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Room Air Resuscitation and Targeted Oxygenation for Infants at Birth in the Delivery Room

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ABSTRACT

The results of several clinical trials suggest that infants born depressed can be successfully resuscitated with room air. In 2010, the American Heart Association, American Academy of Pediatrics, Neonatal Resuscitation Program, and the International Liaison Committee published new guidelines to initiate the resuscitation of the term neonate with 21% oxygen. Although this recommendation cannot be extrapolated to the preterm neonate, the use of oxygen for resuscitation in this population can be used cautiously.

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When a term infant is born, rapid and complex physiological changes must occur for the infant to sustain life. Transitioning from intrauterine to extrauterine life usually occurs spontaneously and does not require intervention from health care professionals. However, approximately 10% of newborns require some assistance to begin breathing at birth (International Liaison Committee on Resuscitation, 2006). The goal of resuscitation is to restore tissue oxygen delivery before irreversible damage occurs, which may lead to adverse long-term neurodevelopmental outcomes and even death. Traditionally, infants receiving resuscitation received 100% oxygen. However, in recent years, the guidelines for oxygen use during neonatal resuscitation have changed significantly based on evidence that high concentrations of oxygen immediately after birth are associated with short- and long-term harm to the organs. The organs primarily affected include the eyes, lungs, and brain. The brain may be affected so severely that the survival rate is decreased (Van Der Walt, 2006). Evidence also indicates a direct correlation between oxidative damage and a carcinogenic effect in these oxygen-exposed infants.

The new standard is to initiate the resuscitation of a term newborn with an oxygen concentration of 21%, the concentration in room air. The resuscitation of premature infants is not yet standardized, but the recommendation is to start at a low concentration of oxygen and titrate the oxygen based on the infant's pulse oxygen saturation. The exposure to high concentrations of oxygen at birth may cause injury to tissues and organs due to resultant oxidative stress. The premature infant is extremely vulnerable to oxidative stress because the protective antioxidant defense system has not developed. Therefore, the choice of oxygen concentration for neonatal resuscitation requires an understanding of the risks and benefits of 100% oxygen and room air.

History of Oxygen

Oxygen was first identified in 1604 by the Polish alchemist and philosopher Michael Sendivogius. He warmed nitre and released the resultant gas that he named "aerial nitre." Sendivogius (2004) described this substance as, "the elixir of life without which no mortal can live" (p. 432). This observation came approximately 170 years prior to the work of Carl Wilhelm Scheele and Joseph Priestly who were honored as the discoverers of oxygen. In 1774, Priestly heated mercuric oxide to release a gas. He demonstrated that mice lived longer in a jar of this "eminently breathable air" than those in the regular atmosphere (Van Der Walt, 2006).

The resuscitation of a term infant in the delivery room should begin with 21% oxygen.

This gas was named "oxygen" by Antoine Laurent Lavoisier in 1775, and it is now the most widely used therapeutic gas in medicine.

Oxygen, the second most common element on Earth, was quickly used in adult medicine and approximately 100 years ago was first used in newborn medicine. Today oxygen remains one of the most widely used drugs in neonatology (Saugstad, 2004). For many years, the safety of oxygen was not questioned. In 1950, as some clinicians started to question oxygen's role in damaging the eyes of premature infants, the Apgar score was introduced. The Apgar score may have contributed to the excessive use of oxygen as clinicians were motivated to have the newborn become as pink as possible after birth. Saugstad reiterated that even as recently as a decade ago, the American Heart Association stated that brief exposure to 100% oxygen around the time of birth did not represent any risk. Although this fact was believed to be an obvious truth a decade ago, it is no longer valid. Recent research now shows that even a brief exposure to 100% oxygen immediately after birth may induce potentially long-term hazardous effects (Richmond & Goldsmith, 2006).

Fetal to Neonatal Transition

Fetal life occurs in a relatively hypoxic environment compared to extrauterine life. The placenta provides the fetus with an arterial partial pressure of oxygen (PaO_2) of approximately 25 to 30 mmHg. Fetal hemoglobin has a greater affinity for oxygen and favors placental oxygen uptake and increased oxygen saturation for a given PaO_2 (Escobar, Cernada, & Vento, 2011). At birth, with the initiation of spontaneous respirations, alveolar-capillary gas exchange begins and escalates the PaO_2 and oxygen saturation of the neonate. By one minute of age, a healthy term infant's oxygen saturation is approximately 70%, and by 3 minutes it is approximately 80%. The PaO_2 will reach the 80 to 90 mmHg target between 5 and 10 minutes of life (Table 1). A term newborn not requiring resuscitation takes a median time of 7.9 minutes to reach oxygen saturation greater than 90% (Vento, Escobar, Cernada, Escrig, & Aguar, 2012).

This indicates that a term neonate experiencing a normal transition may not be pink until 5 to 10 minutes of life. The abrupt change in PaO_2 experienced by the newborn creates physiologic oxidative stress necessary to activate dormant trigger genes to allow successful postnatal adaptation and activation of metabolic pathways (Vento et al., 2012). However, infants that experience perinatal asphyxia after resuscitation generate a burst of reactive oxygen and nitrogen species. This process overwhelms the newborn antioxidant capacity and causes damage to cell structures, enzymes, ribonucleic acid (RNA), and deoxyribonucleic acid (DNA) (Escrig et al., 2008). When a high oxygen concentration is used during resuscitation, the oxidative stress is enhanced, which leads to increased damage of organs and an increase in mortality.

Table 1: Average Oxygen Saturation for Term Infants that Require no Medical Intervention at Birth

Oxygen Saturation Percentage	Time in Minutes
70	1
80	3
Greater than 90	5
Greater than 95	10

Oxidative Stress

The saying *more is better* does not apply to the oxygen used in neonatal resuscitation. The injury that hyperoxia can induce in the neonate can be detrimental, and to better understand this principal, it is important to understand the molecular form of oxygen. The single oxygen atom is unstable and therefore binds to a twin atom to form the molecular oxygen (O2). This bond is quite unstable because the pair share only one pair of electrons. Two unpaired electrons remain in the outer shell and prevent it from forming new chemical bonds. Partial reduction of oxygen with just one electron at a time leads to the formation of reactive oxygen species (Vento et al., 2012). These species may include anion superoxide, hydroxyl radical, and hydrogen peroxide. Some of these chemicals are known as free radicals that increase during hyperoxia. Free radicals are highly reactive substances capable of giving rise to chain reactions (Solberg, Perrone, Saugstad, & Buonocore, 2012). Free radicals are atomic or molecular species that are able to oxidize cellular membranes, structural proteins, enzymes, and nucleic acids. Damage to DNA causes mutations