**Indications for iNO**
1. \( \text{PaO}_2 < 100 \text{ mmHg} \) on \( \text{FiO}_2 \) 100%
2. \( \text{O}_2 \) saturations <92% on \( \text{FiO}_2 \) 100%
3. Evidence of PPHN on \( \text{FiO}_2 \) 60% by:
   1. Echo
   2. Clinical judgment if echo unavailable
4. Oxygenation Index (OI) ≥25

**A. INITIATION OF THERAPY (>34 WK)**

- Start iNO at 20 ppm
- \( \text{PaO}_2 \) response >20 mmHg
- \( \text{FiO}_2 \) wean by 2-5% q30 min for preductal sat ≥92%, \( \text{PaO}_2 \) >60 mmHg, and pre-post sat difference ≤5%

- 30 min
- Get ABG
- \( \text{FiO}_2 \) to ≤60%
- NO
- Stop iNO

**Positive Response Indicators**
1. Increase in \( \text{PaO}_2 \) ≥20 mmHg or ≥20% from baseline, with goal of \( \text{PaO}_2 \) >60 mmHg (avoid higher goals)
2. Increase in oxygen saturation by 10% (if unable to obtain arterial \( \text{PaO}_2 \))
3. Decrease in pulmonary artery pressure ≥20% from baseline (echo or PA line)

**Methemoglobin (normal <5%)**
1. Obtain level prior to starting iNO
2. Obtain with first ABG after starting iNO
3. Obtain daily thereafter
4. If metHgb is >5%, consult physician; begin iNO wean
INHALED NITRIC OXIDE (iNO) PROTOCOL

B. WEANING PROTOCOL (>34 WEEKS)

20 ppm

10 ppm

30 min

Saturations ↓ >5%

YES NO

5 ppm

30 min

Saturations ↓ >5%

NO YES

4 ppm

60 min

Saturations ↓ >5%

YES NO

3 ppm

60 min

Saturations ↓ >5%

NO YES

2 ppm

60 min

Saturations ↓ >5%

YES NO

1 ppm

Saturations ↓ >5%

Discontinue iNO


1. Weaning Considerations
2. If patient falls below the success criteria, return to previous settings and try again in 4 hrs if no lability
3. If there are 2 unsuccessful weans in 12 hrs, hold weaning for 12-24 hrs
4. Consider adjunct therapies:
   a. Sildenafil 0.5 mg/kg IV q6 hrs; titrate up to 4-6 mg/kg/day

Obtain ABG
• If PaO₂ <75 or saturations ↓ ≥5%, restart iNO
INHALED NITRIC OXIDE (iNO) PROTOCOL

Checklist prior to Initiation:
1. Surfactant administered
2. HFOV with lung volumes optimized on Chest X-ray
3. Echo document PPHN and rules out congenital heart defects
4. Hypotension corrected with vasoactive agents and volume as indicated

C. iNO THERAPY <34 WEEKS

<table>
<thead>
<tr>
<th>5 ppm</th>
<th>Oxygenation Response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Post-ductal saturation 90%</td>
</tr>
<tr>
<td></td>
<td>• PaO2 &gt;60 mmHg on FiO₂ 100%</td>
</tr>
<tr>
<td>30 min</td>
<td></td>
</tr>
</tbody>
</table>

YES

1. Wean FiO₂
2. Discontinue iNO over next 2-4 hrs

D. WEANING PROTOCOL <34 WEEKS

Return 1 step if failure to wean

- 20 ppm
  - Wean FiO₂ to 60% over 1-2 hrs; then begin iNO wean in 1-2 hrs
  - Check BG in 15 minutes after iNO initiation
  - May wean with post-ductal saturations >85% and PaO₂ >60 mmHg

- 10 ppm
  - 5 minutes without ventilator/FiO₂ changes
  - Wean over 1-2 hours

- 5 ppm
  - 5 min without ventilator/FiO₂ changes
  - Wean FiO₂ <50% 
  - Wean iNO over 1-4 hours
  - No evidence of shunting; normal pH

- 2 ppm
  - 5 min without ventilator/FiO₂ changes
  - Observe for 30 minutes

- 1 ppm
  - 5 min without ventilator/FiO₂ changes
  - Observe for 30 minutes; pre-oxygenate for 10 minutes with ↑ FiO₂ by 0.2

Discontinue iNO
  - 5 min without ventilator/FiO₂ changes
  - Observe for 30 minutes; then ↓ FiO₂ by 0.05 q30 min. back to baseline

* BG q15 minutes x2

1. Increase by 5 ppm to max 20 ppm; check response at each step
2. Wean FiO₂ to 60% and then begin iNO wean

Failure to Wean:
↑ in pre ductal-post ductal O₂ saturation difference by >5% within 5 minutes of weaning, with no change in vital signs/ventilator settings/FiO₂/inotropes.

Return to previous iNO dose and re-attempt weaning in 1-2 hrs.

Hibbs AM, et al. One year respiratory outcomes of preterm infants enrolled in the Nitric Oxide Chronic Lung Disease Trial
*J Peds* 2008;153(4):525-29
INHALED NITRIC OXIDE (iNO) PROTOCOL

Checklist prior to Initiation:
1. Infant to be in hypoxic respiratory failure or documented pulmonary hypertension per echo
2. Lung volumes optimized on SIMV/HFOV and CXR shows good expansion

E. CONGENITAL DIAPHRAGMATIC HERNIA AND BRONCHOPULMONARY DYSPLASIA/CLD

Oxygenation Response
• Post-ductal saturation >95%
• PaO2 increased by 10-20 mmHg from baseline at 1 hr following initiation (check ABG at 1 hr – no vent changes to be made during this time)

Responder
1. Maintain iNO (max of 96 hrs)
2. Start on Sildenafil:
   a. 0.5 mg/kg PO q 6hr
   b. Titrate up to 4-6 mg/kg/day
3. Follow iNO weaning protocol (see Part B)
4. If continuing for >96 hours, will require approval of two physicians with daily review

Non-Responder
Discontinue iNO therapy, or plan for wean over next 4-6 hrs

The current literature does not support the use of iNO in established BPD/CLD and CDH infants. The role of iNO in treating pulmonary hypertension in CDH infants remains controversial.