is performed in the setting of delayed cord clamping, it is important to consider its potential effect on acid-base status. Continued placental gas exchange and/or neonatal breathing can affect the cord blood gas results by decreasing the pH, base excess, and bicarbonate and by increasing the lactate and pCO2 [6, 16, 17]. Currently, it is recommended that immediate cord clamping takes place for the depressed newborn in order not to delay resuscitation [3, 14, 15, 18].

**Answer: 2**

You correctly interpret the first cord gas results as venous (high pO2) and ask the respiratory therapist to collect an arterial sample from the cord. She gives you the following results: pH 7.07, pCO2 62, pO2 9, and BE -15.

At this time you:

1. Are reassured by the cord gases (since the pH from both the artery and vein is >7.0) and continue standard newborn care.
2. You are concerned by the significant arterial cord acidosis and plan further evaluation.

Once the umbilical cord gas is proven valid (i.e., from the correct vessel, without air bubbles, and not affected by heparin), it may be used to evaluate intrapartum events [4, 5, 9].

Fetal acidosis may be the result of a sudden decrease in placental or umbilical blood flow from conditions such as cord compression or placental abruption [3]. Other potential causes for fetal acidosis include fetal anemia, placental insufficiency, maternal hypoxemia and hypoventilation, and chronic maternal conditions such as preeclampsia [3, 6, 19].

Cord compression, e.g., cord prolapse, decreases blood flow from the placenta to the fetus [4]. When the cord is subjected to compression, the thin-walled umbilical vein is more likely to collapse compared to the thick-walled umbilical arteries [10]. This may lead to a reassuring venous cord gas and acidotic arterial cord gas, underscoring the importance of obtaining both samples [4, 5, 7, 20].

In placental abruption there is decreased perfusion of the placenta. In contrast to umbilical cord compression, the arterial and venous cord blood pCO2 values will be similar although both can potentially be significantly acidotic [4, 9].

Uncommonly there may be a complete occlusion of all three vessels in the umbilical cord with

resulting cessation of blood flow to and from the fetus. In this situation, both cord blood gases could appear to be normal, as they reflect the acid-base state immediately prior to the complete occlusion, although the newborn may be significantly acidotic [4, 10, 21].

**Answer: 2**

Despite the reassuring venous cord gas, you are concerned by the significant arterial cord acidosis and plan further evaluation. What other evaluations might you consider?

1. Neonatal arterial blood gas.
2. Obtain a cord or neonatal lactate level.
3. Perform a neurologic exam.

A systemic arterial blood gas should be obtained within the first hour of life in all depressed newborns. This will help to determine potential intrauterine events and may also reflect the adequacy of resuscitation. An arterial blood gas obtained within the first hour of life that demonstrates significant acidosis coupled with an abnormal neurologic exam can be used to guide time-sensitive treatments such as therapeutic hypothermia. A capillary blood gas (CBG) may be misleading in the first hours after birth since poor perfusion may depress the pH and make the base deficit appear higher. However, a normal CBG at this time is reassuring.

It is possible to obtain an arterial lactate from the umbilical cord. Elevated cord lactate levels may be used to predict the presence of hypoxic-ischemic encephalopathy (HIE) [22]. In the setting of fetal hypoxia, anaerobic metabolism results in the accumulation of lactic acid, resulting in a metabolic acidosis. Unlike volatile acids, such as carbon dioxide, lactic acid is removed at a slower rate by the placenta from the fetal circulation [4, 7, 10]. For this reason, cord lactate levels are thought to reflect fetal acidosis and may be used to help predict neurologic outcomes [22]. However, at this time there is no consensus on the cord lactate level that might predict adverse outcomes [6]. A neonatal arterial lactate might also be helpful in the absence of a reliable cord gas. Shah reported that a plasma lactate level >7.5 mmol/l within the first hour of life was associated with moderate or severe HIE with a sensitivity of 94% and specificity of 67% [23].

An umbilical cord metabolic acidosis in a healthy appearing, vigorous newborn does not predict poor neurologic outcomes [24, 25]. A newborn must also have an exam consistent with moderate to severe encephalopathy in order to consider the possibility of a neurologic insult and to meet criteria for TH [25]. Therefore a thorough evaluation, including a neurological examination, is essential to predict long-term outcomes.

**Answer: 1, 3**

The newborn's arterial blood gas at 55 min of life is pH = 7.22, pCO2 of 49, pO2 of 74, and BE −10. At this time you proceed with a neurologic exam. You observe the newborn has a weak cry and slowly withdraws his legs with stimulation. His arms and legs are extended and his hands are clenched bilaterally. He has a weak suck and an incomplete Moro reflex by spreading his arms and barely pulling them inward.

At this point you should:

1. Refer patient for therapeutic hypothermia.
2. Observe and re-examine baby in 2–4 h with repeat ABG.
3. Start passive cooling.
4. Order ultrasound of the brain.

The Sarnat staging system provides a methodical approach to the neurologic evaluation of a depressed newborn. It employs the following elements: level of consciousness, neuromuscular control including posture and muscle tone, reflexes, autonomic system responses, and the presence or absence of seizures [26] (Table 1.2).

The level of consciousness of the newborn is evaluated as hyperalert, lethargic, stuporous, or comatose. The hyperalert newborn often appears to be staring and irritable and may not sleep for up to 24 h. Per Sarnat, the lethargic newborn would be irritated when disturbed and would have a delayed but completed response to a stimulus. In the more severe cases, the level of

**Table 1.2** Modified Sarnat staging system here

| Stage | Stage 1 | Stage 2 | Stage 3 |
|---|---|---|---|
| Level of consciousness | Hyperalert | Lethargic | Stuporous or comatose |
| Tone | Normal | Decreased | Flaccid |
| Posture | Mild distal flexion | Strong distal flexion, complete extension | Decerebrate posturing |
| Spontaneous activity | Normal or decreased | Decreased | No activity |
| Reflexes | | | |
| Suck<br>Moro | Weak<br>Strong, easily elicited | Weak<br>Incomplete | Absent<br>Absent |
| Autonomic system | | | |
| Pupils | Dilated | Constricted | Variable, nonreactive to light, unequal |
| Heart rate<br>Respiration | Tachycardia | Bradycardia<br>Periodic breathing | Variable<br>Apnea |
| Seizures | None | Common | Uncommon |

Derived from [1, 26]

consciousness is described as stuporous. The stuporous newborn would only respond to painful stimuli by withdrawing or demonstrating decerebrate posturing [26]. Rarely, the newborn could be considered comatose with no arousal nor motor response [27]. When evaluating posture, distal flexion and full extension means that the extremities are extended and the wrists and digits, including the thumb, are flexed (i.e., cortical thumb), where the thumb is flexed and held across the palm. Hypotonia occurs when decreased resistance is met with passive movement of the extremities. Flaccid is described when no resistance is met. The Sarnat system (Table 1.2) has been modified to be used in evaluation of term and near-term newborns for therapeutic hypothermia [1].

Following birth asphyxia, a sequence of events may occur in the brain leading to cerebral injury and long-term neurodevelopmental impairment. Birth asphyxia occurs before, during, or after birth due to many causes including lack of placental blood flow and subsequent poor gas exchange leading to hypoxia and hypercapnia [28, 29]. There are three phases of cerebral injury: (1) primary phase, (2) latent phase, and (3) delayed phase [30, 31]. The primary phase occurs during the asphyxial event and results in hypoxia and decreased cerebral circulation with eventual neuronal cell swelling which, if the event was severe, may lead to necrosis and cell death [29, 31–33]. The latent phase begins with the return of cerebral circulation and occurs over hours 1–6, with partial recovery [32, 33]. The delayed phase occurs at 6–15 h following the hypoxic event, with secondary deterioration leading to neuronal death and clinical deterioration [30–32]. It is the latent phase, which occurs between hours one and six, which is considered the therapeutic window to prevent secondary deterioration and delayed neuronal death [2, 33].

Knowledge that interventions during the therapeutic window might halt neuronal death and positively affect long-term neurodevelopmental outcomes has been an impetus for research into potential treatments for HIE [34]. TH has been established as the standard of care for this condition [2]. With multiple trials, TH has been demonstrated to decrease both mortality and neurodevelopmental impairment among newborns with HIE [33, 35].

The neuroprotective effect of TH is achieved by lowering the core body temperature and subsequently reducing the metabolic rate of the brain in attempt to prevent neuronal cell death [33]. There are two different types of cooling systems for TH that have been studied with large randomized controlled trials: whole body (systemic) hypothermia and selective head hypothermia [1, 36–38]. Both systems are effective in reducing

mortality and neurodevelopmental impairment in moderate to severe encephalopathic newborns [32, 33, 35].

In 2014, the American Academy of Pediatrics' Committee on Fetus and Newborn recommended that the decision to use TH should be guided by two validated protocols [39]. Two protocols that are currently used by a majority of institutions in the United States: the NICHD Protocol for Systemic Hypothermia [1] and the "CoolCap" Study for selective head hypothermia [36]. These protocols use slightly different criteria, which means it is very important for the generalist to be familiar with the specific protocol that is commonly used by their referral institution.

The following inclusion criteria are consistent across most protocols [1, 36–38]:

1. Gestational age greater than or equal to 36 weeks
2. Less than or equal to 6 h of life
3. One or more of the following:
   (a) A pH ≤ 7 or base deficit ≥16 on a cord gas or any blood gas within the first hour of life
   (b) A 10 min Apgar score of ≤5
   (c) Positive pressure ventilation for at least the first 10 min of life
4. An exam indicative of moderate or severe encephalopathy

Each protocol has different requirements to distinguish between moderate or severe encephalopathy by using Sarnat staging (see Table 1.2 above). Whole body hypothermia requires presence of seizures or one or more signs in three of six Sarnat categories [1]. In selective head hypothermia, a newborn is said to have moderate or severe encephalopathy if the level of consciousness is lethargic, stuporous, or comatose and the neurologic exam reveals one or more of the following: abnormal reflexes (including pupillary abnormalities or abnormal oculomotor reflexes), hypotonia, a weak or absent suck, or seizures [36].

Many referral centers that use the selective head cooling protocol require an amplitude electroencephalograph (aEEG) prior to initiation of cooling [36]. An aEEG is a bedside monitor that screens for abnormal brain activity as well as seizures [40].

Exclusion criteria generally include one or more of the following [1, 36–38]:

- Gestational age less than 36 weeks
- Greater than 6 h since birth
- Birthweight less than 1800 g
- Presence of a major congenital abnormality
- A moribund newborn

Some protocols also exclude newborns with gross hemorrhage [37] or intracranial hemorrhage [36].

TH should only be provided in an institution with a neonatal intensive care unit with the following capabilities: an approved and implemented standardized cooling protocol, the necessary equipment (including active controlled hypothermia equipment, core temperature monitoring, mechanical ventilation, EEG or aEEG, and MRI), the necessary subspecialty services (i.e., pediatric neurology), and the availability of long-term neurodevelopmental follow-up [39, 41].

The short therapeutic window (e.g., 6 h) creates a conundrum for outlying hospitals that often lack the capacity to do TH [42–44]. One solution has been to attempt to treat these newborns through passive and uncontrolled active cooling at these outlying hospitals until transport can be arranged [42–45]. Passive cooling involves discontinuing active warming activities by turning off the radiant warmer and removing blankets [45]. Uncontrolled active cooling involves briefly placing ice packs or cool gel packs on the newborn's chest and/or forehead [42, 45]. Both passive cooling and uncontrolled active cooling are risky endeavors, as they place newborns at high risk for severe hypothermia [42]. This is especially true for severely encephalopathic newborns due to their propensity for temperature dysregulation [43, 45]. Overcooling may result in bleeding, thrombosis, sepsis, and arrhythmias [46]. Many transport teams now have controlled active cooling devices that can be initiated on arrival to the outlying hospital [47]. Some centers will treat patients up to 24 h after injury, although

a recent study showed no statistical improvement from newborns cooled beyond 6 h of life [48].

It is also important to avoid *hyperthermia* and hypoglycemia in asphyxiated newborns as they have been associated with increased brain injury and poorer outcomes [2, 41, 49–51].

The most common side effects of active controlled cooling are sinus bradycardia and thrombocytopenia [33].

**Answer: 1**

Denouement: This baby should be referred for TH if not available at your hospital. If you are uncertain that the patient meets criteria, repeat the exam and studies in 1 h and/or consult your neonatologist. Cranial ultrasound will not give any useful information at this early stage in the evolution of a possible HIE, but may demonstrate unexpected findings such as hemorrhage or hydrocephalus. Continued metabolic acidosis or an elevated arterial lactate (> 7.5 mmol/l) and continued hypotonia would tend to favor treatment with TH before 6 h of age.

## Case Presentation

A 38 and 4/7 weeks gestation male is born by cesarean section for failure to progress to a 26-year-old primigravida female. Pregnancy was complicated by poor prenatal care. Membranes ruptured 14 h prior to delivery with clear amniotic fluid. At birth, the baby is limp with a heart rate of 80 bpm. He is noted to have poor respiratory effort and receives 2 min of positive pressure ventilation (PPV). After PPV, he begins to spontaneously breathe and his heart rate improves to 130; however, he continues to have poor tone. Apgar scores of 2, 5, and 7 are assigned at 1, 5, and 10 min of age. An unspecified cord blood gas shows a pH of 7.22, pCO2 of 52, pO2 of 18, and a base excess of −7. You are called to assess whether or not this patient qualifies for cooling.

You perform a history and physical exam and you realize that the history is not consistent with the criteria for TH although the newborn is encephalopathic on exam. Your staff have yet to perform the newborn's measurements including weight, length, and head circumference.

At this time you:

1. Turn off the radiant warmer and call the referral center.
2. Obtain head ultrasound since your referral center prefers one before cooling.
3. Ask staff to perform newborn measurements.

You obtain a head ultrasound preemptively since your referral institution prefers one before cooling. It reveals massive hydrocephalus. While writing your note, you realize the patient's head circumference is 39 cm > 99% while weight and length are 50%, 3290 g and 50 cm respectively.

This case emphasizes the importance of obtaining a full history, performing a complete physical exam, and adhering to the protocol's inclusion criteria for TH. Encephalopathy is a broad entity encompassing multiple etiologies all leading to a depressed mental state [52, 53]. As such, there is a broad differential for neonatal encephalopathy beyond hypoxic-ischemic events including sepsis, meningitis, congenital infection, inborn errors of metabolism, genetic disorders, intracranial abnormalities including perinatal stroke both ischemic and hemorrhagic, hydrocephalus, and neonatal epilepsy syndromes [54]. Therefore, only those newborns that meet the criteria for TH should be cooled. Performing TH on newborns that do not meet criteria could result in delayed or missed diagnoses, resulting in increased morbidity and mortality. Until HIE is confirmed, it has been advised to describe the newborn as having neonatal encephalopathy [53].

Some protocols recommend obtaining a head ultrasound prior to cooling which would have detected the abnormality in this case. The 39 cm head circumference (>99% for gestational age) is disproportionate to the newborn's weight and length, which were in the 50% for gestational age. The head ultrasound revealed undiagnosed hydrocephalus which explained the depressed Apgar scores, hypotonia, and decreased activity noted on the exam.

**Answer: 2, 3**

Newborns that possess an inborn error of metabolism can also demonstrate signs and symptoms of encephalopathy. They may be initially asymptomatic, as the placenta acts as a filter removing the byproducts of their deranged metabolism. Following birth, these patients may go on to develop lethargy and seizures. It is therefore reasonable to include serum ammonia and lactate levels in evaluating neonatal encephalopathy.

Newborns with sepsis can also be lethargic and may readily become acidotic. The early institution of antibiotics in these cases is critical. By evaluating the perinatal events, physical examination, the results of cord blood and post-birth blood gas analysis, and other laboratory evaluations, one can usually differentiate the various causes of neonatal encephalopathy.

## Case Presentation

A 40 and 6/7 weeks gestation female is born by vaginal birth after cesarean (VBAC) delivery to a 32-year-old G2P1. Pregnancy was uncomplicated. Rupture of membranes occurred 28 h prior to delivery revealing clear amniotic fluid. The baby is limp with a heart rate of 70 bpm at birth. She remains apneic and receives PPV via self-inflating bag. Heart rate declines to 60 bpm despite ventilation corrective steps, and she is successfully intubated on the second attempt at 4 min of life. Her heart rate has declined to 40 bpm despite adequate ventilation. She receives 5 min of chest compressions. One dose of endotracheal tube epinephrine and one dose of intravenous epinephrine via an emergent umbilical line results in improvement of heart rate. Due to poor perfusion, she receives a 10 ml/kg normal saline bolus. Apgar scores are 1 at 1 min, 1 at 5 min, 3 at 10 min, 3 at 15 min, and 3 at 20 min. An arterial cord gas shows pH of 6.95/pCO2 83/pO2 19/HCO3 17.8/base excess −15.7. She is transferred to the newborn nursery for stabilization. Her temperature on admission is 37.4 °C, and she is placed under a radiant warmer on manual control. After continuous manual ventilation, an ABG is obtained at 50 min of life revealing pH 6.95, pCO2 66, pO2 26, HCO3 14, and base excess −19, and bedside glucose is 39 mg/dl. On exam, you note with arterial puncture she slowly responds by flexing her arms and demonstrates a facial grimace. Without stimulation she has decreased activity, poor tone, a weak suck, and equal but delayed Moro reflex, pupils appear constricted, heart rate is 120 bpm, and she is now spontaneously breathing above the ventilated breaths.

You call the referral center for transport. How would you proceed to stabilize the newborn while waiting for the transport team?

1. Make patient NPO, start D10W at 60 ml/kg/day, obtain blood culture, and start ampicillin and gentamicin.
2. Make patient NPO, start D10W at 100 ml/kg/day, obtain blood culture, and start ampicillin and gentamicin.
3. Make patient NPO and turn off radiant warmer. Do not start antibiotics.
4. Make patient NPO, turn off radiant warmer, give a 2 ml/kg bolus of D10 W and start D10W at 60 ml/kg/day, obtain blood culture, and start ampicillin and ceftazidime.

Birth asphyxia is the result of poor perfusion to the fetus from either decreased placental or umbilical blood flow [28]. In response, the fetal heart preferentially shunts blood to the vital organs, including the brain, the heart, and the adrenal glands, and, if prolonged, these organs can be adversely affected [24, 55]. Asphyxia can ultimately lead to HIE but can also cause electrolyte and endocrine disturbances, as well as dysfunction of the heart, kidneys, and/or liver [50, 56].

During the stabilization of the depressed newborn, the potential for multi-organ dysfunction should be considered. The depressed newborn should be made NPO, given a bolus of glucose, and started on dextrose containing intravenous fluids. Fluid restriction of 40–70 ml/kg/day is recommended to avoid fluid overload and to theoretically prevent worsening of cerebral edema [51, 56]. Careful fluid balance must be maintained, as too strict a fluid restriction can lead to

hypovolemia with the worsening of acute kidney injury (AKI). Fluid restriction may also increase the risk of hypoglycemia which is associated with poorer neurodevelopmental outcomes [51].

Newborns with HIE should be screened for sepsis with a blood culture and receive empiric antibiotics. If nephrotoxic medications are used, such as gentamicin, it is important to monitor drug levels prior to the subsequent dose to ensure they are within the therapeutic range [51, 57]. If the patient is anuric or oliguric or has an elevated creatinine, nephrotoxic medications should, if possible, be avoided [51, 57]. Antibiotic regimens might include piperacillin-tazobactam or ampicillin and a third-generation cephalosporin such as ceftazidime.

**Answer: 4**

You obtain a point of care blood glucose which is 54 mg/dl. You make the newborn NPO and start D10W at 60 ml/kg/day. A blood culture is obtained and you have ordered ampicillin and ceftazidime. 15 min later, the nurse calls you to the bedside to evaluate jerking movement of the upper and lower extremities associated with increased blood pressure and oxygen desaturation.

At this time you:

1. Continue waiting for the transfer team.
2. Order 20 mg/kg Phenobarbital IV once stat.
3. Obtain BMP, Mg, and ionized Ca.

Neonatal seizures are defined as sudden, abnormal activity causing motor, behavioral, and/or autonomic dysfunction [27, 58]. They may present with tonic, clonic, or myoclonic movements or have a subtler presentation such as apnea, vital sign instability, or horizontal eye deviation with or without nystagmus [27]. With the advent of video EEG, it is now known that seizure-like activity can be easily misinterpreted [58]. Some activities that are characterized as clinical seizures do not show simultaneous EEG changes, and documented electrographic seizures do not always have stereotypical clinical activity [27]. This emphasizes the need for prolonged EEG monitoring [27]. If the newborn has seizure-like activity, the provider should screen for and correct electrolyte and metabolic derangements by obtaining a serum glucose, sodium, ionized calcium, and magnesium level [59]. If the clinician suspects seizures in a patient with HIE, it would be advisable to load with phenobarbital 20 mg/kg [27]. Phenobarbital is effective at suppressing clinical seizures, but electrographic seizures may be ongoing [27]. Therefore, it is important to transfer to a center with full neurologic monitoring capabilities through EEG or aEEG and the availability of neurologic consultation.

**Answer: 2**

The transport team arrives and successfully transfers the newborn to a higher level of care. The mother remains as an inpatient following her C-section. The following day, she asks how the referral center will evaluate her newborn for brain damage.

Your response to her:

1. That is a good question for the referral center.
2. Oftentimes an MRI will be performed within the first week.
3. A brain MRI will be performed and there will be developmental follow-up.

Following therapeutic hypothermia, an MRI is performed between 1 and 2 weeks of age to evaluate the extent of the injury and gather prognostic information for the family [2]. Injuries to the basal ganglia and thalamus are more likely to be associated with a poor prognosis than watershed injuries, and injury to posterior limb of the internal capsule is highly associated with a poor neurodevelopmental outcome [27, 60]. Although TH is associated with an improved MRI, a normal MRI does not preclude neurodevelopmental impairment [61]. Both normal MRIs and those with only mild injuries can be associated with neurodevelopmental impairment; therefore, it is important to be cautious when counseling families on prognosis [61].

**Answer: 3**

**Clinical Pearls**

- After successful resuscitation of a term or near-term neonate, the clinician should determine the cause of the neonatal depression.
- Evaluation of the resuscitated neonate should occur quickly since therapies (i.e., therapeutic hypothermia, antibiotics) are time sensitive.
- An umbilical cord blood gas with a PO2 of >31 mmHg has likely been obtained from the umbilical vein.
- Most (but not all) of the time an umbilical venous blood gas pH will be predictive of the umbilical artery pH.
- In the absence of a cord blood gas, an early arterial blood gas or arterial lactate level may assist in determining if the patient is a candidate for therapeutic hypothermia.
- Neurological evaluation of the neonate using a modified Sarnat scoring system will assist in determining if the baby is a candidate for therapeutic hypothermia.
- *H*yperthermia and hypoglycemia should be avoided in post-resuscitated neonates as they are synergistic with asphyxia injury.
- Apnea in a term neonate has a central nervous system etiology until proven otherwise.

**Conflict of Interest** Both authors declare they have no conflicts of interest with regard to the content of this manuscript.

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