# Retinopathy of Prematurity

*Retinopathy of prematurity (ROP) is the second leading cause of blindness in childhood in the United States. The pathogenesis of ROP includes 2 phases. In the first phase, hyperoxia leads to vessel-growth cessation. In the second phase, hypoxia leads to pathologic neovascularization that extends into the vitreous.*

**ANESTHETIC PATIENT CONSIDERATIONS:**

- Neonatal and premature infant anesthetic considerations including ROP
- Risks of excessive hypoxemia: reopening of ductus arteriosus, vasoconstriction, bradycardia, decreased cardiac output, hypoxic brain injury

**ANESTHETIC PROCEDURE CONSIDERATIONS**

1. Risk of Apnea and bradycardia in infants undergoing peripheral retinal ablation (intra-op and x 3 days)
2. Avoid N2O intra-op and for at least 5 d after the air injection, 10 d after the $SF_6$ injection, and 15–30 d after the $C_3F_8$.

**ANESTHETIC GOALS:**

- PaO2 between 50-80 mmHg, SpO2 88-95%, limit O2 supplementation
- Neonatal resuscitation with room air
- $PaCO_2$ between 35 and 45 mm Hg

**PATHOPHYSIOLOGY**

- In the normal developing retina, there is a gradual transition from vascularized to avascular retina. Blood vessels grow gradually from the macula toward the edges of the developing retina. In patients with ROP, there is an abrupt termination of the vessels, marked by a linear demarcation in the retina.
- The immature retina responds to injury to the developing retinal capillaries by arrest of normal vasculogenesis followed later by disorganized reactive neovascularization and fibrous tissue formation in the retina and vitreous humor.
    - Retinal vasculogenesis is complete by 44 weeks postconception, after which time the risk of ROP is negligible.
- Scarring and lack of normal growth can cause the retinal network to peel away and retinal detachment.
- The pathogenesis of ROP includes 2 phases.
    - In the first phase, hyperoxia leads to vessel-growth cessation.
        - Supplemental oxygen suppresses vascular endothelial growth factor (VEGF), which results in the cessation of normal vessel growth and regression of existing vessels
    - The second phase, precipitated by the increasing metabolic demand of the developing retina with a compromised vascular supply is characterized by relative hypoxia, which leads to pathologic neovascularization that extends into the vitreous
        - The second proliferative phase is associated with an increased VEGF expression in the retina caused by relative hypoxia, which results in pathologic neovascularization
- Supplemental oxygen might be used therapeutically at appropriate time points to downregulate VEGF expression and to limit the neovascular complications of ROP
- There is a lack of evidence indicating that high oxygen sats increase ROP risk after 32 weeks' PGA.
- The spectrum or stages of disease is classified as follows:
    - Stage I. Mildly abnormal blood vessel growth. Many improve with no treatment and eventually develop normal vision.
    - Stage II. Moderately abnormal blood vessel growth. Many improve with no treatment and eventually develop normal vision.
    - Stage III. Severely abnormal blood vessel growth. The abnormal blood vessels grow toward the center of the eye instead of following their normal growth pattern along the surface of the retina. Some infants with no treatment and eventually develop normal vision. However, when infants have a certain degree of stage III and "plus disease" develops, treatment is considered. Plus disease means that the blood vessels of the retina have become enlarged and twisted, indicating a worsening of the disease.
    - Stage IV. Partially detached retina
    - Stage V. Completely detached retina

**HISTORY**

- **RISK FACTORS**
    - Prematurity (<35 weeks PCA, Negligible risk after 44 weeks PCA)
    - Low birth weight (<1500g)
    - Hyperoxia from administered oxygen
    - Duration of Oxygen treatment (no evidence that short duration of O2 as seen in anesthesia, causes or worsens ROP)
    - Timing of O2 (during phase I versus during phase II)
    - Hypoxemia
    - Hyper- and hypocapnia
- **LESS SIGNIFICANT RISK FACTORS**
    - Hypotension, sepsis and infection**,** Congenital Heart disease, intraventricular hemorrhage**,** blood transfusions**,** vitamin E deficiency
- ROP has been documented even in the absence of oxygen therapy
- Risk of retinopathy is inversely related to birth weight and gestational age.

**PHYSICAL**

- STANDARD PHYSICAL EXAM FOR NEONATE
- **EYE EXAM PERFORMED BY OPHTHALMOLOGIST**
    - Examination at 6 weeks of chronologic age or at 32 weeks PGA is recommended in premature infants weighing less than 1500 g at birth and in those born before 28 weeks of gestation.

**INVESTIGATIONS**

- As dictated by procedure, ROP requires no special investigations other than eye exam (see above)

**PREVENTION OF ROP**

- Lack of evidence that short term exposure to high O2 (ex. During anesthesia) increases risk of ROP however best to Minimize O2 exposure to pre-term infants <44 weeks PGA
- The optimal oxygen-saturation targets for preterm newborns are still controversial

- Speculated that low oxygen saturation in the first phase combined with high oxygen in the second phase of ROP pathogenesis might achieve greater protection than low oxygen alone.
- In General PaO2 50-80mmHg is recommended, SpO2 88-95% is it is difficult to know if the neonate is in Phase I or Phase II of ROP generation
    - Meta –analysis shows statistically significant risk reduction of 52% by low oxygen saturation (70%–96%) in the first postnatal weeks (Phase I) and of 46% by high oxygen saturation (>94%–99%) after PGA of 32 weeks (Phase II)
- Neonatal resuscitation with room air (evidence suggests it is as effective as 100% oxygen and may even be associated with reduced mortality rates, and morbidity including ROP
- Vitamin E may protect against ROP and reduce severity

**TREATMENT FOR ROP**

- Transscleral cryotherapy or laser photocoagulation is used to destroy the peripheral avascular areas of the retina, resulting in slowing or reversing the abnormal growth of blood vessels, which may reduce the risk of retinal detachment.
    - Central vision is preserved at the expense of some peripheral vision.
- Laser treatment
    - decreases retinal detachment and reduces blindness by 25%
    - nonblinding ocular morbidity is not reduced by treatment
- In advanced stages, partial retinal detachment can be treated with a scleral buckle or vitrectomy.
- The cryotherapy and laser therapies are usually performed under general anesthesia
- The surgical procedures do not involve blood loss or significant surgical stress, but they do depend on a still surgical field for periods ranging from 30 to 90 minutes.
- Retinal surgery may involve various procedures alone or in combination, including scleral buckling, vitrectomy, gas-fluid exchange, and injection of vitreous substitutes.
    - Scleral buckles are silicone rubber appliances sutured to the sclera to indent the eye wall, thereby relieving vitreous traction and functionally closing retinal tears.
        - This is an external procedure in which the eye may either not be entered at all or entered with a small needle puncture through the sclera for drainage of subretinal fluid.
    - Vitrectomy (removal of vitreous) is commonly performed to reduce traction on the retina (↓retinal detachment), clear blood and debris and remove scar tissue
    - A bubble of gas is sometimes introduced into the vitreous cavity during a scleral buckle or a vitrectomy when the surgeon wants an internal tamponade of retinal tears that cannot be closed adequately by a scleral buckle

**PROGNOSIS**

- 80% to 90% of acute cases of ROP undergo spontaneous regression with little or no residual effects
- Infants who develop ROP are at higher risk of developing ophthalmologic problems later in life including retinal tears, retinal detachment, myopia, strabismus, amblyopia, and glaucoma.

**ANESTHETIC OPTIONS AND ANESTHETIC SETUP**

- As per procedure.
- Adequate monitoring, vascular access, and thermal stability are common challenges to management of neonates**.** Consider monitoring preductal SpO2

**MANAGEMENT OF ANESTHESIA**

- Procedure dependant. Use paralysis for retinal procedures to ensure patient remains still

**DISPOSITION & MONITORING**

- **ANALGESIA**: Procedure dependant
- **OXYGENATION**: PaO2 50-80mmHg
- **MONITORING**: Patients are often premature infants and require inpatient monitoring for apnea after any procedure until 55-60 weeks PGA

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