Royal Hospital for Women (RHW)
NEONATAL BUSINESS RULE
COVER SHEET

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SUMMARY	Retinopathy of prematurity (ROP) is a disease seen in some premature neonates that has the potential to lead to visual impairment and blindness. Screening to detect and treat the disease in a timely manner limits the number of neonates suffering visual impairment.
Key Words	Retinopathy of prematurity, ROP screening, ROP management, treatment

Ref:

Retinopathy Of Prematurity (ROP) (Neonate)

RHW CLIN083

Contents

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Within this document we will use the term woman, this is not to exclude those who give birth and do not identify as female. It is crucial to use the preferred language and terminology as described and guided by each individual person when providing care.

1 BACKGROUND

Retinopathy of prematurity (ROP) is a disease seen in some premature neonates that may 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, fluctuation in oxygen saturation and excess administration of oxygen[1]. Screening to detect and treat ROP limits the number of infants suffering visual impairment.

The International Classification of ROP (ICROP3) classifies the disease in terms of location, extent, stage and severity[2]. Some of the following guideline is based on the document being prepared by the Paediatric Special Interest Group of the Royal Australian and New Zealand College of Ophthalmologists (RANZCO)[3].

2 RESPONSIBILITIES

2.1 Staff (medical, midwifery, Nursing, Allied health)

2.1.1 NCC Medical – Identify and request infant for eye examination. Gain consent from parents to administer eye drops. Prescribes requested mydriatic eye drops.

2.1.2 NCC Nursing

2.1.2.1. NUM maintains a scheduling system to indicate when infants are due for first and subsequent examinations. Liaise with the Ophthamology CNC.

2.1.2.2. Bedside nurse administers requested and prescribed mydriatic eye drops. Assists ophthalmologist when Ophthamology CNC is unavailable. Monitor neonate, pre, during and post examination.

2.1.3 Ophthalmology Medical – Ophthalmologist to conduct screening and follow ups. Document examination in medical records.

2.1.4 Ophthalmology Nursing CNC – Informs NCC NUM of examination timing, gathers necessary equipment and sets up procedure trolley, accompanies ophthalmologist to assist with procedure

3 PROCEDURE

3.1 Equipment

- Mydriatic eye drops
- Sucrose 24% or expressed breast milk
- Eye speculum sterile
- Eye depressor sterile
- Screening equipment provided by ophthalmology team

3.2 Clinical Practice

3.2.1 Who should be screened?

- Gestational age at birth <31+0 weeks regardless of birth weight
- Birth weight ≤ 1250 g regardless of gestational age [4,5]
- Other at-risk neonates determined by the neonatologists and ophthalmologists

3.2.2 Commencment of examination

- First screening
  - GA <28+0 weeks at birth – At 31 weeks postmenstrual age
  - GA ≥28+0 weeks at birth – 5 weeks from birth
  - If birthweight <1250 g or other risk factors determined by neonatologist

Table 1: 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	31 weeks	4 weeks
28 weeks	33 weeks	5 weeks
29 weeks	34 weeks	5 weeks
30 weeks	35 weeks	5 weeks
≥31 weeks or if birthweight <1250 g or other risk factors determined by neonatologist		5 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.

3.2.3 Frequency and cessation of examination

- Determined by the ophthalmology team every 1-2 weeks
- When to cease examination

- Determined by the ophthalmology team
- General guidelines are[3]
  - Once retinal vascularisation had reach zone 3 in infants who have not had evidence of ROP.
  - 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.

3.2.4 Rescheduling/postponing screening

- Rare, when infant is exceptionally unstable
- Consult with senior medical staff
- Document the reason for rescheduling in eRIC

3.2.5 Follow-up after NCC discharge

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

3.2.5 Treatment

- **Indications requiring treatment**
  - Type 1 ROP including Zone 1 disease of any stage with plus disease, zone 1 stage 3 disease without plus disease, and zone 2 stage 2 or 3 with plus disease.
  - Agressive- ROP (A-ROP) requires urgent treatment and may not follow the more typical progression of ROP requiring treatment. A-ROP is characterised by its location (posterior or peripheral), prominence of plus disease, and the ill-defined nature of the retinopathy and rapid progression.
  - There are a small number of infants that have stage 3 disease with extensive fibrovascular proliferation into the vitreous, but do not develop plus disease. These infants may be at risk of developing retinal traction and some ophthalmologists will recommend treatment in this situation.
- **Timing of treatment**
  - Treatment should be undertaken within 72 hours of the diagnosis of type 1 ROP and within 24-48 hours for A-ROP.
- **Methods of treatment**
  - Ablation of the peripheral avascular retina with transpupillary laser photocoagulation is the recommended treatment unless the child has: A-ROP, zone 1 disease, is too sick to tolerate laser treatment or in cases where the view of the retina is inadequate to allow safe laser treatment.
  - In these cases, intravitreal injection of a Vascular Endothelial Growth Factor (VEGF) inhibitor (such as ranibizumab) is preferred. Treatment should be undertaken by a paediatric ophthalmologist or vitreoretinal surgeon experienced in the treatment of ROP.

- All infants having treatment should have a repeat examination within 1 week of this treatment.
- Additional treatment is at the discretion of the treating ophthalmologist. Indications for further treatment may include no evidence of regression (or indeed deterioration) of ROP, worsening plus disease or the presence of laser skip areas. Such treatment may include further laser or VEGF inhibitors.

3.3 Documentation

- eRIC
- Consent form for the administration of mydriatic eye drops

3.4 Education Notes

- ROP is to be classified using the International Classification (ICROP3). The revised classification was published in 2021.[2]
- **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.

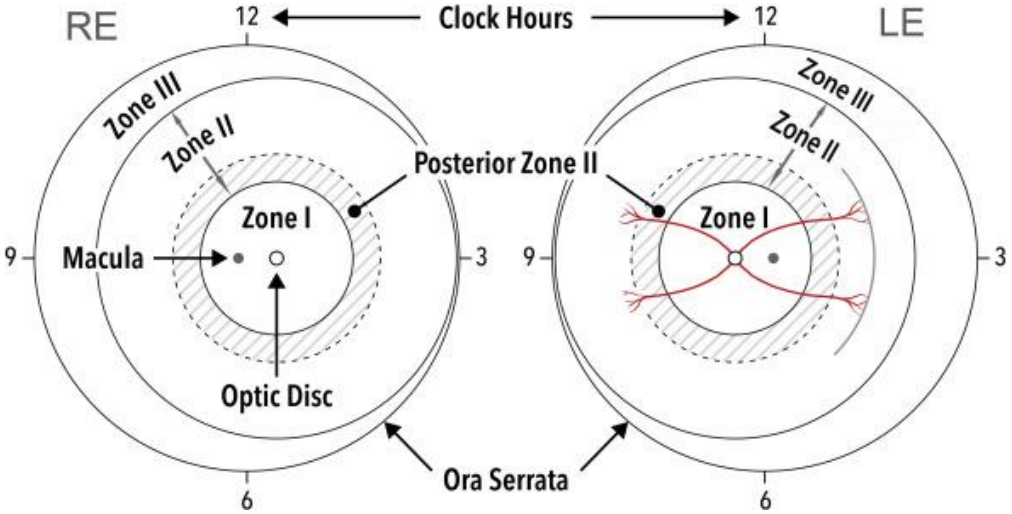

Figure 1: Diagram of right eye (RE) and left eye (LE) showing zone borders and clock hour sectors used to describe the location of vascularization and extent of retinopathy[2]

- **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 of ROP**
  - Type1
    - 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
    - Zone I, stage 1 or 2 ROP without plus disease
    - Zone II, stage 3 ROP without plus disease
  - Aggressive posterior retinopathy of prematurity (AP-ROP)
    - Characterised by its posterior location, prominence of plus disease, and deceptively featureless neovascularisation.
    - Typically seen in Zone I but may occur in posterior Zone II.
    - Usually does not progress through the classic stages 1 to 3, and neovascularisation may be flat and easily overlooked.
    - Eyes with AP-ROP should be promptly treated with laser.
- **Screening criteria**
  - NCC's local Guideline has been developed from the following local data, in consultation with the local ophthalmology group and is based on recommendations from Canadian and Swedish guidelines,[5,7]
  - 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 1160g, 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.
  - Australia and New Zealand[3]

- There are 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.

- UK 2022 Guidelines[4]
  - All babies less than 32 weeks gestational age (up to 31 weeks and 6 days) or less than 1501g birthweight should be screened.
  - 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[5]
  - GA of 30+6 weeks of GA at birth or less (regardless of birth weight); AND
  - Birth weights of 1250 g or less to be screened. 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 Paediatrics 2018[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 2020[7]
  - GA 30+6 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 2021[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.

- **Method of examination**
  - Binocular indirect ophthalmoscopy has historically been the examination method most commonly used to screen for ROP.
  - Wide-field digital retinal photography (WFDRP) such as Retcam3 is considered to be an acceptable method of screening. However, images obtained by this screening need to be interpreted by an expert ophthalmologist and images need to permanently recorded.

- Laser retinal burns should be confluent or near confluent in the avascular region. Some authorities recommend photocoagulation immediately posterior to the vascular ridge in more severe cases of type 1 ROP.
- It is recognised that the treatment of ROP is steadily evolving and modalities such as fundus fluorescein angiography and optical coherence tomography may be integrated in to the standard of care.
- VEGF inhibitors are used as the primary treatment in the indications described above. They are also used as a rescue treatment if laser treatment has failed to control type 1 disease or A- ROP.
- The long-term potential side effects of VEGF inhibitors on the premature infant are not well understood and are still under investigation. The choice of drug and dosage are also constantly changing, so the most recent evidence-base should be consulted prior to administering treatment. Treatment with VEGF inhibitors should be subject to individual institutional policy with appropriate informed consent obtained from the guardians.
- VEGF inhibitors without laser ablation, require far more intensive follow-up for the infant and family, which may not be appropriate in certain geographical locations.
- 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]
- Cryotherapy to the peripheral avascular retina is not an acceptable treatment for ROP in Australia and New Zealand. Its use has been superseded by laser.
- 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.

3.5 Abbreviations

ROP	Retinopathy of Prematurity	RANZCO	Royal Australian and New Zealand College of Ophthalmologists
A-ROP	Aggressive Retinopathy of Prematurity	VEGF	Vascular Endothelial Growth Factor
RE	Right eye	LE	Left eye
AP-ROP	Aggressive Posterior Retinopathy of Prematurity	GA	Gestational Age
WFDRP	Wide-field digital retinal photography		

3.6 CBR Implementation Plan

The revised CBR will be distributed to all medical, nursing and midwifery staff via @health email. The CBR will be discussed at ward meetings, education and patient quality and safety meetings. Education will occur through in-services, open forum and local ward implementation strategies to address changes to practice. The staff are asked to respond to an email or sign an audit sheet in their clinical area to acknowledge they have read and understood the revised CBR. The CBR will be uploaded to the CBR tab on the intranet and staff are informed how to access

3.7 Related Policies/procedures

- RHW NCC Nursing CBR - Eye – Administration of eye drops to a neonate
- RHW NCC Nursing CBR - Eye – Preparing the neonate for eye examination

3.8 References

1. Zin A, Gole GA. Retinopathy of prematurity-incidence today. Clinics in perinatology 2013;40(2):185-200.
2. Chiang, MF, Quinn, GE, Fielder AR et al.International Classification of Retinopathy of Prematurity, Third Edition. Ophthalmology 2021;128 (10):e51-68. https://www.aaojournal.org/action/showPdf?pii=S0161-6420%2821%2900416-4 Accessed on the 29. 6.2024
3. Retinopathy of Prematurity (ROP) Screening and Treatment Guideline. 2021. Royal Australian and New Zealand College of Ophthalmologists. https://ranzco.edu/wp-content/uploads/2022/01/RANZCO-Guidelines-for-Retinopathy-of-Prematurity-ROP_Dec-2021.pdf. Accessed on 29.6.2024.
4. Royal College of Paediatrics and Child Health.UK Screening of Retinopathy of Prematurity Guideline, March 2022 https://www.rcpch.ac.uk/sites/default/files/2024-06/ROP-screening-guideline-Mar-2022-with-alert.pdf. Accessed on 29.6.2024.
5. Jefferies AL. Retinopathy of prematurity: An update on screening and management. Paediatrics & child health 2016;21(2):101-4.
6. American Academy of Pediatrics Section on Ophthalmology. Screening examination of premature infants for retinopathy of prematurity. Pediatrics 2018;142(6):189-95. https://publications.aap.org/pediatrics/article/142/6/e20183061/37478/Screening-Examination-of-Premature-Infants-for?autologincheck=redirected. Accessed on 29.6.2024.
7. Holmström G, Hellström A, Gränse L et al. New modifications of Swedish ROP guidelines based on 10-year data from the SWEDROP register. Br J Ophthalmol. 2020 Jul;104(7):943-949.
8. Dai S, Austin N, Darlow B; New Zealand Paediatric Ophthalmology Interest Group; Newborn Network; Fetus and Newborn Special Interest Group; Paediatric Society of New Zealand. Retinopathy of prematurity: New Zealand recommendations for case detection and treatment. Journal of Paediatrics and Child Health 2015;51:955-9.
9. Fierson WM et al. Screening examination of premature infants for retinopathy of prematurity Pediatrics 2018;142(6):e20183061

4 ABORIGINAL HEALTH IMPACT STATEMENT DOCUMENTATION

- Considerations for culturally safe and appropriate care provision have been made in the development of this Business Rule and will be accounted for in its implementation.
- When clinical risks are identified for an Aboriginal and/or Torres Strait Islander woman or family, they may require additional supports. This may include Aboriginal health professionals such as Aboriginal liaison officers, health workers or other culturally specific services

5 CULTURAL SUPPORT

- For a Culturally and Linguistically Diverse CALD woman, notify the nominated cross-cultural health worker during Monday to Friday business hours
- If the woman is from a non-English speaking background, call the interpreter service: NSW Ministry of Health Policy Directive PD2017 044-Interpreters Standard Procedures for Working with Health Care Interpreters.

6 NATIONAL STANDARDS

- Standard 1 Clinical Governance
- Standard 2 Partnering with Consumers
- Standard 3 Preventing and Controlling Infections
- Standard 4 Medication Safety
- Standard 5 Comprehensive Care
- Standard 6 Communicating for Safety

7 REVISION AND APPROVAL HISTORY

Date	Revision No.	Author and Approval
12.3.2019	1	S Bolisetty (Lead Clinician), Kimberley Tan (SCH Ophthalmologist), Mark Jacobs (SCH Ophthalmologist), Hughie Tsang (SCH Ophthalmologist), Brian Darlow (University of Otago, Christchurch) Approved by NCC LOPs Committee
11.06.2019	2	S Bolisetty (Lead Clinician), Kimberley Tan (SCH Ophthalmologist), Brian Darlow (University of Otago, Christchurch)

		Approved by NCC LOPs Committee
30.06.2024 11.7.2024	3	S Bolisetty (Medical Co-director), E Jozsa (CNS) Endorsed by NCC CBR committee
15.8.24	3	Endorsed RHW BRGC