
بسم الله الرحمن الرحيم

Noninvasive Respiratory Support

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Oxygen Therapy in neonates

Oxygen Therapy

- Oxygen is probably the most commonly used **drug** in neonatal intensive care.
- Appropriate use of O_2 is **highly therapeutic** in most cases of neonatal cardiopulmonary disease:
  - **relieving hypoxemia**
  - **pulmonary vasodilator**
  - . . .
  - . . .

Oxygen Therapy

- **Inadequate O_2** administration with resultant **hypoxemia**, however, may result in severe **neurologic injury**.
- **Excessive O_2** administration has been implicated as one of the most important provocative factors in **retinopathy of prematurity** and in **BPD** and . . . . . .
- **Accurate measurement of O_2 administration and arterial O_2 tension (Pao_2) or oxygen saturation is therefore mandatory in any neonate requiring O_2 therapy.**

Blenders

- Regulation of ambient O_2 concentration during assisted ventilation (Fraction of Inspired Oxygen – **FiO_2**) is performed by **blenders**.

Pulse oximetry

- A pulse oximeter uses a light source and sensor to measure the absorption of red light passing through capillaries in the skin and estimates the portion of hemoglobin that is fully saturated with oxygen.

Pulse oximetry

- The monitor displays the **oxygen saturation**, which ranges from 0% to 100%. This number is not the same as the partial pressure of oxygen (Po2) measured by a blood gas machine.
- The oximeter also displays the baby's **heart rate** by sensing pulsatile blood flow in the capillaries.

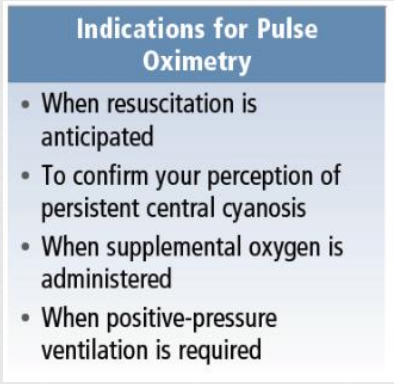
Pulse oximetry (NRP)

- Healthy newborns undergoing normal transition may take several minutes to increase their blood oxygen saturation from approximately **60**%, which is the normal intrauterine state, to more than **90**%, which is the eventual state of air-breathing healthy newborns.

1 min	60%-65%
2 min	65%-70%
3 min	70%-75%
4 min	75%-80%
5 min	80%-85%
10 min	85%-95%

Pulse oximetry (NRP)

- Use pulse oximetry to guide your treatment when:
  - resuscitation is anticipated
  - to confirm your perception of persistent central cyanosis
  - if you give supplemental oxygen
  - if PPV is required.



- With good technique, a pulse oximeter will allow accurate assessment of the heart rate and oxygen saturation within approximately 1 to 2 minutes of birth.
- If the baby has a very low heart rate or poor perfusion, the oximeter may not be able to detect the pulse or oxygen saturation.

O_2 analyzers

- Although blenders are generally very accurate, the clinician must usually employ an additional device periodically to check that the blender is actually delivering the desired O_2 concentration to the patient: **Portable O_2 analyzers** or **continuous in-line sensing devices.**

Oxygen Therapy

- Administration of poorly **humidified oxygen** may result in bronchospasm and airway injury in neonates.
- It is important that oxygen be **warmed** to 35° to 36° C to reduce the risk of airway problems.
- When warming and humidifying any gases administered to patients, excessive humidification may get into the circuit and produce "**rainout**," or the formation of droplets that can drip into the airway.
- A heating wire within the ventilator circuitry can reduce the severity of this problem.

Minimize Supplemental Oxygen

- High Fio_2 injures lung tissues.
- Exposure to excessive Fio_2 begins in the delivery room.
- Many NICU teams routinely resuscitate with **100% oxygen** and do not have a blender in the delivery or resuscitation room with which to administer lower concentrations of oxygen.
- Resuscitation with **room air** may work just as well as resuscitation in 100% oxygen with no apparent difference in long-term outcomes.

Minimize Supplemental Oxygen

- The AAP / AHA (**NRP**) was **recommended** resuscitating premature infants with blended oxygen between 21% and 100%, but quickly decreasing the Fio_2 as soon as the patient achieves an acceptable (Saturation of Peripheral Oxygen) Spo_2:
  - **But today**, one could start with low Fio_2 (21%) in ≥ 35 weeks' gestation and (21%-30%) in < 35 weeks' gestation and increase as needed.
  - These approaches require **blender** and **pulse oximetry** in the delivery room, and the NRP now recommends these capabilities **if routinely resuscitating infants less than 32 weeks' gestation**.

Minimize Supplemental Oxygen

- The cross-sectional, retrospective study of **Tin et al.** reported that patients (gestational age less than 28 weeks) treated with lower target Spo_2 ranges (70%-90% **vs**. 88%-98%) required **fewer ventilator days** (13.9 **vs**. 31.4 days) and **oxygen days** (40 **vs**. 96 days).

Minimize Supplemental Oxygen

- The **BOOST trial** randomized convalescing infants (greater than 2 weeks old) to standard (91%-94%) or higher Spo_2 target range (95%-98%) to improve growth and development:
  - **more pulmonary sequelae with the higher target Spo_2.**
  - **The higher Spo_2 target range did not confer a growth or development advantage**.

Minimize Supplemental Oxygen

- The **STOP-ROP study**, which randomized infants with retinopathy of prematurity (ROP) to one of two target Spo_2 ranges (96%-99% **vs**. 89%-94%), found **more pulmonary complications in those treated with the higher Spo_2 target**:
  - A post hoc analysis of baseline respiratory status showed that patients in the two treatment groups of the STOP-ROP study had similar pulmonary scores at randomization.

Oxygen Toxicity

- In their original description, **Northway et al.** considered the inspiration of high concentrations of **O_2** the most likely cause of **BPD**.
  - In their experience, affected infants had been given **O_2 in concentrations of 80% or higher for at least 6 days**.
  - They stated that BPD was probably “the result of oxygen-induced lesions in the respiratory mucosa, with subsequent defective drainage, combined with lesions in the alveoli and capillaries induced by oxygen and respiratory distress.”
  - They speculated that **intermittent positive pressure ventilation (IPPV) and endotracheal intubation** also may have played a role.

Oxygen Toxicity

- Now more than 40 years after their original description, speculation lingers.
- The individual impacts of **O_2, IPPV, and endotracheal intubation** have yet to be delineated precisely.
- Contemporary consensus holds that all of these factors are **significant**.
- In the years since BPD was first described by Northway et al. successive investigators reported **toxicity at lower O_2 concentrations and with shorter durations of therapy**.

Oxygen Toxicity

- **Edwards et al.** described BPD in babies whose FIO2, though only 0.22 to 0.30, was administered for as long as 53 days.
  - There is no definite FIO_2 at which one can predict the appearance of BPD.
  - **Immaturity of the lungs** is the common denominator.

Oxygen Toxicity

- Increased vulnerability of lung tissue in **smaller premature infants** is well known: the more premature the lungs, the more likely it is that **BPD** will occur (**Oxidant and protease activities are destructive**) :
  - **antioxidant enzyme activity** seems to develop within a timeframe that coincides with the maturation of surfactant synthesis.
  - The level of antioxidant enzymes (as well as that of surfactant) in newborn is significantly increased when maternal **betamethasone** is given 24 and 48 hours before delivery.

Oxygen Toxicity

- **White** reviewed the subject of pulmonary O_2 toxicity:
  - The levels of **O_2 metabolites** (superoxide, hydrogen peroxide, hydroxyl radicals, and others) are augmented during periods of **hyperoxia**; their production in the lung is destructive.
  - Hyperoxia generally incites **a profuse inflammatory response**; but it may injure epithelial cells even in the absence of inflammation.

Oxygen Toxicity

- Infants with RDS who are destined to progress to BPD have been identified in the first postnatal week by demonstration of increased concentrations of **oxyradical markers**.
- Infants with RDS who did not develop BPD show no such increase.

Oxygen Toxicity

- **Defense mechanisms** against toxic O_2 metabolites (radicals) are critical to the prevention or attenuation of oxidant lung damage.
- **Superoxide dismutase** is probably the primary substance of this defense; glutathione peroxidase and catalase are also significant.
- Superoxide dismutase promotes elimination of the superoxide radical; an effective pulmonary response to hyperoxia requires its enhancement.

Oxygen Toxicity

- In human premature infants given **supplemental O_2**, however, superoxide dismutase does not increase in either the lungs or the blood.
- This lack of response is compatible with the immature lung's susceptibility to oxidant injury.
- Clinical studies of the effects of superoxide dismutase are **not conclusive**.

Oxygen Toxicity

- **Davis et al.** reported their multicenter trial of intratracheally administered Cu-Zn superoxide dismutase, which was given for 1 month to extremely premature infants receiving ventilator support:
  - There was neither a difference in mortality nor in the need for oxygen at 36 weeks' PMA, **but** in the treated group at 1 year of age, there was less hospitalization, fewer emergency room visits, and less frequent medication for asthma.

Oxygen Toxicity

- In another study pertinent to the role of hyperoxia in BPD, an attempt was made to determine whether higher oxygen saturations might diminish the severity of prethreshold ROP (**STOP-ROP Study**):
  - Increased incidence of BPD and lung infection were unanticipated outcomes among infants who received the higher oxygen concentrations.

Oxygen Toxicity

- Other attempts to minimize oxidant damage to the lung have been reported in studies that evaluated the antioxidant activity of vitamin E:
  - Vitamin E is a major antioxidant known to diminish peroxidation of polyunsaturated lipids by virtue of its scavenger activity.
  - Vitamin E deficiency is pervasive among premature infants; supplementation would be logical.
  - However, a summary of the several trials that evaluated vitamin E supplementation has indicated its ineffectiveness in diminishing the incidence of BPD.

Oxygen Toxicity

- **Hyperoxia:**
  - inhibits lung growth and maturation, resulting in the development of smaller lungs with fewer alveoli and an inhibition of vascular development.
  - It also causes interstitial edema by increasing capillary permeability.
  - Hyperoxia incites profuse inflammation, setting the stage for subsequent fibrosis.
  - Some investigators have been convinced that O_2 toxicity is the principal cause of BPD, but the evidence is largely derived from animal experiments.

Oxygen Toxicity

- In **human infants**, there is considerable evidence that oxygen radicals cause significant injury early in the course of BPD.
- Davis et al. demonstrated in piglets that a minimal acute injury followed positive-pressure ventilation in room air; but when an FIO2 of 1.0 was added, the severity of lesions increased significantly.

Oxygen Toxicity

- Providing for enhanced antioxidant capacity could reduce vulnerability to lung damage.
- Suggested investigations include antenatal stimulation of antioxidant enzyme production, genetic manipulation to enhance production of enzymes, and perhaps a pharmacologic substitute for the enzymes.

TABLE 8-2 Preferred Acronyms Concerning Continuous Distending Pressure*

Acronym	Definition
BiPAP	Bilevel positive airway pressure
CDP	Continuous distending pressure
CNEP	Continuous negative expiratory pressure
CPAP	Continuous positive airway pressure
ECMO	extracorporeal membrane oxygenation
HFNC	High-flow nasal cannulae
HHNC	Humidified, high-flow nasal cannulae
IFS	Infant Flow system (variable flow nasal CPAP)
NC	Nasal cannulae
NCPAP	Nasal continuous positive airway pressure
NHFV	Nasal high frequency ventilation
NIPPV	Nasal intermittent positive-pressure ventilation
NPCPAP	Nasopharyngeal continuous positive airway pressure
NPSIMV	Nasopharyngeal synchronized intermittent mandatory ventilation
NRS	Noninvasive respiratory support
NSIMV	Nasal synchronized intermittent mandatory ventilation
NV	Nasal ventilation
PEEP	Positive end-expiratory pressure
VFD	Variable flow driver

Box 8-1 CONDITIONS FOR WHICH CONTINUOUS DISTENDING PRESSURE HAS BEEN USED CLINICALLY

- Respiratory distress syndrome (RDS) in premature newborn infants
- Apnea of prematurity (AOP)
- Postextubation management of premature infants
- Postoperative respiratory management:
  - Congenital heart disease
  - Abdominal wall defects (gastroschisis, omphalocele)
  - Other abdominal or thoracic surgical conditions
- Differentiating congenital cyanotic heart disease from pulmonary disorders
- Meconium aspiration syndrome (MAS)
- Other aspiration syndromes (e.g., blood or gastric aspiration)
- Transient tachypnea of the newborn ("wet lungs")
- Pulmonary edema
- Congestive heart failure
- Patent ductus arteriosus (PDA)
- Pneumonia
- Laryngo-, broncho-, and/or tracheomalacia
- Resuscitation of infants in the delivery room
- Increased work of breathing
- "Other" disorders with radiographic findings of atelectasis, poor lung expansion, or pulmonary infiltrates
- Persistent pulmonary hypertension of the newborn (PPHN)
- Pulmonary hemorrhage
- Provision of high PEEP during extracorporeal membrane oxygenation (ECMO)

PEEP, Positive end-expiratory pressure.

Contraindications to CPAP

Some contraindications to CPAP include the following:

- Infants who have progressive respiratory failure and are unable to maintain oxygenation, $PaCO_2$ levels greater than 60 mm Hg (8 kPa), and/or pH levels of 7.25 or less
- Certain congenital malformations: congenital diaphragmatic hernia, tracheoesophageal fistula, choanal atresia, cleft palate, gastroschisis
- Infants with severe cardiovascular instability (hypotension, poor ventricular function)
- Neonates with poor or unstable respiratory drive (frequent apnea, bradycardia, and/or oxygenation desaturation) that is not improved by CPAP.

Conclusions

- Cochrane collaborative reviews have addressed diverse CPAP RCTs.
- To date the following conclusions have been made:

  (1) there is insufficient evidence to assess the benefits and risks of prophylactic NCPAP in the preterm infant.

  (2) early use of CPAP may reduce the need for mechanical ventilation.

  (3) early therapy with surfactant and NCPAP may be of benefit.
- Concerning overall CPAP use, there are no definitive conclusions in the Cochrane evaluations. All of the reviews stress the need for further large, prospective RCTs.

خسته نباشید