Pathogenesis of ROP and the role of oxygen

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ROP and oxygen

- Described in animal models by Patz et al in 1952
- Inadequately regulated oxygen remains an important risk factor, but other factors also play a role e.g., sepsis, blood transfusions
Retinal blood vessels in the preterm eye

In term infants the retina is completely vascularized at birth.

In preterm infants the retinal vessels are immature and do not reach the edge of the retina.
Normal retinal vascularization

- The retina develops from the optic disc outwards
- Relative hypoxia of the developing peripheral retina stimulates the production of local growth factors, such as vascular endothelial growth factor (VEGF), which stimulate normal vessel growth
- Maternal nutrients and growth factors also play a role e.g., insulin-like growth factor
Retinal response to high oxygen saturation

- Endothelial damage
- Obliteration of developing retinal blood vessels
- Increasing hypoxia of the developing peripheral retina stimulates over production of growth factors such as VEGF
- Abnormal blood vessel development
Mouse model of oxygen induced retinopathy (OIR)

Kim CB et al. Eye and Brain 2015

Vaso-obliteration
Vaso-proliferation
ROP develops at the junction of vascular and avascular retina

Proliferation of abnormal vessels and fibrous tissue

Retinal detachment in advanced disease

From CyberSight
Premature birth

Decreased
Maternally derived factors
(ω-3 PUFA, IGF-1)

Supplemental oxygen

Vasoobliteration

Increased
ROS
Free radicals
Lipid peroxidation
Prostanoids and isoprostanes
trans-AAs
Nitration

Decreased
HIF-1 stabilization
Growth factors (VEGF, Epo, IGF-1)
ω-3 PUFA

Hypoxia
Increasing metabolism

Neovascularization

Increased
HIF-1 stabilization

Growth factors (VEGF, Epo)
Metabolic factors (succinate, adenosine)

Decreased
ω-3 PUFA

Sapiieha et al J Clin Invest 2010