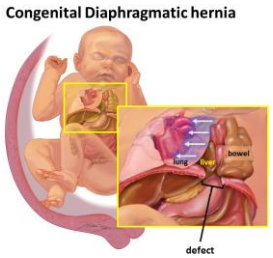
JOHNS HOPKINS
CHILDREN'S CENTER



Appendix 1. Congenital Diaphragmatic Hernia Guidelines

I. Pre-Delivery Preparation
   a. Pre/Post-ductal saturation monitor
   b. Umbilical line tray, umbilical lines (5 Fr double & single lumen catheters)
   c. Foley catheter
   d. IV fluids (D10W) flushed through lines
   e. Conventional ventilator and oscillator at bedside
   f. iNO available and ready
   g. Charge nurse to identify PCVC nurse for each shift prior to delivery
   h. Provider to obtain blood, umbilical line and PCVC consent
   i. Provider to notify General Pediatric Surgery, Pediatric Cardiology and PICU of impending delivery
   j. Delivery team should bring an 8F and a 10F Replogle to delivery

II. Delivery Room Management
   a. Supplemental oxygen set at 50%
   b. NeoPIP set with PIP 20 cm H2O and PEEP 5 cm H20
   c. Immediate intubation by NICU Fellow or Attending Physician

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i. Avoid routine drying/stimulation prior to intubation
ii. Avoid bag and mask ventilation prior to intubation
iii. For meconium stained infants, no tracheal suctioning unless obvious meconium visualized below vocal cords during primary intubation attempt
iv. Do NOT cut ETT

d. Nurse to place preductal pulse oximeter probe on right wrist
e. Nurse to place 8-10 French Replogle for stomach decompression using a 30mL syringe for intermittent decompression while in delivery room
f. May adjust PIP as needed based on heart rate. Heart rate should be used as primary indicator of appropriate ventilation (120-150 wnl). 0_2 Sat adjunct when available.
g. May adjust supplemental oxygen as needed to meet target preductal saturations of 90% per NRP guidelines.
    i. If adjusting supplemental oxygen, increase or decrease FiO2 by 10% every 90 seconds.
    ii. Avoid hyperoxia = preductal oxygen saturation above 95% in the DR
h. Routine use of surfactant in preterm AND term infants with CDH should be avoided. Surfactant should be administered only after careful

consideration. Surfactant administration may be associated with a higher mortality rate, greater use of ECMO therapy and more chronic lung disease in term infants with CDH. In preterm infants with CDH, surfactant administration was also associated with a lower survival rate.

III. NICU Admission Goals (child should be admitted to area of NICU determined to be low stimulation)
    a. First 15 minutes:
        i. Determine appropriate mode of ventilation
        ii. Peripheral IV placement
        iii. Place Replogle to low intermittent suction (20cm H2O)
        iv. Obtain chest x-ray
        v. Notify general pediatric surgery via PING and PICU, Red Attending (4-6039) of admission
        vi. Routine NICU admission measures
    b. Next 15 minutes:
        i. Sedate as needed: see “Sedation and Analgesia” for dosing
            1. Avoid morphine because of possible hypotension
        ii. Restrain infant for umbilical line placement

c. By 30 minutes:
    i. CXR obtained to confirm appropriate ETT placement and diagnosis
    ii. Attempt umbilical line placement
    iii. Obtain admission labs via umbilical lines:
        1. Blood gas
        2. Type and screen
        3. Lactate
        4. CBC with differential
        5. Blood culture
d. By 1 hour:
    i. Ampicillin and Gentamicin administered
    ii. Umbilical lines placed
        1. If UVC placement unsuccessful, prepare for PCVC placement
        2. Keep UVC in subhepatic location (if unsuccessful appropriate functional central placement) until PCVC placed
        3. Consider 2 views to determine appropriate UVC placement (i.e. AP and cross-table lateral view)
    iii. Second blood gas (obtained within 30 minutes of initial blood gas)
    iv. Foley placed
e. By 4 hours:
    i. Echocardiogram
    ii. Head ultrasound
    iii. Baseline pro-BNP

IV. Guidelines for Management in NICU

These guidelines are meant to direct care in the first 48 to 72 hours of life during the initial stabilization period and can be adjusted by the care team as needed thereafter.

a. Ventilation Management (AVOID BAROTRAUMA and VOLUTRAUMA)
    i. Chest x-ray should be obtained as soon as possible upon admission and repeated as needed based on clinical condition and mode of ventilation.
        1. Chest x-ray will help define adequate expansion of the lungs (contralateral lung expansion of 8 ribs visible above diaphragm).
        2. Avoid overinflation, defined as contralateral lung expansion of more than 9 ribs visible above diaphragm.
    ii. Pressure-controlled conventional ventilation: initial settings are a PIP of 20–25 cm H2O and a PEEP of 5 cm H2O; ventilator rate of 40–50/min
        1. Based on concept of "**gentle ventilation**" which incorporates use of lower PIP and higher rates to achieve target PaCO2 in range of 50-65mmHg
        2. If requiring PIP above 25 cm H20 or rate above 50/min, then consider high-frequency oscillatory ventilation (HFOV)

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iii. HFOV: initial setting mean airway pressure 13–17 cm H2O, frequency 10-12 Hz, amplitude (Delta P) depending on chest wall vibration
    1. The mean airway pressure should be adjusted to have an adequate expansion of the lungs determined by chest x-ray.
    2. Avoid overinflation (contralateral lung expansion of more than 9 ribs visible above diaphragm).
iv. After stabilization, the FiO2 should be decreased if preductal saturation is above 95% AND appropriate PaO2 (see below) by weaning supplemental oxygen by 5% every hour.
    1. Target preductal saturations 92-98%
    2. If weaning oxygen:
        a. No pre/post gradient should be present
        b. Post-ductal saturation > 92%
v. Postductal arterial blood gas goals:
    1. pH: 7.25-7.35
    2. PaCO2: 50-65
    3. PaO2: 60-80

b. Hemodynamic Management
i. Arterial line placement for blood pressure monitoring (UAC or peripheral arterial line)
ii. Monitor for appropriate end-organ perfusion as evidenced by heart rate within normal range, capillary refill below 3 seconds, urine output

over 1mL/kg/hr, lactate level below 3 mmol/L and no symptoms of poor perfusion.

iii. Mean arterial blood pressures (MAP) should be appropriate for gestational age (i.e. MAP 40-50 in term infant).

iv. Signs of poor perfusion should help guide decision to start inotropic support and include:
    1. Lactate > 3 mmol/L
    2. Capillary refill > 3 seconds
    3. Tachycardia (HR > 170/min in sedated infant)
    4. Urine output less than 1mL/kg/hr

v. If there are signs of poor perfusion or if blood pressure is below normal level for gestational age:
    1. Give 10mL/kg normal saline bolus, repeat as needed.
    2. If perfusion or blood pressure has not improved after a max of 3 fluid bolus(es), initiate inotropic support with Dopamine then Dobutamine (See Policy PED105 for dosing recommendations)
    3. Hydrocortisone should be considered for refractory hypotension once on maximum Dopamine (20mcg/kg/min) and starting on Dobutamine without improvement.
        a. Recommend loading dose 20 mg/m^2
        b. Maintenance dose: 20 – 30 mg/m^2/DAY, divided Q8H

4. If infant remains hypotensive, epinephrine should be considered.

vi. Consider use of milrinone if echocardiogram shows evidence of right ventricular dysfunction.

c. Pulmonary Hypertension Management

i. Pediatric cardiology/pulmonary hypertension service consultation

ii. Echocardiogram within first 4 hours of life

iii. Blood pressure support should be given to maintain arterial blood pressure levels at normal levels for gestational age.

iv. iNO should be considered when there is:

1. Evidence of right-to-left shunting with difference between preductal and postductal saturation of oxygen > 5 % - OR -
2. Infant is requiring more than 70% FiO2 despite maximized ventilator settings (before or after transition to HFOV)

v. Use of adjuvant therapies such as inhaled prostacyclin [Epoprostenol Sodium (Flolan)] or phosphodiesterase inhibitor [Sildenafil citrate (Revatio)] should be only be done in consultation with the Pulmonary hypertension service.

Sedation and Analgesia

i. Sedation is of utmost importance.

ii. Recommended medications: alternatives may be considered based upon specific patient needs

1. Opioids:
    a. Avoid morphine due to possible hypotension
    b. Fentanyl: initial: 1 – 3 mcg/kg/hour, titrated to effect in 1 mcg/kg/hour increments. Maximum: 5 mcg/kg/hour.
    c. If fentanyl at maximum dose is not providing adequate sedation, consider hydromorphone. Initial: 0.0075 mg/kg/hour.

2. Benzodiazepines:
    a. Diazepam: 0.05 – 0.1 mg/kg IV every 4 hours as needed
    b. Lorazepam: 0.05-0.1mg/kg/dose every 4 hours as needed
    Maximum effective dose is usually 0.1mg/kg/dose every 3-4 hours. Propylene glycol toxicity is a concern if given more frequently.
    c. Midazolam infusion: initial 0.05 mg/kg/hour
        i. If inadequately sedated on maximum doses of intermittent agents
        ii. Use with caution in preterm infants and infants with underlying CNS disorders due to risk of seizures.

iii. Dexmedetomidine: initial dosing range 0.2 – 0.6 mcg/kg/hour

iv. Neuromuscular blocking agents should only be used if all sedative measures have failed to prevent patient activity from causing severe gas exchange dysfunction

e. Fluids/Electrolytes/Nutrition

i. 50 to 60 ml/kg/day including medication for the first 24 h, intake should be increased thereafter.

ii. TPN/IL should be initiated after first 24 h of life.

iii. Monitor fluid balance closely with goal of net even.

iv. Nursing to calculate urine output every 2 hours with goal of 1mL/kg/hr or greater.

d. Infectious Diseases

i. CBC with differential and blood culture should be obtained on admission.

ii. Start Ampicillin and Gentamicin for suspected sepsis, regardless of sepsis risk factors.

iii. Duration of antibiotic therapy to be determined by care team.

e. Laboratory monitoring

i. Admission labs:

1. Blood gas
2. Type and screen
3. Lactate
4. CBC with differential
5. Blood culture

6. SNP array (obtained from cord blood if possible)

ii. Arterial blood gas monitoring:
    1. Every 30 minutes x 2
    2. Every hour x 2
    3. Every 2 hours x 2
    4. Then every 4 hours
iii. Lactate every 6 hours
iv. Complete blood count every 12 hours
v. Electrolytes every 12 hours (alternating BMP and CMP) with ionized calcium
vi. Ongoing lab schedule to be determined by care team

V. ECMO Guideline Criteria

All criteria assume optimal support of respiratory and/or cardiovascular failure including HFOV, pulmonary vasodilator therapy, inotropic support and sedation (including paralysis)

a. Respiratory Criteria
    i. OI
        1. > 40 for 30 minutes (i.e two ABGs in a row)
        2. > 35 for 2 hours
        3. > 30 for 4 hours
        4. Persistent need for MAP > 18,
    ii. Barotrauma
        1. Severe air leak unresponsive to other therapies
    iii. Acute deterioration without rapid resolution
        1. PaO2 < 30 or preductal SaO2 < 70%

b. Cardiovascular/Oxygen Delivery Criteria
    i. Plasma lactate > 5 mmol/L and not improving despite volume expansion and inotropic support
    ii. Rapidly deteriorating or severe ventricular dysfunction
    iii. Intractable arrhythmia with poor perfusion
    iv. Cardiac arrest
c. ECMO should be explicitly addressed q12hr between NICU and GPS attendings/fellows
d. Pulmonary vasodilators and right heart function should be optimized if possible before ECMO initiation; dose titration and gatekeeper approval for these agents should be discussed with the pulmonary hypertension service.
    i. Inhaled NO; max dose 20 ppm
    ii. Sildenafil (Revatio); 0.25-1mg/kg po q6hrs
    iii. Inhaled inhaled prostacyclin [Epoprostenol Sodium (Flolan)]; max dose 50 mg/kg/min
    iv. Bosentan 0.25 - 2mg/kg po q12 hr
    v. Trepostonil (Remodulin); 5-20 ng/kg/min IV

After ECMO cannulation controlled transfer to PICU should occur

VI. Surgical Management
a. Timing guideline criteria for repair
    i. <u>Respiratory Criteria (maintained for 24hrs)</u>
        1. FiO2 < 50%
        2. Preductal SaO_2 >90%, P_aO_2>60 mmHg

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3. PIP ≤ 25
4. MAP ≤ 16
5. Minimized edema
6. OI ≤ 20
7. PCO_2 ≤ 65mmHg

ii. <u>Hemodynamic Criteria (maintained for 24hrs)</u>
1. Dopamine <10 mcg/kg/min
2. Appropriate MAP for GA
3. Sub-systemic PA pressures on Echo
4. Lactate < 3 and pH >7.25
5. Euvolemic
6. Resolved right ventricular failure

iii. Some patients will never reach these criteria after a reasonable amount of time; these patients may be candidates for ECMO

b. Repair on ECMO
i. Timing under study but trend is toward early repair (1-3 days)
ii. Amicar
iii. Open repair (see repair types)
iv. Leave chest tube (see chest tube section)

c. Repair types
i. Consider thoracoscopic repair in any child not currently on ECMO
ii. For patch repairs, consider Goretex vs. Dual Mesh Patch

d. Chest tube usage: routine chest tube use is not required even in the setting of large pneumothorax

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VII. Post-repair/Post ECMO guidelines

a. **Gentle Ventilation** strategy should be continued
b. Initial ventilation and hemodynamic management guidelines should generally be followed
c. Feeding should be initiated as soon as feasible
    i. Feeds should generally be nasoduodenal to start
    ii. A trial of NG feeds should be entertained depending on respirtatory status

SUMMARY OF GOALS

Minimize barotrauma

Heart rate less than 170/min in sedated infant

Mean arterial blood pressure 40-50 mmHg in term infant

Pre-ductal oxygen saturation 92-98% and post-ductal >92% with appropriate PaO2

Capillary refill less than 3 seconds

Urine output at least 1mL/kg/hr

Blood gas: pH: 7.28-7.35 / PaCO2: 50-65 / PaO2: 60-80k

Lactate < 3 mmol/L, Hematocrit > 40%

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Congenital Diaphragmatic Hernia Medication Use Guidelines

- These recommendations are relevant to patients with CDH and may not be appropriate to extrapolate to other disease states
- Medication use and dosing should be based on patient-specific needs and response

Hemodynamic Support

Medication	Initial Dosing	Maintenance Dosing
Hydrocortisone	1 mg/kg IV once OR 100 mg/m^2 IV once	NICU: • <34 weeks: 0.5 mg/kg IV q12h • ≥ 34 weeks: 0.5 mg/kg IV q6 – 8h PICU: • 25 mg/m^2 IV q6h
Vasoactive infusions	Refer to the following Policies: • (PICU0137) Vasoactive Therapy, Management of the Pediatric ICU Patient • (PED105) Vasoactive Therapy	

Pulmonary Hypertension Medications:

- Approval by a Pediatric Pulmonary Hypertension (PPH) Attending Physician must be obtained prior to order verification
  - Refer to LexiComp Online Formulary PPH Attending approval information for each PH medication
- PPH Attendings will provide dosing and titrations plans for patients receiving PPH medications

Medication	Dosing	Information
Inhaled Nitric Oxide (iNO)	Initial: 10 – 20 ppm Maximum: 20 ppm	• Doses > 20 ppm not recommended due to lack of efficacy and risk of methemoglobinemia • Abrupt discontinuation may lead to worsening oxygenation and rebound pulmonary hypertension – weaning parameters located in • Refer to (CLN002) Inhaled Nitric Oxide Administration
Inhaled Epoprostenol (Flolan®)	0.05 mcg/kg/minute	Refer to (MDU046) Continuous Nebulized Therapies for Pediatric Patients >> Appendix B: Use of Continuous Nebulized Epoprostenol (Flolan) for Pediatric Patients
Sildenafil (oral)	Initial: 0.25 - 0.5 mg/kg PO Q8H • Titrate in 0.25 – 0.5 mg/kg/dose increments Maximum: 1 mg/kg PO Q8H	Patients initiated on sildenafil require a consent form prior to initiation • Available via Forms on Demand (search blank forms for "Sildenafil")
Treprostinil (IV)	Usual range: 2-40 ng/kg/minute • Doses up to 80 ng/kg/minute have been used	Dosing and titration dictated by pulmonary hypertension provider

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Bosentan (oral)	Initial: 0.25 – 0.5 mg/kg PO Q12H Maximum: 2 mg/kg PO Q12H	REMS program is in place to increase awareness and minimize risk of hepatotoxicity • LFTs should be routinely monitored in patients receiving bosentan

Sedation and Analgesia

Medication	Dosing	Information
Opioids		
Fentanyl	Initial: 1 – 3 mCg/kg/hour Titrate by 0.5 - 1 mCg/kg/hour Max: 5 mcg/kg/hour	
Hydromorphone	Initial: 0.0075 mg/kg/hour	If fentanyl at maximum doses is ineffective, replace with hydromorphone
Benzodiazepines		
Diazepam	0.05 – 0.1 mg/kg IV Q4H PRN	
Lorazepam	0.05 – 0.1 mg/kg IV Q4H PRN Max: 0.1 mg/kg IV Q3-4H	Propylene glycol toxicity may occur at high doses or with renal impairment **(see below)** [1]
Midazolam	Initial infusion: 0.05 mg/kg/hour	Indicated if inadequately sedated on maximum doses of intermittent agents
Other		
Dexmedetomidine	Initial: 0.2 – 0.6 mCg/kg/hour	Can cause bradycardia secondary to AV blockade
Vecuronium	Intermittent Doses: 0.1 mg/kg/dose Q1 – 2H PRN Initial Continuous Infusion: 0.1 mg/kg/hour • Titrate to goal level of paralysis	Train-of-Four (TOF) Monitoring recommended when feasible: • Refer to (MDU027) Neuromuscular Blocking Agents for Mechanically Ventilated Patients >> Appendix C: Train of Four • Goal is typically 1 – 2 twitches (85 – 90% blockade)
Cisatracurium	Intermittent Doses: 0.15 mg/kg/dose over 5 – 10 seconds Initial Continuous Infusion: 0.03 – 0.05 mg/kg/hour • Titrate to goal level of paralysis	
Information		

[1] Propylene Glycol Toxicity	• Propylene glycol undergoes metabolism to lactic acid, leading to lactic acidosis
	• Toxicity has been associated with propylene glycol doses > 1,000 mg/kg/day
	• Monitoring:
	  ○ Increased anion gap
	  ○ Increased osmolar gap ([measured serum osmolarity – calculated osmolarity] > 10
	  ▪ Indicates significant quantities of an unmeasured solute
	  ▪ Calculated osmolarity = 2 x [Na] + [glucose/18] + [urea/2.8]
	  ○ Serum lactic acid
	  ○ Blood gas
	  ○ Serum electrolytes and renal function markers	

Hemostatic Agents for Patients on ECMO

Medication	Dosing	Information
Aminocaproic Acid	• Loading dose: 100 mg/kg (max 5,000 mg) to be given at least 1 hour prior to procedure • Initial maintenance infusion dosing: 33.3 mg/kg/hr (Max 1,000 mg/hr)	• Use and dosing is dictated by per surgical team: Refer to (ECMO831) Amicar Administration • Aminocaproic acid is renally eliminated and dose adjustments may be warranted in patients with renal dysfunction
Tranexamic Acid (TXA)[1]	• Loading dose: 10 – 15 mg/kg (Max 1,000 mg) • Initial maintenance infusion dosing based on eGFR:[2] ○ ≥ 60 mL/min: 2 mg/kg/hr (Max 125 mg/hr) ○ 30 - < 60 mL/min: 1.5 mg/kg/hr (Max 100 mg/hr) ○ 15 - < 30 mL/min: 1 mg/kg/hr (Max 60 mg/hr) ○ < 15 mL/min: 0.5 mg/kg/hr (Max 30 mg/hr) ○ CRRT: 1 mg/kg/hr (Max 60 mg/hr) ➢ TXA infusions can be titrated to a maximum of 10 mg/kg/hr; higher dosing is associated with increased incidence of seizures, especially in patients with deceased renal function	

1 Evidence for use of the intravenous TXA continuous infusion is limited to treatment durations of 10 hours for pediatric patients. The safety and efficacy of longer treatment durations is not known.

2 Estimated Glomuerular Filtration Rate (eGFR) = 0.413 x ht (cm) / SCr

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