Inhaled Nitric Oxide (iNO)

**PHYSIOLOGY:** NO is a free radical, produced by the endothelium, that relaxes vascular smooth muscle (via its second messenger, cGMP) producing vasodilation. It is likely that pulmonary NO production is critical for the successful transition from fetal to postnatal circulation. Infants with PPHN have decreased serum levels of NO metabolites (nitrates) and decreased serum cGMP levels. Controlled studies in infants with PPHN have shown that iNO is a safe and effective pulmonary vasodilator, improves oxygenation, has minimal systemic effects and decreases the need for ECMO.

iNO is a selective pulmonary vasodilator because hemoglobin binds NO with high affinity, thus eliminating systemic vascular effects. However, this oxidation of hemoglobin results in the production of methemoglobin (metHgb), which is restored to its usual oxygen-carrying state by enzymatic reduction. **Methemoglobinemia** (metHgb >5%) occurs in approximately 10% of newborns treated with iNO and resolves with decreasing the iNO dose. Infants receiving iNO therapy should have a metHgb level measured daily.

**DOSE of iNO:** Usual dose is 20 ppm. This produces maximal pulmonary vasodilation in the vast majority of infants with PPHN.

**WEANING of iNO:** As oxygenation improves, decrease FiO₂ to ≤0.50. Then, iNO can usually be weaned from 20 to 5 ppm in decrements of 5 ppm every 1 to 2 hours. After that, wean by 1 ppm every 1 to 2 hours. Reduction of iNO from 1 to 0 ppm must be done with care as hypoxemia may result (See below). During the weaning process, monitor the infant closely for decreases in oxygen saturation and increase FiO₂ as needed. In infants with severe PPHN or congenital diaphragmatic hernia, an echocardiogram may be useful to evaluate right ventricular function and pressure before discontinuing iNO.

**REBOUND PULMONARY HYPERTENSION:** Sudden discontinuation of iNO will cause rebound pulmonary hypertension that may be severe. This probably results from suppression by iNO of endogenous NO production. Rebound pulmonary hypertension is a risk with cessation of iNO from even low doses (i.e., <5 ppm), after only a few hours of iNO therapy, and regardless of whether the infant initially responded to iNO.

Because of the risk of rebound pulmonary hypertension, be certain that the bag system (for manual ventilation) is set up to deliver iNO at the time of the onset of iNO therapy. This will ensure that the infant will continue to receive iNO during suctioning of the airway and in the event of a malfunction of the ventilator.