Nitric Oxide Usage in Neonates

Guideline Responsibilities and Authorisation

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Target Audience	Consultants, Registrars, NNPs, CNSs, RNs
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Guideline Review History

Version	Updated by	Date Updated	Summary of Changes
3	Kathryn Thorn	2019	New template Full review
	Lee Carpenter	2020	Added references, weaning flow diagram
3.1	Miranda Bailey-Wild	2023	Added table for assessment of efficacy at time of commencing iNO (section 2.4)

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1 Overview

1.1 Background

Nitric oxide (NO) is a potent vasodilator used to treat pulmonary hypertension. It is a gas that is given into the ventilator or CPAP circuit and is inactivated instantly in blood, by reacting with haemoglobin. Therefore, it produces rapid and localized effects on the pulmonary vasculature with presumed minimal action on the systemic vasculature or systemic blood pressure.

1.2 Purpose

This guideline describes the process to administer inhaled nitric oxide (iNO) either via conventional ventilator or CPAP.

1.3 Scope

Consultants, Registrars, NNPs, CNSs, & Registered Nurses

1.4 Patient / client group

- Neonates with symptomatic Persistent Pulmonary Hypertension of the Newborn (PPHN) – proven clinically (i.e. 10% differential in pre/postductal saturations, only in babies with known patent ductus arteriosus), or by point of care ultrasound/echocardiography
- Neonates with severe hypoxaemic respiratory failure (i.e. oxygenation index>20, PaO2 <60 mmHg or <8kPa despite 100% FiO2), caused by e.g. meconium aspiration/exposure, postoperative pulmonary hypertension.
- Used with **caution** in preterm infants < 34 weeks GA, as rescue treatment for severe hypoxic respiratory failure on a case-by-case basis.

1.5 Definitions

CNS	Clinical Nurse Specialist
CPAP	Continuous Positive Airway Pressure
FiO_2	Fraction of inspired oxygen
iNO	Inhaled Nitric Oxide
IVH	Intravascular Haemorrhage
NNP	Neonatal Nurse Practitioner
NO	Nitric Oxide
NO2	Nitrogen Dioxide
OI	Oxygenation Index

PPHN	Persistent Pulmonary Hypertension of the Newborn
PVR	Pulmonary vascular resistance

2 Clinical Management

2.1 Equipment

- iNO delivery circuit set up guideline is available at: J:\WomenChildren\NICU\Education\CheatSheets2020

  Hard copy also on Inosys trolley and Cheat Sheet folders in Nursery 1 and 2.
- Spare equipment for setup of NO delivery circuit can be found in Technician NICU workroom

2.2 Indications for use

- PPHN
- Severe hypoxia (oxygenation index >20, PaO2 <60 mmHg or <8kPa despite 100% FiO2.)

Oxygenation Index (OI)

$$OI = \frac{\text{Mean Airway Pressure} \times FiO_2 \times 100}{PaO_2}$$

SSH OI calculator: see

https://www.starship.org.nz/health-professionals/calculators/respiratory-indices-calculator/

2.2.1 Entry Criteria

- Echocardiogram to exclude cyanotic (duct dependant) congenital heart disease
- Gestation >34 weeks. (In exceptional circumstances inhaled nitric oxide may be used in preterm infants <34 weeks as a rescue remedy but requires discussion with Consultant)
- Absence of lethal congenital malformation
- Careful consideration in presence of IVH (grade 2-4) or coagulopathy

2.3 Commencement of inhaled Nitric Oxide

2.3.1 Ventilator

- Assemble equipment according to **iNO delivery circuit set up guideline** (available on shared drive as above)
- Use in-line suction catheter to avoid interruption of circuit.
- Optimise lung inflation: Efficacy of iNO is dependent on the degree of lung inflation (i.e. less effective if lung under-expanded).
- Do not turn off ventilator during procedures such as reintubation or hand bagging.

2.3.2 CPAP

- SMO decision to use iNO via CPAP
- Assemble equipment according to **iNO delivery circuit set up guideline** (iNO delivery circuit set up guideline).
- Cautiously discontinue any intravenous vasodilators if in use.

NOTE: Neopuff should be set up and connected to iNO supply, so it can be used immediately if manual IPPV is needed (Refer to Nitric Oxide-Inhaled (iNO): Nursing Management in Newborn Intensive Care Unit (NICU) procedure (4938))

2.4 Initiating treatment with inhaled Nitric oxide (iNO)

- ***before starting iNO:*** document clinical parameters to categorise iNO response
- ***start iNO at 20ppm:*** do NOT change other parameters or touch the baby
- ***+15 minutes:*** document clinical parameters and iNO response

	Before iNO	15 mins after iNO
Mean Airway Pressure		
FiO_2		
PaO_2		
Pre-ductal SpO_2		
Post-ductal SpO_2		
Systolic blood pressure		
If available:		
Bi-directional shunt		
Estimated Pulmonary artery pressure		

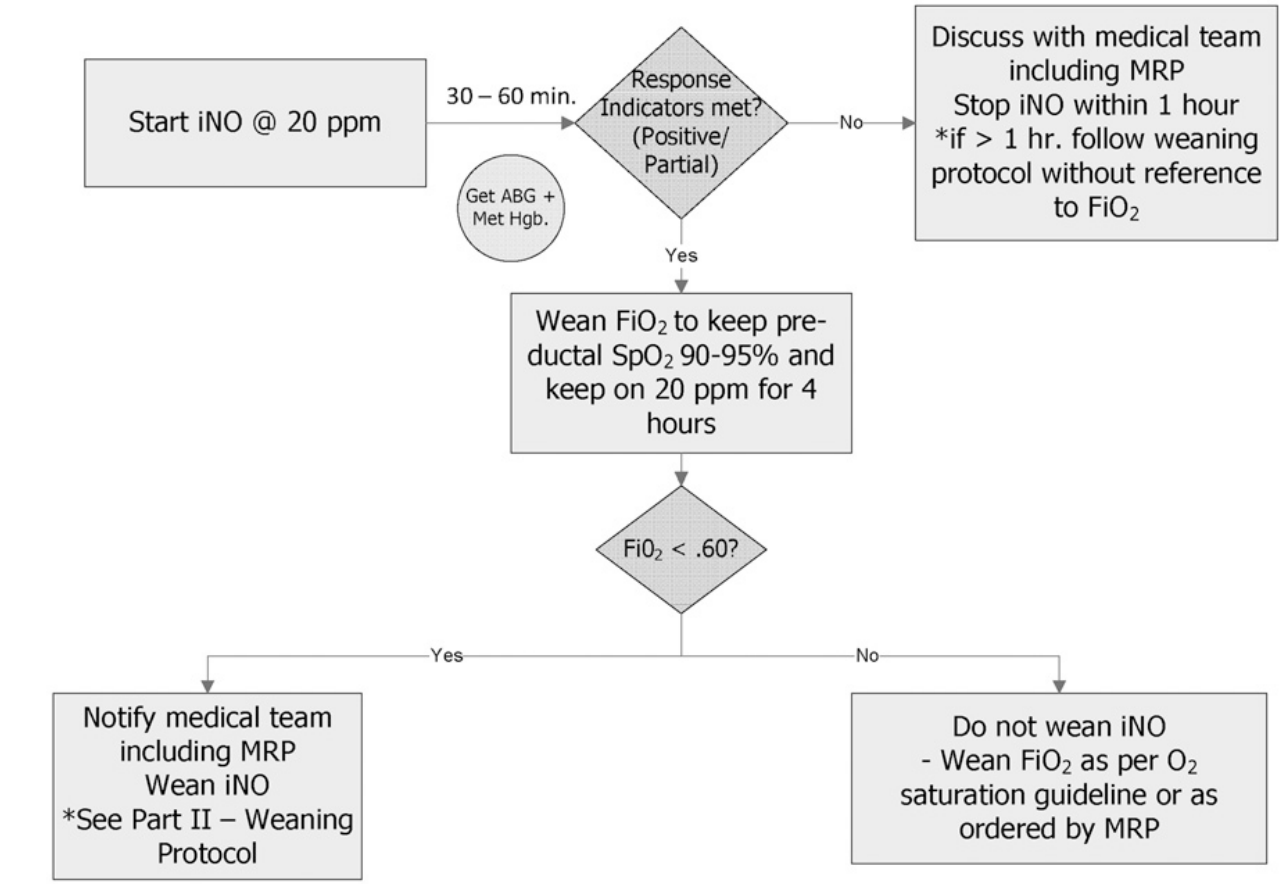
- If there is a **positive response** follow the flowchart as below (2.5)
- If there is **NO response** to iNO treatment, iNO should be discontinued again.

2.5 Treatment with inhaled nitric oxide

Indications for iNO
PPHN or HRF or as indicated by echo
O.I > 20 (consider at 15-20)

Ensure optimal lung recruitment (recent CXR to assess)

Obtain baseline vital signs and ABG



Response Indicators:
Positive
↑PaO_2 ≥ 20 mmHg
↑SpO_2 by 10%
Or able to drop FiO2 by at least 0.20

Partial -
↑PaO_2 by 10 – 20 mmHg
↑SpO_2 by 5 – 10 %
Or able to drop FiO2 by at least 0.10 – 0.20

Methemoglobin (Normal < 2.5%)
Obtain level is first ABG after starting iNO
Obtain q24h thereafter

If Methemoglobin Hgb
> 10% - Discontinue
5 – 10% Decrease iNO by 50% and repeat level
< 2.5% Safe

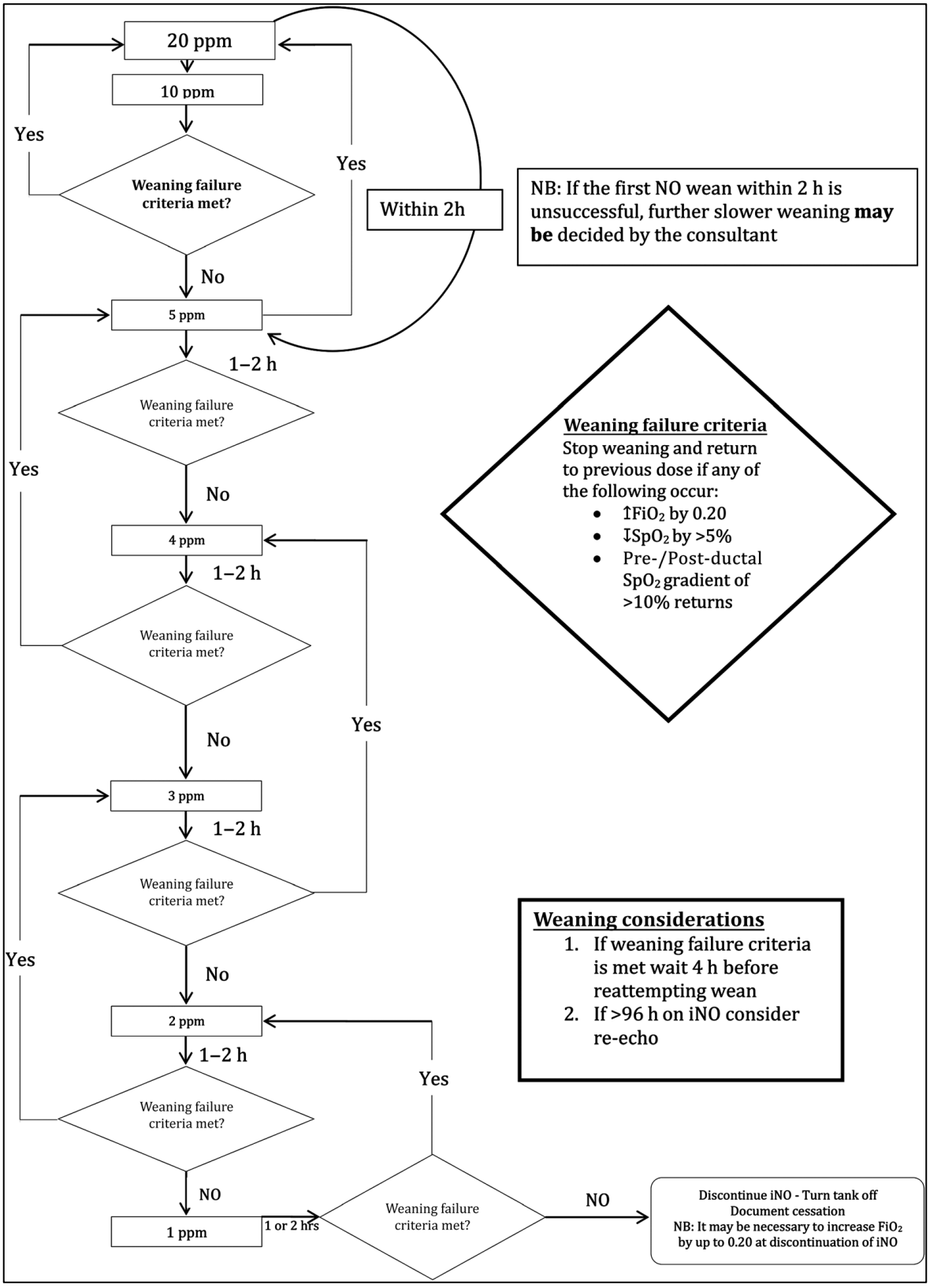
2.5 Monitoring

Continuous monitoring of heart rate, blood pressure and (arterial) oxygen saturation (refer Oxygen Therapy for Newborns in NICU protocol) with hourly documentation

- OI calculation (see above) on arterial blood gases
- Pre and post ductal saturation monitoring
- Measure Methaemoglobin (from blood gas) after 1 hour and 12 hours (approximately) following commencement of iNO therapy to exclude methaemoglobin reductase deficiency. If methaemoglobin >5%, need to stop NO, inform SMO, and consider rescue therapy with methylene blue.
- Monitor Nitrogen Dioxide (NO_2) levels in inspiratory gases (upper limit 5ppm).

2.6 Weaning

Exogenous iNO suppresses production of endogenous NO, therefore slow weaning, especially for the last few ppm is advised in order to avoid rebound PPHN.



2.7 Potential Complications

1. Platelet dysfunction and bleeding
2. Methaemoglobinaemia (upper limit 5%)
3. Nitrogen Dioxide (NO_2) poisoning – pulmonary oedema, ARDS
4. Reduced FiO2 in inspiratory gases due to displacement by NO (probably negligible)
5. Prevents pulmonary vascular bed remodelling (prolonged use in animal experiments)

NOTE: There are no restrictions for pregnant staff members to care for babies treated with iNO.

3 Audit

3.1 Indicators

- All neonates, receiving iNO, meet the entry criteria (2.2.1)
- All neonates commence iNO at 20ppm (unless contraindicated)
- Methaemoglobin levels are measured and documented in clinical notes at 1 hour and 12 hours after the commencement of iNO
- Documentation of OI in clinical notes

4 Evidence base

4.1 Bibliography

- Ahearn J., Panda M., Carlisle H., & Chaudhari T. Impact of inhaled nitric oxide stewardship programme in a neonatal intensive care unit. Journal of Paediatrics and Child Health 56 (2020) 265–271 © 2019 Paediatrics and Child Health Division (The Royal Australasian College of Physicians)
- P. Chandrashekharan et al. Early use of iNO in Preterm Infants. Is there a rationale for selective approach? Am.J.Perinatol. 2017 Apr 345(5):428-440
- M. Busè et al. Inhaled nitric oxide as a rescue therapy in a preterm neonate with severe pulmonary hypertension: a case report. Ital J Pediatr. 2018; 44: 55.
- Nitric oxide for respiratory failure in infants born at or near term. Finer N. and Barrington K Cochrane Library, 18.10.2006.
- Nitric oxide – inhaled. Retrieved April 18th 2020 from: https://www.starship.org.nz/guidelines/nitric-oxide-inhaled
- SSH OI calculator: see https://www.starship.org.nz/health-professionals/calculators/respiratory-indices-calculator/

4.2 Associated Te Whatu Ora Waikato Documents

- Nitric Oxide-Inhaled (iNO): Nursing Management in Newborn Intensive Care Unit (NICU) (4938)
- Oxygen Therapy for Newborns in NICU (3115)