Approved by Quality & Patient Care Committee
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RETINOPATHY OF PREMATURITY – SCREENING AND TREATMENT

This Local Operating Procedure is developed to guide safe clinical practice in Newborn Care Centre (NCC) at The Royal Hospital for Women. Individual patient circumstances may mean that practice diverges from this Local Operating Procedure.

INTRODUCTION

Retinopathy of prematurity (ROP) is a disease seen in some premature infants that has the potential to lead to visual impairment and blindness. ROP is the result of disordered retinal vascular development. It has strong associations with low birth weight, extreme prematurity, poor weight gain and excess administration of oxygen.[1]

The International Classification of ROP classifies ROP in terms of location, extent, stage and severity.[2] Screening to detect and treat in a timely manner limits the number of infants suffering visual impairment.

Some of following guidelines are based on the working document being prepared by the Paediatric Special Interest Group of the Royal Australian and New Zealand College of Ophthalmologists (RANZCO).[3]

1. AIM

- To provide a guideline for ROP screening and treatment program at the Royal Hospital for Women

2. PATIENT

- Newborns

3. STAFF

- Medical and nursing staff

4. EQUIPMENT

- As per ophthalmology team

5. CLINICAL PRACTICE

Whom to screen

- Gestational age at birth <31^{+0} weeks (regardless of birth weight)
- Birth weight of 1250 g or less (regardless of gestational age)[4,5]
- Other at-risk neonates determined by the neonatologists and ophthalmologists

NOTE:
The aim of screening is to identify infants who require treatment early AND minimise the number of examinations for infants at low risk.

When to screen

<u>First screening</u>[5]

- GA <28^{+0} weeks at birth – At 31 weeks postmenstrual age
- GA ≥28^{+0} weeks at birth – 5 weeks from birth

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Table: Timing of first ROP screening for each gestational age week

GA at birth	Postmenstrual age	Chronological age
23 weeks	31 weeks	8 weeks
24 weeks	31 weeks	7 weeks
25 weeks	31 weeks	6 weeks
26 weeks	31 weeks	5 weeks
27 weeks	32 weeks	5 weeks
28 weeks	33 weeks	5 weeks
29 weeks	34 weeks	5 weeks
30 weeks	35 weeks	5 weeks
≥31 weeks*		5 weeks

*If birthweight <1250 g or other risk factors determined by neonatologist

Subsequent screening

- Every 1-2 weeks or as determined by the ophthalmology team[3]

When to cease screening

- To be determined by the ophthalmologists
- General guidelines are as follows:[3]
  - Examinations can be discontinued once retinal vascularisation had reach zone 3 in infants who have not had evidence of ROP
  - This degree of vascularisation is rarely seen before 37 weeks postmenstrual age
  - Infants that have had ROP but have not required treatment should be followed until the ROP has been observed to clearly regress and the vascularisation has entered zone 3
  - It may be necessary to continue screening examinations well beyond 40 weeks of postmenstrual age

Follow-up after NCC discharge

- Arrange a follow-up check at Sydney Children's Hospital Ophthalmology clinic at 6 months of age
- Subsequent follow-up will be determined by the clinic

Informed Consent

- Obtain written informed consent from parent/s for cyclomydril eye drops administered prior to eye examination
- Counsel parents about the purpose, the importance and possible side effects of ROP screening in a timely manner

Rescheduling/postponing screening

- Rescheduling or postponing the screening can only be allowed after discussion with senior medical staff
- Document the reason for rescheduling in eMR

6. DOCUMENTATION

- eMR
- Medication Chart
- Consent Form
- NICUS database

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7. EDUCATIONAL NOTES

- ROP is to be classified using the International Classification of ROP. The revised classification was published in 2005.[2]
- The location of disease is described by its zone. Zone I is the posterior pole, and its border is strictly defined as a circle with the optic nerve in its centre and with a radius twice the distance from the centre of the optic nerve to the centre of the macula. Zone II extends from the edge of zone I to a circle with radius equal to the distance from the optic nerve to the nasal ora serrata. Zone III is the residual crescent anterior to zone II. By definition, an eye with vascularisation to within 1 disc diameter of the nasal ora serrata and temporal ROP has disease in zone III, regardless of the location of the temporal disease.

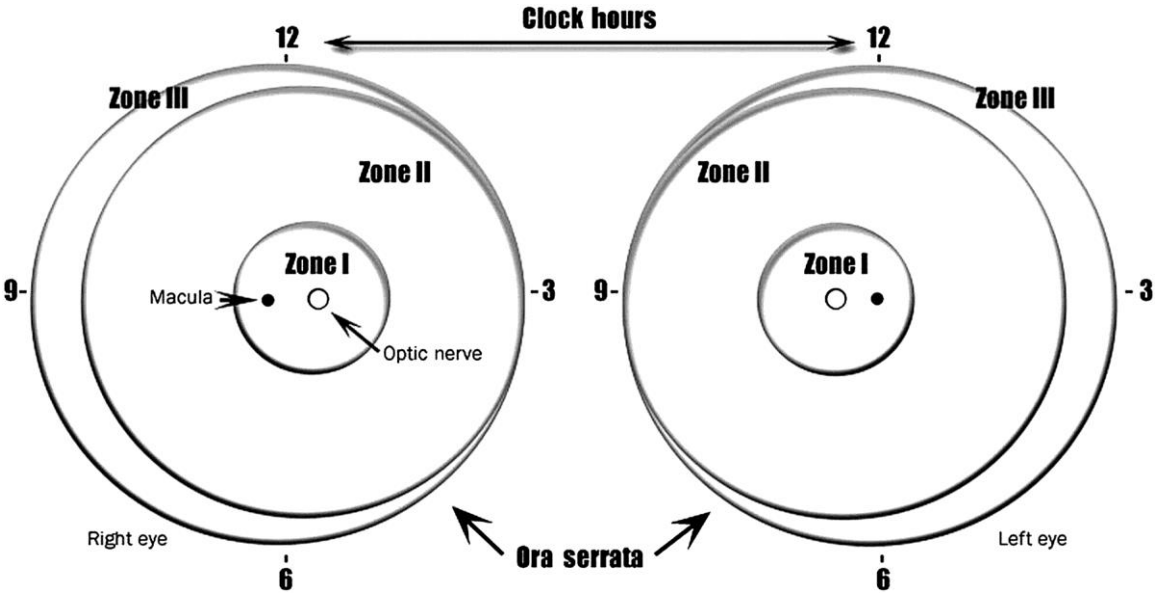

Figure. Zones of the eye.[6]

- Severity of disease is described by stages:[2,9]
  Stage 1: Demarcation line separating avascular and vascularized retina. Line is flat and not raised.
  Stage 2: Ridging of the demarcation line with height and width.
  Stage 3: Extraretinal fibrovascular proliferation.
  Stage 4A: Extrafoveal retinal detachment.
  Stage 4B: Subtotal retinal detachment involving the fovea.
  Stage 5: Total retinal detachment.
  Plus disease: Vascular dilation and tortuosity of vessels in at least 2 quadrants of the eye.
  Pre-plus disease: More vascular tortuosity than normal, but insufficient for diagnosis of plus disease.
  Type 1 ROP:
  Zone I, any stage ROP with plus disease
  Zone I, stage 3 ROP with or without plus disease
  Zone II, stage 2 or 3 ROP with plus disease
  Type 2 ROP:
  Zone I, stage 1 or 2 ROP without plus disease
  Zone II, stage 3 ROP without plus disease

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AP-ROP: Aggressive posterior retinopathy of prematurity, or AP-ROP is characterized by its posterior location, prominence of plus disease, and deceptively featureless neovascularization. AP-ROP is typically seen in zone I but may occur in posterior zone II. AP-ROP usually does not progress through the classic stages 1 to 3, and neovascularization may be flat and easily overlooked. Eyes with AP-ROP should be promptly treated with laser.

- Screening criteria: In Australia and New Zealand there is some variation in recommendations regarding gestational age and/or birth weight of infants to be referred for ROP screening. Some centres use birth weight of 1500 g or gestational age of 32 weeks while others use a cut off of 1250 g or 30 weeks.[3]
    - UK 2008 Guidelines recommend the following:[4]
        - Good Practice Point: All babies less than 32 weeks gestational age (up to 31 weeks and 6 days) or less than 1501g birthweight should be screened for ROP.
        - Grade B recommendation: All babies less than 31 weeks gestational age (up to 30 weeks and 6 days) or less than 1251g birthweight **must** be screened for ROP.
    - Canadian Guidelines 2016 recommend the following:[5]
        - GA of $30^{+6/7}$ weeks or less (regardless of birth weight); AND
        - Birth weights of 1250 g or less. Some centres may choose to extend the birthweight to 1500g or less.
        - First screening at 4 weeks postnatal age for 27^{+0} weeks and over and at 31 weeks postmenstrual age for GA<27^{+0} weeks
    - American Academy of Pediatrics 2013 guidelines recommend the following:[6]
        - Birth weight of ≤1500 g or GA of 30 weeks or less
        - Selected infants with a birth weight between 1500 and 2000 g or GA >30 weeks with an unstable clinical course.
    - Swedish Guidelines for ROP recommend the following:[7]
        - GA $30^{+6/7}$ weeks or less (regardless of birth weight)
        - First screening at 5 weeks postnatal age for 27^{+0} weeks and over and at 31 weeks postmenstrual age for GA<27^{+0} weeks
    - New Zealand Guidelines 2015 recommend the following:[8]
        - All infants <1250 g birthweight, or less than 30 weeks' gestation.
        - Selected infants ≥1250 g or ≥30 weeks with an unstable clinical course who are believed to be a high risk by their attending neonatologist.
        - Initial screening: GA of 26 weeks or less at 30-31 weeks PMA; GA 26-30 weeks and over (<1250g) at 4 weeks postnatal age.
- Our local data on ROP over 5.5 years between January 2013 and June 2018 indicate that 46 neonates at 31 weeks GA were screened for ROP and 2 cases of ROP were found. Case 1 was found to have stage 1 ROP with a birthweight of 1160 g, which would have been screened with new birthweight criteria. Case 2 was a baby with a birthweight >1500g and with no significant respiratory illness showed stage 1 ROP that resolved spontaneously.
- Based on our local data, latest recommendations from Canadian and Swedish guidelines,[5,7] and in consensus with our local ophthalmology group, we developed local screening criteria as follows:
    - GA of $30^{+6/7}$ weeks or less (regardless of birth weight)
    - Birth weights of 1250 g or less.
    - First screening at 5 weeks postnatal age for GA 27^{+0} weeks and over and at 31 weeks postmenstrual age for GA<27^{+0} weeks
- Timing of first screening: ROP takes longest to develop in very immature infants, therefore, first examination for these very immature infants is based on the postmenstrual age rather than postnatal age.

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- Method of examination: Binocular indirect ophthalmoscopy has historically been the examination method most commonly used to screen for ROP. Wide field angle digital retinal imaging (e.g. Retcam3) is also being used as a method of screening. However images obtained by this screening need to be interpreted by an expert ophthalmologist and images need to permanently recorded.
- Treatment for ROP:[3,4,5]
    - Standard treatment of ROP is by transpupillary diode laser ablation.
    - Treatment is warranted in type 1 ROP, unless there are some special circumstances when close observation may be acceptable.
    - APROP requires urgent treatment and may not follow the more typical progression of ROP requiring treatment.
    - Retinal ablation is done with laser photocoagulation.
    - Intravitreal injection of vascular endothelial growth factor (VEGF) inhibitors (such as bevacizumab) can be used in certain situations. These situations may include: APROP, zone 1 disease, an infant who is too sick to tolerate laser treatment, in cases where the view of the retina is inadequate to allow safe laser treatment and rescue treatment if laser treatment has failed to control type 1 disease or APROP. The long-term potential side effects of VEGF inhibitor on the premature infant are not well understood and such treatment is still considered investigational. It is a requirement of anti-VEGF treatment that there is careful tracking of the patient and long-term follow-up because of the risk of late recurrence of neovascular disease. The AAP recommends such follow-up continue to at least 65 weeks postmenstrual age.[10]
    - Arrangements for follow-up should be discussed by all parties (paediatricians, ophthalmologists, parents) and arranged before discharge/transfer with a paediatrician having prime responsibility, and parents having copies of all letters documenting eye results and follow-up arrangements.
- Possible side effects noted around the procedure include feed intolerance, abdominal distension, apnoeas and increased respiratory support.

8. RELATED POLICIES/PROCEDURES/CLINICAL PRACTICE LOP

- Eye – Administration of eye drops to the neonate
- Eye – Preparing the neonate for eye examination

9. RISK RATING

- Medium

10. NATIONAL STANDARD

- Standard 1 Clinical Governance
- Standard 2 Partnering with Consumers
- Standard 4 Medication Safety
- Standard 5 Comprehensive Care
- Standard 6 Communicating for Safety

11. ABBREVIATIONS AND DEFINITIONS OF TERMS

NCC	Newborn Care Centre	AP-ROP	Aggressive Posterior ROP
ROP	Retinopathy of Prematurity	VEGF	Vascular Endothelial Growth Factor
GA	Gestational Age		

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