Retinopathy of prematurity (ROP)

ROP is a potentially sight threatening condition which is confined to the retinal vessels of premature infants. Although many preterm infants develop ROP, severe disease is infrequent; 18% of neonates <1251g have Stage 3 disease or more and only 6% of these require treatment. In the UK, ROP accounts for 3% of childhood visual impairment.

Stages of ROP (1)

Outcomes
With pre-threshold ROP, the incidence of blindness was 9% for early treated eyes compared to 15% for conventionally treated eyes (treated after progression to threshold ROP). The incidence of myopia was around 70% for both treatments.

For threshold ROP, the incidence of blindness was 36% for treated eyes compared to 55% for non-treated eyes. Incidence of myopia was high in both groups (around 80%).

Threshold ROP: Zone I or II; five contiguous or eight composite hours of Stage 3 with plus disease.
Pre-threshold ROP: (1) Zone I any ROP (2) Zone II Stage 2, with plus (3) Zone II any amount of Stage 3, no plus (4) Zone II Stage 3 with plus but less than required Threshold clock hours.

Pathogenesis
Current concept of pathogenesis or ROP supports a two-stage process. After preterm birth, high partial pressure of oxygen (pAO₂) suppresses expression of growth factors (IGF-1, VEGF, Epo), and interrupts normal retinal vascular development (Phase I). After a few weeks (variable, around 29-30 weeks corrected gestation), continued development of the non-vascularised retina leads to relative hypoxia (due to increased metabolic demands), and results in increased expression of vascular growth factors and abnormal vascularisation (Phase II).

Location and Position
Position of ROP on the retina is measured by clock hours.

The Three Zones of the Retina

Typical diagram of the zones of the retina.

Zone I is the most posterior part of the retina and includes the optic nerve.

Zone III is the most peripheral zone, where vessels are often absent in ROP, but present in the normal eye.
Who requires screening?^5
- All infants less than 32 weeks gestational age (up to 31 weeks and 6 days) OR
- All infants with a birth weight less than 1501g

Infants that require screening each week should be entered into the ROP diary in advance. Mr Patrick Watts (Consultant Ophthalmologist) or his registrar comes to the neonatal unit, usually on a Monday morning. The eye drops are prescribed by the neonatal team and administered by the nurse looking after the baby. After screening, the ophthalmologists fill in an ROP sheet which summarises the Zone, the stage, and the presence of plus for each eye. The plan for follow up is recorded on the yellow ROP sheet and in the ROP diary. Many infants will require an outpatient appointment with Mr Watts following discharge. The timing of this appointment is decided by ophthalmology.

When should the first screening occur?^5
- Infants born up to 26 weeks and 6 days: at 30 to 31 weeks postmenstrual age.
- Infants born up to 31 weeks and 6 days: between 4 to 5 weeks (i.e. 28-35 days) postnatal age
- Infants >32 weeks gestational age but with a birthweight <1501 grams: between 4 to 5 weeks (i.e. 28-35 days) postnatal age
- All infants that require screening should have their first ROP examination prior to discharge.

<table>
<thead>
<tr>
<th>Gestational Age(weeks) at birth</th>
<th>Timing of first ROP screen</th>
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<tbody>
<tr>
<td>22, 23, 24, 25, 26</td>
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<td>27</td>
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Drug administration prior to and after screening
One drop of Proxymethacaine (local anaesthetic) is given before starting the examination. One drop of Phenylephrine 2.5% (sympathetic stimulant affects pupillary dilator muscle) and Cyclopentolate 0.5% (parasympathetic blocker inhibits pupillary sphincter muscle) is instilled into each eye twice, 5 minutes apart one hour prior to the examination. Comfort care offered to infants during examination, including sucrose solution, nesting, swaddling, dummy etc. Paracetamol is considered for all babies IV/PO.

Management^3

<table>
<thead>
<tr>
<th>Prevention of ROP</th>
<th>Infants included</th>
<th>Hypothesis</th>
<th>Main intervention</th>
<th>Recommendations</th>
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</thead>
<tbody>
<tr>
<td>LiGHT-ROP</td>
<td>&lt;1251 gm, &lt;31 weeks</td>
<td>Light reduction reduces ROP</td>
<td>Goggles vs No goggles</td>
<td>No difference in ROP incidence</td>
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<tr>
<td>STOP-ROP</td>
<td>Pre-threshold ROP, &lt;94% SpO2 in room air</td>
<td>Higher target SpO2 prevents 2nd stage of ROP development</td>
<td>Target 89-94% vs 96-99% SpO2</td>
<td>No difference in ROP needing treatment</td>
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<tr>
<td>HOPE-ROP</td>
<td>Pre-threshold ROP, &gt;94% SpO2</td>
<td>Less infants with higher SpO2 progress to threshold ROP</td>
<td>Observational: &lt;94% vs &gt;94% SpO2</td>
<td>No difference in ROP needing treatment</td>
</tr>
</tbody>
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Treatment of ROP

| CRYO-ROP          | <1251 gm, survived to 28 days | Treatment reduces poor outcome | Cryotherapy vs observation | Hypothesis proved |
| ET-ROP            | <1251 gm, pre-threshold ROP | Early treatment reduces poor outcome | Treat high-risk pre-threshold vs threshold | Hypothesis proved |
| BEAT-ROP          | Stage 3+, zone I or II | Bevacizumab reduces recurrence of ROP | IV bevacizumab vs laser treatment | Hypothesis proved in Zone I patients |

Analysis of oxygen-regulation trials (STOP-ROP, SUPPORT and BOOST I & II) suggest avoiding high SpO2 in the first few weeks of life (<95% targets) as prevention for ROP.
Three treatment trials of ROP have established trans-pupillary diode laser therapy as first line of therapy.
Due to long term side effects of laser therapy, intravitreal bevacizumab should be considered for zone 1 stage 3 ROP with plus disease^4 (please see separate guidelines for intravitreal bevacizumab).

References
5. RCPCH Evidence Based Guideline for the screening and treatment of Retinopathy of Prematurity (ROP), 2008

Dr M Chakraborty, Dr S Barr and Mr P Watts; April 2014, requires review April 2017.