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 associated lung injury (VALI), 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 upon the feasibility and indications for offering ECMO.
- This guideline is for the medical management of newborns with CDH both pre and post-surgical repair as the principles are the same.
- All neonates undergoing surgery for CDH should be enrolled in multidisciplinary follow up including looking at neurodevelopmental outcomes.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1st May 2021	**Review Period**: 3 years
Team Leader:	Clinical Nurse Consultant	**Area/Dept**: GCNC CHW

Date of Publishing: 22 April 2021 7:59 AM Date of Printing: 22 April 2021

CHANGE SUMMARY

- List the sections/items that have changed from the previous version.
- References updated
- Drug information and dosages updated to align with Australasian Neonatal Medicines formulary
- Ventilation information updated
- Supportive nursing care information added

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 standardised tests. This is in keeping 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 associated lung injury (VALI)
- 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

Stabilisation in the delivery room and initial perinatal period should include attention to:

- Physiologically based cord clamping, unless there is a contraindication, as this has shown benefit in animal models of CDH[4] and in other high risk newborns
- Early intubation and avoidance of bag-mask ventilation
- Measurement and documentation of the tidal volume of spontaneous breaths: low tidal volumes may predict risk of chronic lung disease or mortality[5]

On admission the initial stabilisation should address the following:

- Cardiorespiratory support
- Avoidance of bag-mask ventilation to prevent barotrauma and distension of the stomach, which may also limit expansion of the ipsilateral 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, however pre-ductal (right radial) arterial access is preferred as it reflects cerebral oxygenation

- $TcCO_2$ monitoring
- Pre- and post-ductal O_2 saturation monitoring. Assessment of oxygenation is based on pre-ductal O_2 saturation, but both are measured to continuously monitor right-to-left shunt indirectly
- Arterial blood gas and initial FBC, Electrolytes, Urea, Cr, Ca, Mg, coagulation profile, glucose, lactate
- Chest X-ray and abdominal X-ray
- Cardiology referral. An echocardiogram is required to document cardiac structure and to assess the degree of pulmonary hypertension, ductal status and ventricular function and dimensions. This is suggested to be performed within the first 4-12 hours after birth, after the initial transitional period and due to the potential for early cardiac dysfunction[6].
- Subsequent echocardiography or clinician performed cardiac ultrasound should be considered thereafter to guide decision-making in the pre- and post-operative periods, during unexpected deterioration and when weaning support[6].
- Consult the paediatric surgeon

General Measures and Monitoring

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

- Minimal clinical handling to ensure that adverse physiological responses are avoided.
- Supportive parent touching is encouraged within clinical parameters.
- 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
- 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 for the first 48 hours and then review.

Associated congenital anomalies are present in 10-40% of neonates with CDH[1,7]. Cardiac anomalies have been reported in up to 25% of neonates with CDH and worsen the prognosis[2]. A CGH array is recommended in all neonates with CDH[7].

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

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.

Permissive hypercapnoea and gentle ventilation is recommended as it has been reported to increase survival[8, 9, 10,11].

Ventilation strategy

The preferred ventilation modes are either Synchronised Intermittent Mandatory Ventilation (SIMV) or Assist Control (AC), with tidal volume monitoring[11]. Low PEEP, PIP and TV are the important aspects of ventilation for an infant with CDH, irrespective of ventilation mode.

Recommended ventilation strategies include:

Ventilation parameter	Recommendation
Peak Inspiratory Pressure (PIP)	• Maintain a PIP < 26 cm H_2O
Positive end expiratory pressure (PEEP)	• 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.

Ventilator rate	• Use a ventilator breath rate of 40 – 60 /min to allow permissive hypercapnoea (pCO_2 45 – 65 mmHg), Ph 7.25 – 7.35 • Maintain spontaneous respiration if possible
Tidal volume	• Aim for 3 - 4 mL/kg tidal volume
Oxygenation	• Titrate FiO_2 to maintain pre-ductal saturations 85 – 88% and post-ductal saturations above 70% • In individual cases, pre-ductal levels down to 80% may be accepted, providing organs are well perfused as indicated by pH > 7.25 and urinary output above 1 ml/kg/hr

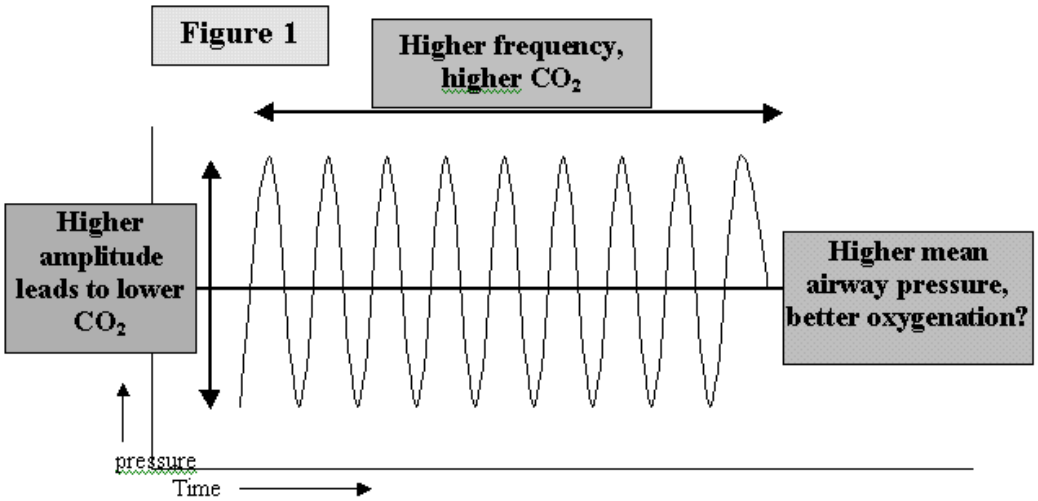
Safety alert: If these ventilator parameters cannot be maintained and the pCO_2 is >80 mmHg and the pH is <7.25 then in the presence of neonatologist/intensivist/fellow, consider commencing HFOV.

HFOV

HFOV is a lung protective strategy to reduce ventilator associated lung injury (VALI). 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 [12, 13]. One prospective randomised trial did not show any significant difference in the combined outcome of mortality or chronic lung disease when comparing HFOV with conventional mechanical ventilation[14]. A shorter duration of ventilation and a reduced need for both medical treatment of pulmonary hypertension and ECMO were observed in infant's initially ventilated using conventional ventilation in this study[14].

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[15].
- "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[15]. As seen in Figure 1 below.



The following settings recommended when commencing HFOV (for more detail refer to the Respiratory Support in Neonates - GCNC - CHW policy):

HFOV setting	Recommendation
ETT	• Preferably cuffed and with minimal leak of between 10-20%
Mean Airway Pressure (MAP)	• Commence with a MAP 2 cm above what was required on conventional ventilation (13-17cm H_2O)
Frequency (Hz)	• Usually set at 8-10. A higher frequency may be appropriate in specific circumstances, e.g. for preterm infants or those with air leak, following discussion with the consultant.
Amplitude (Delta P)	• Adequate to produce desired pCO_2 — (30-60cm H_2O depending on chest wall vibration). Consider starting with an amplitude approximately double the set MAP
Oxygen (FiO_2)	• To maintain a pre-ductal oxygen 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 (7-8 posterior ribs and curved normal hemidiaphragm) and to rule out over distension (≥10 posterior ribs and flattened normal hemidiaphragm). 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.
- In the NICU setting for additional information on HFOV and management of ventilated patients refer to the Respiratory Support in Neonates - GCNC - CHW policy

Supportive Nursing Care

Infants with CDH require supportive nursing care due to their level of illness and treatment. Considerations include:

Parent	- Facilitate parent involvement in caregiving from admission - Opportunities for involvement include: assisting with cares, immuno-supportive oral care (ISOC), supportive containment/holding (hand hugs), reading and talking to their baby
Positioning	- Maintain flexion and utilise a high nest to minimise insensible losses and support muscle relaxed infants - Alternate position as able - Consider the use of a gel pillow in muscle relaxed infants
Noise	- Reduce noise, particularly for muscle relaxed infants - If utilising HFOV, use ear muffs and provide periods of time off when there is less activity and noise in the unit - ideally when parents are present to encourage exposure to language/talking
Light	- Adapt light to the infant's needs - Avoid direct light in the face
Touch	- The infant may be sensitive to touch - encourage still resting hands - If skin-to-skin cuddles are not possible, encourage modified skin-to-skin
Taste/scent	- Utilise ISOC and scent pads - Encourage reciprocal scent pad exchange (infant/parent and parent/infant)
Caregiving	- The infant may require additional support during nursing care giving interventions - Consider the use of four handed care (i.e. two people – nurse/nurse or nurse/parent), supportive wrapping (seat belt swaddling), paced caregiving responsive to the infants cues

Refer to the following policies for additional information supportive care:

- Respiratory Support in Neonates - GCNC - CHW
- Developmental supportive care for newborn infants

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. Echocardiography or clinician performed cardiac ultrasound may be a valuable adjunct to assessment. Haemodynamic management should be aimed at achieving appropriate end-organ perfusion.

- Intervention must take into account 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 ischaemia, sepsis or a strangulated bowel must be considered.

Inotropic/Vasopressor support of the cardiovascular system

The general aim is to maintain an adequate systemic arterial pressure to maintain organ perfusion. Systolic, mean and diastolic blood pressure components should be taken into consideration and can provide valuable information about the cause of haemodynamic compromise. Although blood pressure should not be considered in isolation, a 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) is often considered adequate. Other haemodynamic parameters, such as heart rate, pulse volume, serum lactate, urine output and adjunctive cardiac ultrasound measures should also be considered when assessing the adequacy of the circulation.

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

- The initial management of hypotension thought to be representative of impaired circulation may include sodium chloride 0.9% bolus (10 -20 mL/kg). Further fluid boluses should not be given unless discussed with the neonatal consultant or intensivist.

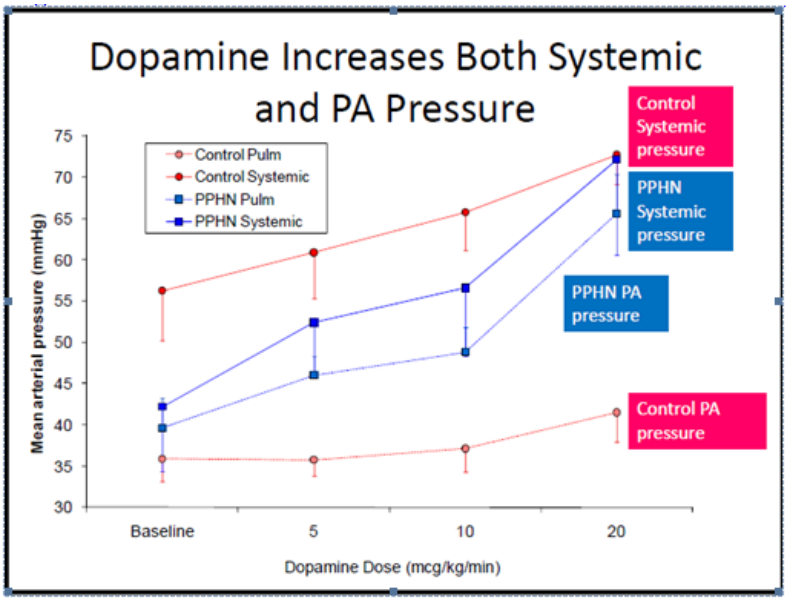
The choice of inotropic and/or vasopressor support should be considered carefully according to the underlying problem and current cardiovascular status clinically and on echocardiogram or clinician performed ultrasound. Frequent reassessment should be undertaken when starting and titrating inotrope and vasopressor medications.

Drug	Dose	Action
Adrenaline	0.05-1 microgram/kg/min	• At **low** doses of 0.01 – 0.1 microgram/kg/min, adrenaline primarily stimulates cardiac and vascular beta-1 and beta-2 receptors, leading to increased inotropy, chronotropy, conduction velocity and peripheral vasodilatation. • At **high** doses of >0.1 microgram/kg/min, adrenaline also stimulates cardiac and vascular alpha-1 receptors, causing vasoconstriction and increased inotropy. The net effects are increases in blood pressure and systemic blood flow resulting from increases in systemic vascular resistance and cardiac output.[16] • Beware higher doses (>1microgram/kg/min) will increase systemic vascular tone.
Milrinone	0.2-0.75 microgram/kg/min Starting dose is generally 0.33 microgram/kg/min (range 0.33 – 0.75 microgram/kg/min) Starting dose for prematurity or renal impairment is 0.2 microgram/kg/min (range 0.2 – 0.5 microgram/kg/min)	• Is an inodilator and lusitrope, which increases cardiac output, lowers peripheral vascular resistance and improves diastolic function.[17] • Milrinone may also reduce pulmonary vascular resistance and improve right ventricular performance and oxygenation in the setting of PPHN.[18-20] • It is long-acting, and takes 6-12 hours to reach steady state. Be wary as may precipitate hypotension sometime after commencement. Use with caution if there is existing diastolic hypotension. • Consider co-treatment with a vasopressor (e.g. noradrenaline) if the patient is hypotensive • Not recommended for use in newborns with coexistent hypoxic-ischaemic encephalopathy due to the potential for the drug to accumulate • Unlike catecholamines, milrinone does not increase myocardial oxygen consumption.
Noradrenaline	0.05-1 microgram/kg/min	• Raises blood pressure mainly by peripheral vasoconstriction, or almost pure alpha effect and only moderate β1 receptor effects. • Indicated where cardiac output is normal and vasoconstriction is desirable – for example, in sepsis.

		• Noradrenaline may improve right ventricular performance and have a favourable effect on pulmonary vascular resistance.
Dobutamine	5-20 microgram/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.
Hydrocortisone	≥ 35 weeks pma/corrected gestational : Loading dose of 1-2 mg/kg[21] followed by 1 mg/kg/dose 6–8 hourly (range 1−2 mg/kg/dose). < 35 weeks: Loading dose of 1-2 mg/kg[21] followed by 1 mg/kg/dose 6–12 hourly (range 1−2 mg/kg/dose).	• May be used for treatment of hypotension after conventional treatment has failed. [22] • Should be considered where there is persistent hypotension despite treatment with 2 vasoactive agents • Ensure that a random cortisol level is sent prior to commencement of this strategy.

- Inotrope/vasopressor infusions must be administered continuously and avoid fluctuations during line changes. This means the quick change method is required 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 doses raise pulmonary pressures along with systemic pressure and are therefore not recommended in this setting. See Figure 2.

Figure 2 [23]



Pulmonary Hypertension

The physiological basis for 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 ductal shunting after birth. This may result in hypoxaemia and a difference in pre-and post-ductal oxygen saturations. However, absence of a pre-/ and post-ductal gradient in oxygenation does not exclude the diagnosis of pulmonary hypertension, since the right to left shunting may be intrapulmonary or occur through the foramen ovale. Therefore, echocardiography or clinician performed cardiac ultrasound remains one of the best modalities for real time assessment of pulmonary arterial pressure and right and left 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.[24]

If pre-ductal saturation falls below 85% and there are signs of inadequate organ perfusion, treatment of pulmonary hypertension should be initiated by optimising cardiac function and blood pressure. Adequate intravascular volume should be maintained and transfusion of packed red blood cells may be required to optimise 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/vasopressors are employed to maintain blood pressure at the normal level for gestational age[13] and optimise cardiovascular function.

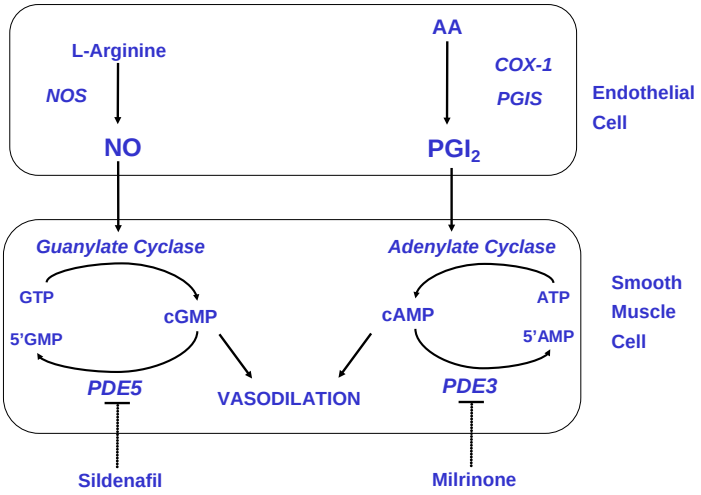
If pulmonary hypertension persists, pulmonary vasodilator therapy should be given, with Inhaled Nitric Oxide as the first choice.

Drug	Dose	Information
Inhaled Nitric Oxide (iNO)	10-20 parts per million (ppm)	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: • FiO2 >0.75 to maintain saturation targets. • Echocardiography/cardiac ultrasound findings consistent with pulmonary hypertension. Commence inline iNO at 10-20 ppm, increasing to 20 ppm if no response after a few minutes
Alprostadil Prostaglandin E_1 (PGE_1)	5-10 nanogram/kg/min (Maintenance dose range 3-20 nanogram/kg/minute)	• PGE_1 is indicated when there is severe pulmonary hypertension and echocardiography/ultrasound evidence of a restrictive ductus arteriosus, in order to ameliorate right heart strain. Can be commenced 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[23]. • Prior to commencing PGE_1, obtain an echocardiogram or clinician performed ultrasound to document pulmonary hypertension and cardiac function • Commence infusion at 5-10 nanogram/kg/min and titrate according to clinical response and/or echocardiogram/cardiac ultrasound findings. • It is recommended PGE_1 is administered via a dedicated IV line. • Commencement of PGE_1 may be associated with systemic hypotension
Sildenafil	Loading dose: 0.4 mg/kg administered over THREE hours followed by: IV	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

	1.6 mg/kg/day as a continuous IV infusion <u>Oral</u> 0.5 – 1 mg/kg every 6-8 hours Increase by 0.5-1 mg/kg/day to total 2 mg/kg/**dose** May increase to a maximum of 3 mg/kg/dose 6 hourly	• May assist with weaning of iNO and mechanical ventilation Data in neonates are limited. Sildenafil may be used when there is severe ongoing pulmonary hypertension[25, 26] • To augment pulmonary vasodilatation, particularly where there has been a poor response to iNO or • When trying to wean ventilator support and persistently unable to cease iNO

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

Figure 3[27]



ECMO

The benefits of ECMO in CDH are still controversial, since there are only few randomised trials demonstrating the advantages of this therapeutic option. At present, there is no precise prenatal and/or early postnatal prognostication parameter to predict reversibility of PPHN in CDH patients. Indications for initiating ECMO include either respiratory or circulatory parameters, which are also undergoing continuous refinement.[28]

Criteria to consider ECMO[29]:

- Clinical instability or inadequate tissue oxygen delivery despite maximal medical therapy (e.g. rising lactate, worsening metabolic acidosis, signs of end organ dysfunction)
- Severe hypoxic respiratory failure with acute decompensation. The impression of a reversible component to an acute cardiopulmonary deterioration
- Absence of pre-existing major compounding factors e.g. congenital, genetic or other comorbid conditions that inform a poor prognosis, severe brain injury, or vessel size too small for cannulation (by assessment of cardiac surgeon)
- Parental informed consent

The Neonatal consultant / paediatric intensivist, surgeon and cardiothoracic surgeon will meet to discuss suitability for ECMO.

Fluid Management and Feeding

- Restrictive fluid management in the first 24 hours consists of 40 mL/kg/day of fluids
- Glucose concentration in intravenous fluids may need to be increased to ensure provision of an adequate glucose infusion rate.
- 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 overly positive, particularly where urine output is low, provided the cardiovascular status is otherwise stable
- Enteral feeding should be started postoperatively combined with ‘anti-reflux’ (anti-acid) medication
- EBM/colostrum can be commenced from birth at trophic levels (no more than 1 mL 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 stabilisation, which is loosely defined as 24 hours of the following:

- Mean arterial blood pressure normal for gestational age off inotropes/vasopressors
- Preductal saturation levels of > 85% in an FiO_2 of <0.5 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 neurodevelopmental clinics.

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

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