Winnipeg Regional Health Authority / Office régional de la santé de Winnipeg — Caring for Health / À l'écoute de notre santé	**Title:** **Management of Patent Ductus Arteriosus in Neonates**	
NEONATAL CLINICAL PRACTICE GUIDELINE	**Approval Date:** January 2015	**Pages:** *1 of 6*
	Approved by: Neonatal Patient Care Teams, HSC & SBH Child Health Standards Committee	**Supercedes:** *N/A*

1.0 PURPOSE and INTENT

To provide clinical guidance to practitioners caring for neonates diagnosed with Patent Ductus Arteriosus (PDA) in the Neonatal Intensive Care Units in Winnipeg.

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 neonatologist performing IENH and the attending neonatologist.

2.0 PRACTICE OUTCOME

Promote assessment and care management for PDA based on best available evidence, reducing practice variation, improving care and reducing incidence of adverse consequences of treatment.

3.0 GUIDELINES FOR ASSESSMENT

3.1 Conduct a comprehensive clinical assessment and Integrated Evaluation of Neonatal Hemodynamics (IENH). Assess for the following (Responsibility of both the neonatologist performing IENH and the attending neonatologist):

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3.1.1 Indicators of pulmonary over-circulation:

- Pulmonary hemorrhage.
- Escalating respiratory support.
- Worsening of oxygenation and/or ventilation.
- CXR : cardiomegaly and pulmonary congestion.

3.1.2 Indicators of systemic hypo-perfusion

- Diastolic blood pressure less than 3rd percentile for GA.
- Both systolic and diastolic pressure below 3rd percentile for GA with the requirement for inotropic support.
- Lactic acidosis unexplained by other causes (more than 2.5 umol/dl).
- Renal impairment with oliguria (less than 1ml/kg/hr).

3.1.3 Biochemical markers:

- Brain type natriuretic peptide (BNP) (if applicable)

3.2 Conduct Targeted Neonatal Echocardiography (TNE) to determine the following (Responsibility of the neonatologist performing IENH) :

3.2.1 PDA morphology: shunt size (pulmonary and aortic end), direction (L-R, bidirectional), gradient (mean + peak)

3.2.2 Left Heart Volume Loading: LV dimensions (LVEDD), LA dimensions (LA size, LA:Ao ratio), Pulmonary artery diastolic flow (Level of MPA, Left branch), Right upper pulmonary vein peak diastolic velocity, Mitral valve inflow VTI

3.2.3 Left Heart Function: systolic (LV FS and/or EF) and diastolic (E/A ratio, IVRT) function, left ventricular output (LVO)

3.2.4 Systemic Hypo-perfusion: Absent or retrograde diastolic flow in post-ductal aorta, SMA, celiac and middle cerebral arterial Doppler.

3.3 Determine whether the PDA is hemodynamically significant based on the echocardiography criteria as outlined above. Classify the PDA as moderate or large in SIZE, and moderate or large in VOLUME SHUNT according to the following descriptive table

	A **PDA DIAMETER**	**B** **Pulmonary over-circulation**	**C** **Systemic hypo-perfusion**
Moderate size-Moderate volume shunt	1.5-3.0 mm or PDA:LPA= 0.5-1 with unrestrictive Pulsatile flow (Vmax<2 m/s)	At least 2 of the following: -LA: Ao 1.5-2.0 - IVRT 45-55 ms - E:A 1.0 - LVO 300-400 mL/kg/min	Absent diastolic flow in at least 2 of the following: - Abdominal aorta - Celiac trunk - Middle cerebral artery
Large size-large volume shunt	>3.0 mm or PDA: LPA >1 with unrestrictive Pulsatile flow (Vmax<2 m/s)	At least 2 of the following: - LA: Ao >2.0 - IVRT <45 ms - E:A >1.0 - LVO >400 mL/kg/min	Reversed diastolic flow in at least 2 of the following: - Abdominal aorta - Celiac trunk - Middle cerebral artery

4.0 GUIDELINES FOR MEDICAL MANAGEMENT (see also APPENDIX A)

4.1 Limit the fluid intake but ensure *ADEQUATE caloric and electrolyte requirement for normal growth.*

4.2 Maintain oxygen saturation alarms as per unit oxygen management guidelines.

4.3 With blood gas analysis accept a pH of 7.2-7.25 (will limit magnitude of L→R shunt).

4.4 Maintain adequate PEEP during medical treatment course. (Evidence in animal studies. PEEP decreased left to right shunt and increased systemic blood flow.

4.5 Maintain the hemoglobin above 110 g/L; may increase pulmonary vascular resistance and reduce left-to-right shunting, (No trials have evaluated the effect of blood transfusion on PDA closure).

4.6 Treat medically with NSAID (Ibuprofen or Indomethacin) once PDA deemed hemodynamically significant by IENH. A second course may be given If there are no contraindications or side effects from a first course. Furosemide is not recommended to be given together with NSAIDs. Medical treatment can be offered to a preterm infant at any post natal age.

4.7 Consider a course of acetaminophen if the PDA is still hemodynamically significant after a 2nd course of above medication (Decision to treat if agreed to by the neonatologist performing IENH and the attending neonatologist; not strongly supported by the current levels of evidence).

4.8 Conduct comprehensive IENH after each treatment course.

4.9 Continue feeding during medical treatment.

4.10 Assess for contraindications of NSAIDs (Ibuprofen or indomethacin):

4.10.1 Active bleeding, especially those with active intracranial hemorrhage or gastrointestinal bleeding.

4.10.2 Thrombocytopenia less than 60 X10^9 (absolute contraindication) or 60-100 X10^9 (Relative contraindication); the trend should be considered if significantly decreasing until stabilized.

4.10.3 Coagulation defect.

4.10.4 Necrotizing enterocolitis (NEC) (Stage 2 or greater).

4.10.5 Significant impairment of renal function with oliguria (less than 1ml/kg/hr and/or creatinine more than 100 umol/l).

4.10.6 Hyponatremia less than 130 mmol/l.

4.10.7 Congenital heart disease in which patency of the ductus arteriosus is necessary.

5.0 GUIDELINES FOR SURGICAL MANAGEMENT (PDA LIGATION)

5.1 The decision for PDA ligation should be a consensus among: the *neonatologist performing IENH, the neonatologist on service, and the paediatric surgeon performing the procedure.* A third neonatologist should be officially consulted if the decision is debatable.

5.2 A PDA may be considered for ligation if it is large both size and shunt volume, with clinical indicators of pulmonary over-circulation (Intubated with escalating respiratory support) with or without clinical indicators of systemic hypo-perfusion.

5.3 In case of absence of the neonatologist performing IENH then the decision will be based on echocardiography done by paediatric cardiology, consensus of the neonatologist on service and a second neonatologist. A third neonatologist should be officially consulted if the decision is debatable. To arrange for this contact the neonatology section head or the assistant medical director of the neonatal unit.

5.4 The reason for surgical ligation of the ductus arteriosus should be clearly indicated and documented by the neonatologist on service.

5.5 A comprehensive two-dimensional echocardiogram should be performed by paediatric cardiologist *at least once* before PDA ligation to exclude duct-dependent congenital heart disease (Pre-TNE), and document sidedness of aortic arch.

5.6 On the day before PDA ligation surgery:

5.6.1 Chest x-ray: As baseline prior to surgery.

5.6.2 Provide arterial access and monitoring with preoperative placement of an indwelling arterial line. Systolic (SAP) and diastolic (DAP) arterial pressures, not merely the mean, are necessary to provide hemodynamic information.

5.6.3 Assess adrenal performance **(**ACTH stimulation test): Hydrocortisone therapy is occasionally indicated for refractory hypotension. These patients are typified by an early fall in both SAP and DAP. We recommend consideration of hydrocortisone in patients who are unresponsive to a single cardiotropic agent, provided hypovolemia and lung overexpansion have been excluded, AND have an impaired ACTH stimulation response test (post-cortisol < 500 umol/L).

5.7 Postoperative Care

Note: Recent evidence describes a post ligation cardiac syndrome (PLCS) occurring in up to 50% of infants undergoing ligation. PLCS is characterised clinically by a fall in systolic blood pressure (usually < 3rd centile for age) requiring one or more cardiotropic agents, and increasing ventilator requirements, necessitating an increase in mean air way pressure and FiO_2 by at least 20%. This usually becomes apparent 6 to 12 hours post-surgery and coincides with postoperative

impairment in left ventricular dysfunction. One paper reported a significantly higher mortality in infants with PLCS compared to controls (33% vs. 11%). The following should be considered when managing the patients in the immediate postoperative period.

5.7.1 Do a chest x-ray within one hour of surgical intervention to exclude air leaks or hyperinflation.

5.7.2 Pay close attention to post-operative respiratory management (consider frequent blood gases) due to expected improvement of lung compliance after resolution of pulmonary over circulation.

5.7.3 Perform an IENH assessment within 1 hour of surgical intervention as this may improve the prediction of the postoperative course. Specifically, left ventricular output < 200 ml/kg/min and fractional shortening < 30% predict later need for cardiotropic support. Recent evidence suggests that early targeted therapy with milrinone leads to decreased risk of postoperative cardiorespiratory instability. Intravenous milrinone should be commenced if LVO < 200 mL/kg/min [infusion of 0.3 mcg/kg/min and no milrinone bolus is needed] with judicious co-administration of 15 mL/kg 0.9% Saline bolus over the first hour to minimize any preload related compromise. Subsequent TNE assessments should be performed at the discretion of the medical team.

5.7.4 Cardiovascular therapy: In the setting of low SAP < 3rd percentile (Table 2), low LVO and/or low fractional shortening, inodilator therapy is preferable. Common agents used in this setting may include dobutamine or milrinone, although there is little published data regarding the efficacy of milrinone in premature infants of comparable gestation. In the setting of low SAP< 3rd percentile, low DAP < 3rd percentile (Table below) and low LVO, volume support, vasopressor agents or hydrocortisone may be preferable. Common agents used in this setting may include dobutamine or dopamine.

Post-conceptional Age (weeks)	SYSTOLIC 3rd Centile	MEAN 3rd Centile	DIASTOLIC 3rd Centile
24	32	26	15
25	34	26	16
26	36	27	17
27	38	27	17
28	40	28	18
29	42	28	19
30	43	29	20
31	45	30	20
32	46	30	21
33	47	30	22
34	48	31	23
35	49	32	24
36	50	32	25

6.0 PRIMARY AUTHOR

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7.0 REFERENCES

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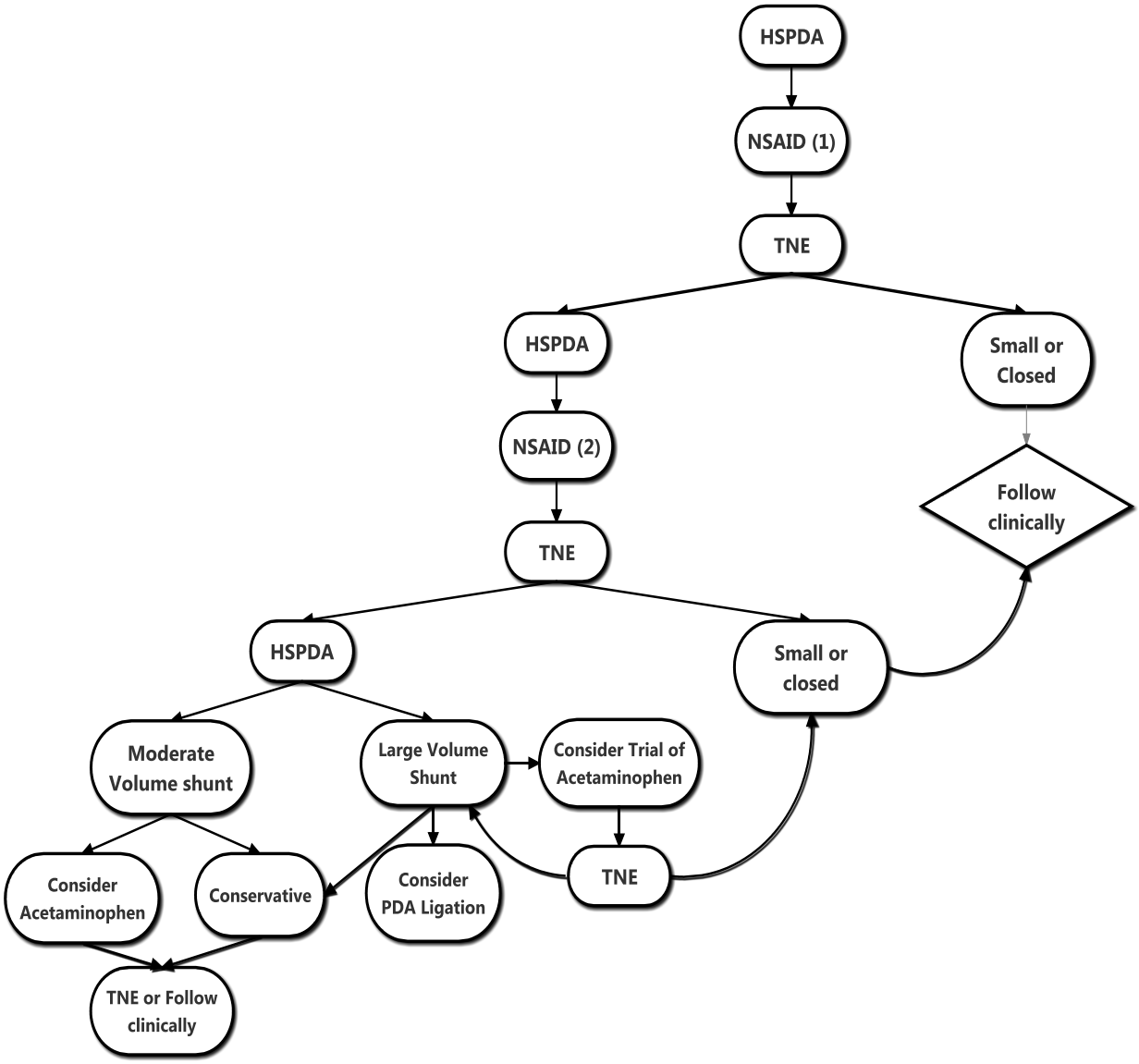
APPENDIX A

Medical management of Patent Ductus Arteriosus in Preterm infants



Prior to Pharmacological Intervention, Consider Risks Versus Benefits