Introduction: In evaluating neonatal resuscitation practices, the use of 100% oxygen for resuscitation of asphyxiated infants has been questioned. Evidence in animal models has determined that exposure to hyperoxia during and after the hypoxic period can generate excessive neurotoxic compounds and that resuscitation with room air may result in better neurologic outcome. Two controlled clinical trials concluded that there was no difference in mortality whether the infants were resuscitated with room air or with 100% oxygen. We hypothesized that there are age related differences in oxygen’s effect on neurodegeneration in the developing brain.

Methods: Organotypic hippocampal slices were prepared from Sprague-Dawley rat pups (PND 4, 7, 14 and 21) as described by Stoppini et al. with some modification and maintained in culture for 7-14 days. Hypoxia (>5% oxygen) was administered via a hypoxic chamber and maintained for 10 minutes. All conditions were maintained within 37 +/- 3 °C. Neuronal cell death was assessed 3 days after exposure to hypoxia using Sytox staining and expressed as mean optical density.

Results: In slices from PND 4 and 7 pups, less than 10% of CA1 neurons (relative to controls exposed to air) were lost after a 10 min exposure to 5% oxygen. The greatest effect on cell death was noted in PND 21 slices (>50% neuronal cell loss), exposed to 5% oxygen for 10 min (p <0.001) and was similar to the amount of neuronal cell death observed in the PND 14 slices. (Figure 1)

Discussion: It has been shown in a hippocampal model of isolated neurons, in addition to our own organotypic slice culture model that neurons or slices prepared from early neonatal neurons (<PND 7) are more resistant to the harmful effects of hypoxic oxygen conditions. (9) From a clinical perspective, this maybe intuitive, knowing that infants prenatally survive in a hypoxic environment in utero. During human hippocampal development, the NMDA receptor subunits undergo age-related changes. These changes in the NMDA receptor subunit composition are an adaptive response that protects the infant to the normal hypoxic conditions in utero. These changes in the NMDA subunit composition occur also in the perinatal rat brain and can possibly explain the findings in this investigation.
**Conclusion:** Hypoxia induces neurodegeneration in the developing rat brain that is dependent on the postnatal age of the rat pup studied. This effect is hypothesized to be a function of the relative NMDA receptor subunit expression that occurs during the ontogenetic development of the brain. Further investigation will determine the impact of brain development on commonly used resuscitation practices.

**References:**
Cherici G et al: Ischemia does not induce the release of excitotoxic amino acids from the hippocampus of newborn rats. 1991. *Dev Brain Res* 60; 235-240.;