1.0 PURPOSE AND INTENT

1.1 To provide a process for the management, monitoring, treatment, and documentation of cardiorespiratory events including apnea, bradycardia, and desaturations in premature infants in neonatal units who are not intubated.

1.2 To provide for safe, effective, and consistent use of caffeine to treat apnea of prematurity.

Note: All recommendations are approximate guidelines only and practitioners must take in to account individual patient characteristics and situation. Concerns regarding appropriate treatment must be discussed with the attending neonatologist.

2.0 PRACTICE OUTCOME

2.1 Prevent and minimize the potential long-term neurodevelopmental impact of these events.

2.2 Reduce length of stay and readmission rates.

2.3 Decrease inter-provider variability.

3.0 DEFINITIONS

3.1 Clinically Significant Cardiopulmonary Event (CSCPE), include any one of the following:

a. Apneic event with a respiratory pause ≥ 20 seconds
b. Apneic event with a respiratory pause < 20 seconds accompanied by a bradycardia < 80 bpm for any duration or with a systemic oxygen desaturation < 85% or accompanied by central cyanosis (if no pulse oximeter was being used) for any duration
c. Bradycardia: a heart rate < 80 bpm for > 5 seconds
d. Oxygen desaturation: systemic oxygen saturation (SpO2) < 80% for > 5 seconds or central cyanosis (if no pulse oximeter was being used).

3.2 Apnea of Prematurity: Apneas occurring in infants less than 37 weeks post-menstrual age (PMA) in the absence of any other condition that may cause apnea (i.e. sepsis).

3.3 Periodic Breathing: A series of 3 or more respiratory pauses per minute, each longer than 3 seconds with intervals of respiration between pauses. This pattern of breathing is common in newborns and is usually not associated with significant bradycardia or desaturation. In those with decreased pulmonary reserve, periodic breathing may culminate in oxygen desaturation albeit brief.

3.4 Bradycardia:

3.4.1 Infant current weight less than 1250 grams
3.4.1.1 A heart rate less than 100 beats per minute

3.4.2 Infant current weight greater than 1250 grams
3.4.2.1 A heart rate less than 80 beats per minute

3.4.3 Profound Bradycardia
3.4.3.1 Heart rate less than 60 beats per minute for 5 seconds or more irrespective of weight).

3.5 Desaturation: Oxygen saturation (SpO2) less than 85% for 10 seconds or more unless otherwise specified in physician's/NNP's order.
3.5.1 Hypoxemia: Oxygen Saturation (SpO2) less than 80% for 10 seconds or more
3.5.2 Intermittent hypoxemic events are desaturations below 80% for more than 10 seconds and/or an abnormal histogram in an infant on room air with more than 10% of the time below 90%).

3.6 Respiratory Support: An artificial means of mechanical support which includes intubation, tracheostomy, nCPAP (nasal continuous positive airway pressure) or non-invasive ventilation, an oral or nasal airway or low flow oxygen (i.e., nasal prongs) regardless of oxygen level.

3.7 Positive Pressure Ventilation (PPV): the application of positive pressure using a self-inflating or flow inflating anaesthesia bag through a full-face mask encompassing the nose and mouth.

3.8 Stimulation is of four types as follows:

a. Self: no stimulation was required by a caregiver for the infant to recover from the event.
b. Gentle: gentle tactile stimulation such as touching or rubbing of the back was required by a caregiver for the infant to recover from the event.
c. Moderate: flicking the sole of the foot, re-positioning the infant side to side, using blow-by oxygen was required by the caregiver for the infant to recover from the event.
d. Vigorous: ventilation with bag and mask or greater resuscitative efforts were required by a caregiver for the infant to recover from the event.

3.9 Self-Resolved Event: Infant recovered spontaneously with respect to respiration and oxygen saturation.

3.10 Mild Event: Infant recovered respiration and oxygenation recovery within 10 seconds of minimal tactile stimulation.

3.11 Moderate Event: Infant recovered respiration and oxygenation within 30 seconds of the beginning of the event after moderate tactile stimulation.

3.12 Severe Event: Infant did not show recovery of respiration and oxygenation within 30 seconds of the beginning of the event in spite of moderate tactile stimulation.

3.13 Gestational Age (GA) (completed weeks, not rounded up): Time elapsed between the first day of the last menstrual period and the day of delivery. If pregnancy was achieved using assisted reproductive technology, gestational age is calculated by adding 2 weeks to the conceptual age.

3.14 Chronological Age (days, weeks, months, or years): Time elapsed since birth.

3.15 Postmenstrual Age (PMA): Gestational age plus chronological age. This is the preferred term to use during the perinatal neonatal hospital stay.

3.16 Preterm: A preterm (premature) infant is one born at a gestational age of 259 days (37 weeks) or less.

3.17 Methylxanthines: Methylated derivatives of xanthine, including caffeine, theobromine and theophylline that serve as a smooth muscle relaxant and cardiac muscle and central nervous system stimulant.

4.0 GUIDELINES

4.1 General Management

Provide cardiorespiratory monitoring, including oxygen saturation histograms, to all infants who are less than 35 weeks 0 days gestational age. Cardiorespiratory monitoring, including oxygen saturation histograms, should be continued for at least 72 hours from the last documented cardiorespiratory episode. If the infant was on caffeine, continue cardiorespiratory monitoring, including daily histograms for at least 5-7 days after discontinuation of caffeine.

If the infant has frequent cardiorespiratory episodes or significant increase in respiratory support, or failure to wean the present respiratory support, a full clinical examination should be considered including assessment of airway patency, thermal stability, blood pressure, glucose regulation and Lung Ultrasound (LUS)/Chest XR. Other potential causes of apnea should also be considered.

Consider treatment with methylxanthine medications (see section 4.3) or CPAP.

Consider a control of breathing study in infants meeting all the following inclusion criteria:

a. Having persistent apneas, bradycardias, and/or desaturations after a corrected post conceptional age greater than 36 weeks 6 days.
b. Feeding ad lib demand.
c. Not on caffeine maintenance.
d. No other medical condition keeping the infant from being discharged home.

If an immature breathing pattern is recognized during the sleep study that improves after a loading dose of caffeine, consider discharge home on caffeine after a few days of observation in the unit at the discretion of the neonatologist.

4.2 Management of Events

4.2.1 When the monitor alarms, evaluate the infant for airway patency, noting if hyperextension or flexion of the neck is present. Reposition the head and neck if necessary. Maintain the head and neck in a neutral position. Additionally, respiratory movements, color, and heart rate should be assessed.

4.2.2 If the infant continues to be apneic or bradycardic after the assessment and position change, initiate appropriate tactile stimulation.

4.2.3 If the infant continues to have inadequate respiratory effort after 30 seconds from the beginning of the event, discontinue stimulation, administer positive pressure ventilation (PPV) **and call for assistance.** If the infant has some respiratory effort, provide only Positive End Expiratory Pressure (PEEP) of 5-6 cmH2O. If the infant shows no respiratory effort, provide breaths at a rate of 40-60 per minute. Avoid hyperventilation as this may decrease the infant's pCO2 level and suppress the stimulus to breathe triggering apnea itself. Administering free-flow oxygen or continuing to provide tactile stimulation to an apneic or

bradycardic infant will not treat the resultant hypoxemia as no oxygen is being delivered to the alveoli.

4.2.4 Reassess respiratory effort, heart rate and oxygen saturation ongoing once PPV is established. Increase the inspired oxygen (FiO2) only if the baby's heart rate and oxygen saturation do not show any improvement at this point.

4.2.5 Continue PPV until regular respiration and normal heart rate have returned to baseline.

4.2.6 Document on the Neonatal Cardiorespiratory Events Record:

a. Any respiratory pause that is greater than 20 seconds or shorter periods with an associated bradycardia or desaturation not caused by care/interventions (i.e., suctioning, or gastric tube insertion).
b. The duration of the episode from the time that the monitor indicates the episode began (using the events record or Oxygen feature) until the episode resolves.

4.2.7 DO NOT RECORD on the Neonatal Cardiorespiratory Events Record:

a. Episodes of periodic breathing, bradycardia, or respiratory pauses less than 20 second duration that are not associated with significant bradycardia or desaturation.
b. Decreased oxygen saturations that are not associated with a respiratory pause or bradycardia.
c. Transient episodes of bradycardia that are self-resolved within 10 seconds and are not associated with a desaturation below 85% or respiratory pause.
d. Any events that were not witnessed, assessed, and responded to, but were found only on the monitor on retrospective review.
e. Any events caused by interventions such as gastric tube insertion or suctioning.
f. Any events reflective of monitor artifact.

g. Such events as described in sections a-f while not recorded may be discussed on patient rounds as to whether they require further investigation or not.

4.3 Caffeine for Apnea of Prematurity

4.3.1 Intravenous (IV) and oral Caffeine is ordered as 'Caffeine', not caffeine citrate.

Adjust dosing and frequency according to the following:

a. Oral and IV doses are the same.
b. Usual loading dose: 10 mg/kg.
c. If there is an ineffective clinical response to the initial load there may be additional loading doses at the discretion of the Neonatologist.
d. Usual maintenance dose: 2.5-5 mg/kg/day given once a day.
e. A higher maintenance dose may be considered, with the neonatologist approval, especially in extreme low gestational age infants to prevent reintubation

4.3.2 Additional loading doses of 5 mg/kg may be given after 4 hours up to maximum of 20 mg/kg/day total.

4.3.3 Consider discontinuing caffeine between 32- and 34-weeks PMA if: a) the infant is off NCPAP b) no significant or frequent events are observed; and c) daily histogram is considered acceptable by the team.

4.3.4 Continue cardiorespiratory monitoring for 5 to 7 days after discontinuing caffeine and until the baby demonstrates no episodes of apnea for at least 3 days. Note: Caffeine half life has a mean of approximately 100 hours in the preterm infant with longer half lives at the lowest gestational ages at birth. (REF: Abdel-Hady H, Nasef N, Shabaan AE, Nour I. Caffeine therapy in preterm infants. *World journal of clinical pediatrics*. 2015;4(4):81-93.

5.0 Discharge criterion

5.1 Off caffeine for 5-7 days and no CSCPE.

5.2 72 hours CSCPE free post last CSCPE.

5.3 For those who have met all goals for discharge but continue to demonstrate a need for caffeine therapy, discharge may be done with planned continuation of caffeine in the home. If this is being considered, consult with the neonatal control of breathing lab prior to discharge.

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APPENDIX A – CARDIO-RESPIRATORY EVENT MANAGEMENT ALGORITHM