CONGENITAL DIAPHRAGMATIC HERNIA MANAGEMENT

PRACTICE GUIDELINE ©

DOCUMENT SUMMARY/KEY POINTS

- Congenital diaphragmatic hernia (CDH) is a high risk, complex congenital malformation consisting of a defect that allows herniation of the abdominal contents into the thorax. The combination of pulmonary hypoplasia and abnormal morphology of the pulmonary vasculature often leads to severe respiratory insufficiency accompanied by pulmonary hypertension.
- Management strategies aim to limit ventilator induced lung injury (VILI), address the short and long term management of pulmonary hypertension, optimise haemodynamic and respiratory status before surgery, avoid cardiac failure and fluid overload and attend to nutrition.
- High frequency oscillation should be considered as an alternative to synchronised conventional ventilation.
- Treating physicians (Neonatologist, Paediatric Surgeon, Cardiothoracic surgeon & Paediatric Intensivist) will discuss and decide the feasibility and indications for offering ECMO.
- All neonates undergoing surgery for CDH should be enrolled in multidisciplinary follow up including looking at neurodevelopmental outcomes.

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1st August 2014	**Review Period:** 3 years
Team Leader:	Staff Specialist, Neonatologist	**Area/Dept:** NETS

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CHANGE SUMMARY

- N/A – new document.

READ ACKNOWLEDGEMENT

- All neonatal clinical staff are to read and acknowledge they understand the contents of this document.

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Introduction

Congenital diaphragmatic hernia (CDH) is a high risk, complex congenital malformation consisting of a defect that allows herniation of the abdominal contents into the thorax. The majority (80%) are left sided. The combination of pulmonary hypoplasia and abnormal morphology of the pulmonary vasculature often leads to severe respiratory insufficiency accompanied by pulmonary hypertension

The mortality of neonates with CDH in the SCHN has fallen dramatically in the last 10 years to around 10-15%. Although there is evidence of long term disability associated with this condition, [1-3] recent unpublished data from Melbourne presented at the European CDH workshop in Rotterdam in June 2013, showed no difference in developmental outcomes at two years of age on standardized tests which is in accordance with data from three year follow-up from the Grace Neurodevelopmental clinic.

This guideline is for the management of neonates with CDH who require significant mechanical ventilation and often complex cardiovascular support. Less critically ill neonates will not require many of the following interventions. The management strategies that follow will aim to:

- Limit ventilator induced lung injury (VILI)
- Address the short and long term management of pulmonary hypertension
- Optimise haemodynamic and respiratory status before surgery
- Avoid cardiac failure and fluid overload

Stabilisation on Admission

On admission the initial stabilisation should address the following:

- Cardiorespiratory support
- Avoidance of bag mask ventilation and subsequent barotrauma and also distension of the stomach which may limit expansion of the hypoplastic lung
- Placement of an oro-/ or nasogastric tube on continuous free drainage with 4th hourly aspiration in order to prevent gastric and bowel distension and further lung compression.
- Central venous access: triple lumen UVC should be inserted
- Arterial access: the umbilical artery can be used. Pre-ductal (right radial) arterial access is preferred as it reflects cerebral oxygenation
- $TcCO_2$ monitoring
- Pre-/ and postductal O_2 saturation monitoring. Assessment of oxygenation is based on preductal O_2 saturation, but both are measured to indirectly continuously monitor right-to-left shunt.
- Arterial blood gas and initial FBC, Electrolytes, Urea, Cr, Ca, Mg, coagulation profile, glucose, lactate.
- Chest X-ray and abdominal X-ray.

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- Cardiology referral. An echocardiogram is required to document normal cardiac structure and to assess the degree of pulmonary hypertension, ductal status and ventricular function.
- Consult the paediatric surgeon

General Measures and Monitoring

Each neonate will have an individualised plan formulated each day. General principles of care include:

- Minimal handling to ensure that adverse physiological responses are avoided.
- Normothermia through the use of a radiant warmer and servo control.
- Blood sampling. The frequency of sampling for ABGs and other parameters (FBC, U&E, Cr, etc.) will largely be determined by the cardiorespiratory status of the neonate as well as previous results. A plan for frequency of blood sampling should be clarified at each ward round.
- Monitor urine output (keep > 1 mL/kg/hr.). Insert a urinary catheter if the neonate is heavily sedated or muscle relaxed.
- Continuous invasive blood pressure monitoring.
- Monitoring with aEEG if available
- Intravenous nutrition should be commenced as early as practical. The aim is to provide adequate nutrition and hydration without causing fluid overload, particularly in the heavily sedated or muscle relaxed neonate. The usual daily total fluid requirement would be 40 - 60 mL/kg/day.

Associated congenital anomalies are present in 10-40% of neonates with CDH[1]. Cardiac anomalies have been reported in up to 25% of neonates with CDH and worsen the prognosis[2]. Recent as yet unpublished data suggest CGH array is recommended in all neonates with CDH [22].

Sedation and Analgesia

Neonates with severe pulmonary hypertension will require analgesia and sedation to facilitate optimal ventilation. Pain score assessment needs to be attended and recorded at least every four hours.

- A narcotic infusion would normally be commenced in a ventilated neonate. Clinical evidence of ongoing pain and/or distress (pain scores) should be managed with additional boluses, increased infusion rate and consideration of another drug or additional sedation.
- In addition to optimised analgesia and sedation, muscle relaxation with bolus or infusion should be considered in any neonate who is difficult to stabilise.
- A midazolam infusion might also be considered in a neonate requiring muscle relaxation or escalating doses of morphine.

Ventilatory Support

Permissive hypercapnoea and gentle ventilation is recommended as it has been reported to increase survival[4, 5].

Synchronised conventional Ventilation (SIMV) with tidal volume monitoring is the preferred initial ventilator strategy

- In preparation for the arrival of a neonate with CDH –the ventilator should be set up to be able to provide inhaled nitric oxide quickly if unable to oxygenate adequately on admission.
- Maintain a PIP < 26 cm H_2O
- Use a PEEP of 2-5 cm H_2O. If oxygenation is a problem consider trialling increased PEEP if the chest X-ray reveals under inflation. Also consider a longer inspiratory time and I:E ratio of 1:1 to maintain airway pressure.
- Use a ventilator breath rate of 40 – 60 /min to allow permissive hypercapnoea (pCO_2 45 – 65 mmHg), ph 7.25 – 7.35
- Aim for 3 - 4 mL/kg tidal volume
- Titrate FiO_2 to maintain pre-ductal saturations 85 – 88% and post ductal saturations above 70% (In individual cases levels down to 80% may be accepted, providing organs are well perfused as indicated by pH > 7.25and urinary output above 1 ml/kg/h).
- Add iNO as discussed below
- Maintain spontaneous respiration if possible

If these parameters cannot be maintained and the pCO_2 is >80 mmHg and the ph is <7.25 then in the presence of neonatologist/intensivist/fellow consider commencing HFOV.

HFOV

HFOV is a lung protective strategy to reduce ventilator induced lung injury (VILIV). The physiological rationale for use of HFOV derives from its ability to preserve end-expiratory lung volume while avoiding over-distension, and therefore lung injury. Retrospective studies have demonstrated effective CO_2 reduction and increased survival in neonates with CDH[6, 7]. A prospective randomized controlled trial on the use of HFOV as an initial ventilation mode is still lacking.

HFOV can be seen as CPAP with “wobbles” and this reflects the physiological goals of:

- CPAP – sustained inflation and recruitment of lung volume by the application of distending pressure (mean airway pressure or MAP) to achieve oxygenation[16].
- “wobbles” – alveolar ventilation and CO_2 removal by the imposition of an oscillating pressure waveform on the MAP at an adjustable frequency (Hz) and amplitude. [16] As seen in Figure 1 below.

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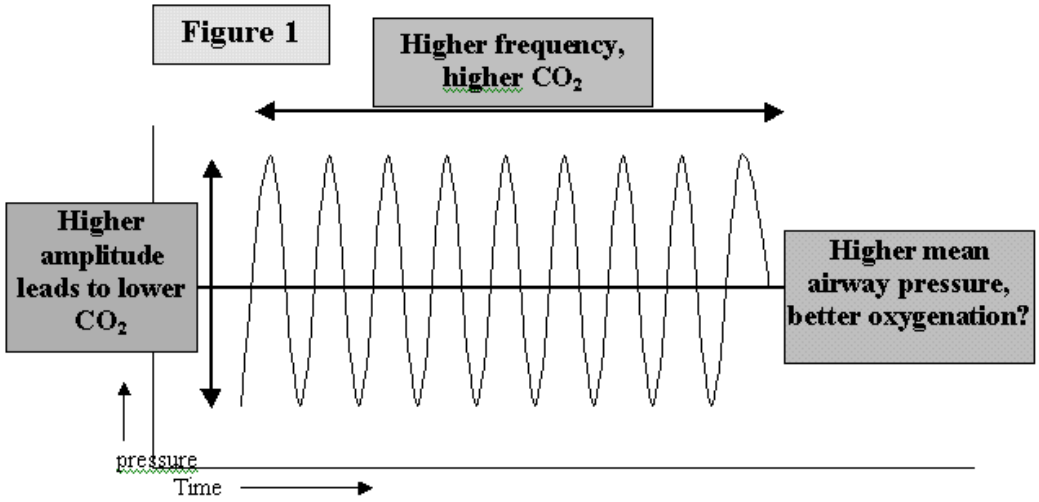

The following settings are a reasonable way to commence with HFOV. For more detail see the HFOV guideline.

- Ensure the ETT size is adequate with minimal leak of less than 10%.
- Commence with a mean airway pressure equal to that required on conventional ventilation (13- 17cm H_2O).
- Set the Hz at 8-10.
- Delta P adequate to produce desired pCO_2 — (30-60 cm H_2O depending on chest wall vibration).
- FiO_2 to maintain a pre-ductal saturation of 85 -88%
- When commencing HFOV have the neonate initially well sedated and consider muscle relaxation. Consider not continuing muscle relaxation once the neonate is stable on HFOV.
- Obtain a CXR within an hour of commencement to determine adequate lung distension (8 posterior ribs and curved normal diaphragm) and to rule out over distension (≥10 posterior ribs and flattened normal diaphragm). Adjust MAP as necessary.

Care of the ventilated neonate

- Neonates who are ventilated require vigilance in observation and assessment to avoid complications of the treatment.
- All ventilated neonates require skilled nursing care and the guidelines are followed and if there are concerns referral to the neonatologist/fellow occurs immediately.
- Please refer to the following guidelines:
  - Endo-Tracheal Suctioning in Neonates: http://chw.schn.health.nsw.gov.au/o/documents/policies/guidelines/2012-0002.pdf
  - Respiratory Support in the Neonatal Intensive Care Unit: http://chw.schn.health.nsw.gov.au/o/documents/policies/guidelines/2007-0005.pdf

Cardiovascular Support

The assessment of circulatory adequacy and therefore decisions about intervention to augment systemic and/or pulmonary blood flow should be multidimensional and include consideration of blood pressure, acid-base status, arterial lactate, urine output and capillary refill. Hemodynamic management should be aimed at achieving appropriate end-organ perfusion.

- Intervention must take account of the degree of respiratory support required
- Targeting a specific blood pressure in an effort to close a pre-post ductal saturation difference where oxygen delivery/utilisation is not overly compromised is generally discouraged.

In the presence of an ongoing metabolic acidosis, myocardial ischemia, sepsis or a strangulated bowel must be considered.

Inotropic support of the cardiovascular system

The general aim is to maintain a systemic mean arterial blood pressure of > 40 mmHg in the term neonate, and in the preterm neonate equivalent to their gestational age (the 10th percentile for each gestation).

Consider excessive mean airway pressure as a cause of hypotension and adjust if possible.

- The initial management of hypotension is a normal saline bolus (up to 20mL/kg). Further fluid boluses should not be given unless discussed with the neonatal consultant or intensivist.

The choice of inotropic support should be considered carefully according to the underlying problem and current cardiovascular status on echocardiogram.

- Dobutamine (5 – 15 micrograms/kg/min) raises blood pressure by increasing cardiac output and decreasing peripheral vascular resistance. Compared to dopamine, dobutamine achieves a greater increase in O_2 delivery for a given increase in O_2 consumption.
- Low dose adrenaline (0.5 -1.0 micrograms/kg/min) – raises the blood pressure by increasing cardiac output and decreasing peripheral vascular resistance. Beware higher doses (>1.0 micrograms/kg/min) will increase systemic vascular tone.
- Milrinone (0.5 -0.75 microg/kg/min) is an ino-dilator which increases cardiac output and lowers peripheral vascular resistance. It is long acting and takes 6-12 hours to reach steady state. Be wary as may precipitate hypotension some time after commencement.
- Hydrocortisone may be used for treatment of hypotension after conventional treatment has failed.[8] Ensure that random cortisol level is sent prior to commencement of this strategy.
- Noradrenaline (0.5-1microg/kg/min) – raises blood pressure mainly by peripheral vasoconstriction or – almost pure αlpha effect and only moderate β1 receptor effects. Indicated where cardiac output is normal but need vasoconstriction – for example in sepsis.

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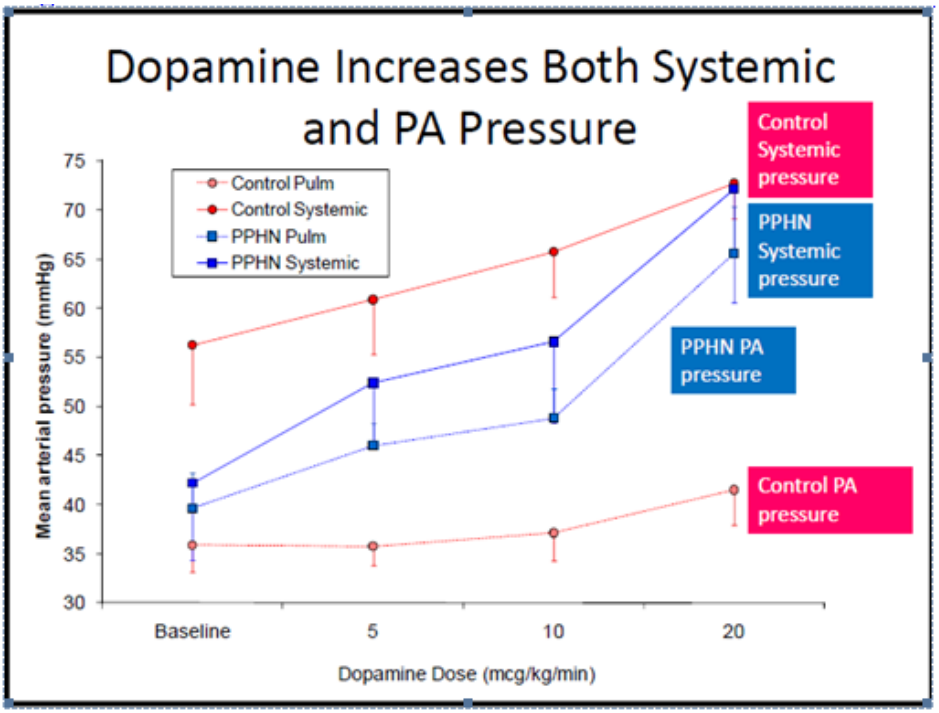
- Inotrope infusions must be administered continuously and avoid fluctuations during line changes. Be aware of incompatibilities when used with other drug additives.
- Note that there is evidence that in the presence of PPHN dopamine and other adrenergic agents in high dose raise pulmonary pressures along with systemic pressure and are not recommended in this setting. See Figure 2.

Figure 2 [20]



Pulmonary Hypertension

The physiological basis of pulmonary hypertension in neonates with CDH is a decreased number of pulmonary arterial structures associated with significant adventitial and medial wall thickening due to an increased amount of smooth muscle cells in pulmonary arteries. As a result, elevated pulmonary vascular resistance may lead to right to left shunting after birth. This may result in hypoxaemia and a difference in pre-and postductal oxygen saturation. However, absence of a pre-/ and postductal gradient in oxygenation does not exclude the diagnosis of pulmonary hypertension since the right to left shunting may occur through the foramen ovale. Therefore echocardiography remains one of the best modalities for real time assessment of pulmonary arterial diameter and right heart function. In patients with CDH left ventricular dysfunction, either caused by right ventricular overload or a relative underdevelopment of the left ventricle, is associated with a poor prognosis. [9]

If pre-ductal saturation falls below 85% and there are signs of inadequate organ perfusion, treatment of pulmonary hypertension should be initiated by optimising blood pressure. Adequate intravascular volume should be maintained, transfusion of packed red blood cells may be required to optimize tissue oxygen delivery. No studies show the benefit of increasing systemic vascular resistance to treat right to left shunting, but it is accepted practice that inotropes are employed to maintain blood pressure at the normal level for gestational age[10].

If pulmonary hypertension persists, pulmonary vasodilator therapy should be given, with inhaled Nitric Oxide as the first choice.

Inhaled Nitric Oxide (iNO)

iNO is a selective pulmonary vasodilator and thus improves pulmonary blood flow. It is indicated when there is evidence of severe pulmonary hypertension such as:

- FiO_2 >75% to maintain saturation targets.
- Echocardiography findings consistent with pulmonary hypertension.

Commence inline iNO at 10 ppm, increasing to 20 ppm if no response after a few minutes

Prostaglandin E_1 (PGE_1)

PGE_1 is indicated when there is severe pulmonary hypertension, in order to ameliorate right heart strain. It may be commenced in conjunction with iNO. Excessive right ventricular overload due to pulmonary hypertension causes right heart failure, particularly when the ductus arteriosus closes. Maintaining the ductus open creates a vent for the right ventricle, allowing a right to left shunt and reduction of overload, especially at times of pulmonary hypertensive crisis[11].

- Where possible, obtain an echocardiogram prior to starting PGE_1 in order to document pulmonary hypertension and/or cardiac dysfunction.
- Commence infusion at 10 ng/kg/min and titrate according to clinical response and/or echocardiogram findings.
- PGE_1 requires a dedicated IV line.

Sildenafil

Sildenafil is a phosphodiesterae-5 inhibitor which:

- Augments the endogenous levels of cGMP in vascular smooth muscle causing pulmonary and systemic vasodilation
- Enhances the vasodilator effects of iNO
- May assist with weaning of iNO and mechanical ventilation

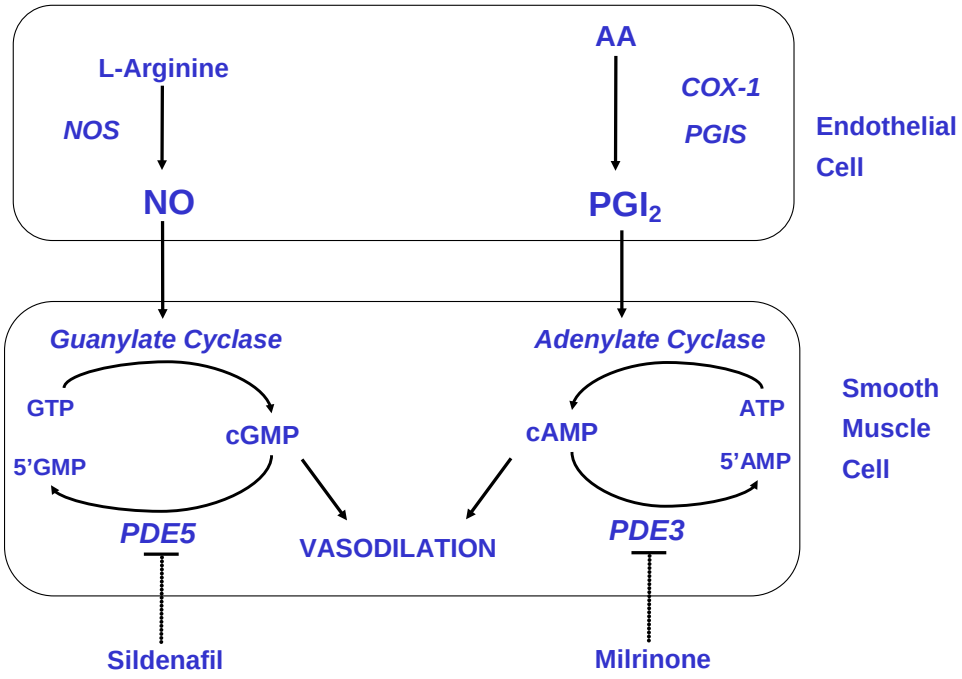
It is used when there is severe ongoing pulmonary hypertension[12, 13]

- To augment vasodilatation or
- When trying to wean ventilator support where unable to cease iNO

It is available in the SCHN as an oral preparation and it may be given to a neonate who is otherwise nil by mouth. The dose is 0.5 mg/kg TDS, increasing in 0.5 – 1 mg/kg increments daily to a total of 3 mg/kg TDS.

Figure 3 outlines the cellular mechanisms whereby iNO, milrinone and sildenafil work synergisitically to lead to pulmonary vasodilation.

Figure 3[21]



ECMO

The role of Extracorporeal Membrane Oxygenation in the treatment of neonates with CDH is still unclear[14]. A meta-analysis of retrospective studies suggests that the introduction of ECMO has improved survival in neonates with CDH[15], however, a meta-analysis of randomized controlled trials with small sample sizes indicated a reduction in early mortality with ECMO, but no long term benefit. [15]

Criteria to consider ECMO

- Clinical instability on maximal medical therapy
- The impression of a reversible component to an acute cardiopulmonary deterioration
- Absence of pre-existing major compounding factors eg. congenital heart disease, sepsis, significant VILI, other congenital or genetic conditions that inform a poor prognosis
- Parental informed consent

The Neonatal consultant / paediatric intensivist, surgeon and cardiothoracic surgeon will discuss the situation.

Fluid Management and Feeding

- Restrictive fluid management in the first 24 hours consists of 40 mL/kg/day of fluids for intravascular filling.
- Thereafter, fluid and caloric intake should be increased based on clinical condition.
- Early administration of parenteral nutrition is recommended.
- Diuretics should be considered where fluid balance is overtly positive.
- Enteral feeding should be started postoperatively combined with anti-reflux medication
- EBM/colostrum can be commenced from birth at trophic levels (no more than 1mL 4th hourly) via gastric tube. Patency and continuous free drainage of the gastric tube must be maintained to allow adequate venting of the stomach.

Timing of Surgical Repair

Delayed surgical repair is now considered best practice. It allows for stabilisation of pulmonary hypertension, the systemic circulation, cardiac function, ventilation and the correction of any haematological or biochemical disturbances

Surgical repair of the defect in the diaphragm is normally performed after physiological stabilization, which is loosely defined as 24 hours of the following:

- Mean arterial blood pressure normal for gestational age off inotropes
- Preductal saturation levels of > 85% SaO_2 in an FiO_2 of < 50% off iNO
- Lactate < 3 mmol/L
- Urine output > 2 mL/kg/hr

Follow-up

Due to the complex nature of this disorder it is desirable for neonates discharged from intensive care to be followed-up by surgical, respiratory and developmental clinics.

There is a support group - http://cdh.org.au/ which may be recommended to families.

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