Screening for Retinopathy of Prematurity (ROP) - Full Clinical Neonatal Guideline – Joint Derby and Burton

Reference no.: NIC SS 02/May 2022/v002

Contents

1. Introduction

Retinopathy of prematurity (ROP) is one of the few causes of childhood visual disability which is largely preventable. Many extremely preterm babies will develop some degree of ROP although in the majority this never progresses beyond mild disease which resolves spontaneously without treatment. A small proportion, develop potentially severe ROP which can be detected through retinal screening. If untreated, severe disease can result in serious vision impairment and consequently all babies at risk of sight-threatening ROP should be screened. Untreated severe ROP is associated with a significant risk of blindness. Appropriate screening can detect babies who require treatment with laser therapy.

The most significant change from the 2008 guideline is that the gestational age screening criterion has been lowered to less than 31 weeks (i.e., up to and including 30 weeks and 6 days). The birth weight criterion of less than 1501g has not been changed.

2. Main body of Guidelines

Indications for Screening for ROP

All babies who are less than 31 weeks gestational age (up to 30 weeks and 6 days) **OR** less than 1501g birthweight should be screened for ROP. One criterion to be met for inclusion. Screening must take place prior to discharge.

When Should Babies be screened?

Gestational age at Birth	Time of Screening
< 31 weeks and 0 days (i.e. up to 30 weeks and 6 days)	**Between 31 weeks and 31 weeks and 6 days postmenstrual age, or at 4 completed weeks' postnatal age (28 – 34 days), whichever is later.**
≥ 31 weeks and 0 days but with birth weight < 1501g	**At 36 weeks' postmenstrual age or 4 completed weeks' postnatal age (28 – 34 days), whichever is sooner.**

Use the ROP screening calculator to determine appropriate date of screening Probability of ROP Requiring Treatment.

Table 1 below presents recommended timings of first examination for each gestational age.

GA (wks*)	PMA (wks*)	PNA (wks*)
22	31	9
23	31	8
24	31	7
25	31	6
26	31	5
27	31	4
28	32	4
29	33	4
30	34	4
31 (BW<1501g)	35	4
32 (BW<1501g)	36	4
33 (BW<1501g)	36	3
34 (BW<1501g)	36	2
35 (BW<1501g)	36	1

**wks: completed weeks (i.e., 22 = 22+0 to 22+6, etc.), GA: gestational age, PMA: postmenstrual age, PNA: postnatal age, BW: birthweight*

Frequency of screening

Minimum frequency	Where…
Weekly	1. The vessels end in zone I or posterior zone II with or without any stage of ROP, *or* 2. Any plus or pre-plus disease, *or* 3. Any stage 3 disease in zone II or III
Continue until the criteria for treatment or two weekly examination or termination have been reached.	
Every two weeks	1. The vessels end in mid or anterior zone II or in zone III; *AND* 2. There is no plus or pre-plus disease; *AND* 3. There is no ROP or stage 1 or 2 ROP
Continue until the criteria for treatment or weekly examination or termination of screening have been reached.	

All babies fitting the above screening criteria should have their name entered into the eye book on the appropriate page on admission and the date for ROP screening recorded in their notes.

The eye book is organised into weeks of screening. Choose the week which fits the above criteria and stick an identity sticker for the baby onto the page.

If a decision is made not to screen a baby, the reasons for not doing so should be clearly stated in the baby's medical record and the examination should be rescheduled within one week of the intended examination.

For babies who are discharged before screening is due:

- An appointment must be made for the appropriate time for screening and given to parents before discharge. The reason for the appointment and the importance of attending on the correct date must be conveyed to parents. A referral letter is not necessary.

At RDH

- Children are seen in the Ophthalmology Clinic on Thursday mornings. "ROP outpatients" slots are available each week and children can be booked into these directly by the receptionist. As screening on NICU occurs on a Monday, please ensure that babies deemed to require **1 week** follow up at discharge are seen no later than 7 days after last review. This will require families to attend on a Thursday in outpatients 3 days after last review (should not be booked 10 days after last review).

At QHB

- Children are seen in the Ophthalmology Outpatient clinic on a day arranged via the eye clinic and agreed with the ophthalmologist

- Where possible babies should have their ROP screening **prior** to discharge.

Advise the parents that their baby will require eye drops instilling and then will need to wait whilst they take effect. The visit will take at least 1-1.5 hours.

Delayed Examination

Only in rare circumstances, consider postponing the examination or performing a limited examination without an eyelid speculum and scleral indentor, when an infant is exceptionally unstable.
This decision should be made at consultant/senior level, and the rationale, its implications, and next steps in screening should be discussed with parents/carers and recorded in the infant's medical records.
Reschedule the next examination no later than one week beyond the intended examination.

Protocol for screening

The screening examination can be stressful for both babies and parents. The examination requires a well dilated pupil so the peripheral retina can be fully visualised.

- In addition to oral communication all parents should receive written information (Information leaflet Appendix 1) about ROP screening in advance of the procedure.

- Eye drops should be prescribed (see below) by a Doctor/ANNP on the night shift proceeding the day of examination to avoid delays.

- **Eye drops:-**

  To achieve effective mydriasis in preparation for ROP screening, 1 hour prior to examination administer:

  0.5% Cyclopentolate - 1 drop per eye (repeat dose after 5 minutes)
  2.5% Phenylephrine - 1 drop per eye (repeat dose after 5 minutes)

Note: Tropicamide 0.5% may be used as an alternative to cyclopentolate 0.5%, noting that it has a shorter duration of action

The Doctor/ ANNP must inform the nurse looking after the baby that the eyes are to be checked the following day and that the drops MUST be given at the appropriate time.

The eye drops are inserted on the day of examination by the nurse responsible for the baby.

Pain Relief

Use proxymetacaine 0.5% as topical anaesthesia just prior to examination when an eyelid speculum is to be used.

Babies will be swaddled and given sucrose as required during eye examination. The attending ophthalmologist may choose to administer topical anaesthetic eye drops to the babies prior to the examination at their own discretion.

The findings of the examination will be documented electronically on Badger detailing zone, stage and extent in terms of clock hours of any ROP and the presence of any plus or pre plus disease. Any discussions with parents will also be documented on Badger together with treatment undertaken and response.

Documentation

Record ophthalmological findings of each ROP examination in the infant's medical records, including detailed information on:

- Extent of vascularisation by zone in the absence of ROP
- Zone and stage of ROP
- Extent of ROP stage in clock hours
- Presence and extent in quadrants of any pre-plus or plus disease
- Name of the examiner
- Date of the next examination or discharge from screening.

Also, record in the infant's medical records that information has been given to parent/guardian and that consent has been gained, and by whom.

Ophthalmologist to document the findings in badger ROP screening result section after each screen.

Termination of ROP Screening

For infants without ROP, continue examinations until vascularisation has extended into zone III – as a guide, this is unlikely to have occurred prior to 36 completed weeks' postmenstrual age (36 weeks 0 days). If there is uncertainty about the zone, consider a further confirmatory examination two weeks later.

For infants with any stage ROP, consider discontinuing screening examinations when any of the following characteristics of regression are detected on at least two consecutive examinations:
- Partial resolution progressing towards complete resolution
- Change in colour of the ridge from salmon pink to white
- Growth of vessels through the demarcation line.

3.0 Treatment for ROP

Refer infants for treatment when criteria have been met:

- Zone I with plus disease and with any stage of ROP
- Zone I without plus disease but with stage 3 ROP
- Zone II with plus disease and with stage 3 ROP (zone II stage 2 with plus disease is borderline for treatment and may be treated or re-examined in one week or less) (note: plus disease should be present in at least two quadrants)
- A-ROP

Discuss with treating ophthalmologist within when referral warranted ROP is present:
- Any pre-plus or plus disease in two or more quadrants in any zone.
- Any zone I or posterior zone II disease.
- Any stage 3 disease in any zone.

Babies who are deemed to require treatment should be treated within 48 hours.

Consent

Discuss with parents/carers the need for ROP screening and provide parents/carers with access to written information (the Parent/Carer Information Leaflet available at UK-screening-retinopathy-prematurity-information-parents-carers.pdf (rcpch.ac.uk)) with enough time before the examination to allow for questions.

Consent for all ROP treatment options will be required from parents/guardians. Where using the Bevacizumab consent form, a copy should be given to parents/guardians, and a copy obtained for filing in the baby's medical notes. Clear documentation should be made in the medical notes around conversations with parents and consent for all procedures

considered and carried out.

ROP Laser Surgery (RDH site only)
Babies at QHB requiring laser treatment are currently managed through the West Midlands ROP Outreach Service – see separate document under guidelines.

Treatment of ROP protocol
The decision to treat will be made according to the 2022 ROP guidelines. This will comply with the guideline recommendation to treat severe disease within 48 hours in most cases. Consent will be sought from parents [Bevacizumab specific consent form – see appendix 2] and documented in case notes.

Laser treatment for ROP
The 810 indirect diode lasers will be used for laser treatment of ROP. This laser together with the charged headset will be sent to NICU from ophthalmic theatres. The upkeep and maintenance of this equipment will be undertaken by the ophthalmology department.

The baby will be required to be on a flat surface at approximately waist height. It will be difficult to treat with the baby in a crib and impossible in an incubator. Treatment will be in a separate room that has all the windows covered. Ophthalmic theatre staff can advise on making a room laser safe. The ophthalmic team will bring signage indicating laser treatment is occurring and entrance is restricted. All present in the room will be required to wear protective goggles which will also be brought by ophthalmic team along with laser equipment. The laser is the size of a large suitcase. All other persons are to be excluded from this room during the treatment session. Those present will be the ophthalmologist, an ophthalmic nurse to attend the laser, neonatologist and a neonatal nurse. The baby will require full monitoring with the ability to intubate and ventilate if necessary.

30 minutes prior to procedure, the baby will be intubated and ventilated following RDH intubation and ventilation protocol (drugs used: Rocuronium and Fentanyl). Sedation will be in the form of a morphine infusion. The dose required is 10 micrograms/kg/hour six hours prior to the procedure and between 20-40 micrograms/kg/hour during the procedure depending on the baby's response. Morphine needs to be reviewed on individual basis i.e., older babies may need more than 10 micrograms/kg/hour and at times may need to be given a maximum dose 30 minutes before the procedure.

One hour prior to the procedure Cyclopentolate 0.5% and Phenylephrine 2.5% will be instilled every 10 minutes to dilate the pupils. Immediately prior to treatment, each eye will have Tetracaine 1% instilled. A 10 ml syringe with sterile water is required to irrigate the cornea during the procedure. The procedure takes about 20 minutes per eye. The main discomfort is from manipulating the eye during the procedure rather than from the laser

itself. Oral Paracetamol to be prescribed post procedure for when required use, dosing as per BNFc.

Informed consent must be taken from the parents. This will be done by the treating ophthalmologist. It will be made clear that in spite of adequate treatment there is still a 10-20% risk of failure and severe visual impairment and that sometimes further treatment is required. It is impractical to have the parents in the room at the time of treatment, and parents should be informed of this at point of gaining consent.

After laser treatment, the morphine infusion should be weaned down over 6 hours with the aim to extubate when the child is ready with good respiratory effort and blood gases stable and consistent with pre intubation values. There is little pain once the treatment is completed. The eyes will be examined next day. Any decision to re-treat will be made within five to ten days. The baby will be examined weekly until it is determined that the ROP has regressed in each eye.

Laser may be indicated after a baby has been discharged from the neonatal unit. This includes babies requiring laser following initial treatment with anti-VEGF agents. Under these circumstances, laser treatment will be arranged under general anaesthesia in ophthalmic theatres at the King's Treatment Centre.

Post laser eye drops:- Maxitrol eye drops 1 drop QDS plus Cyclopentolate drops 0.5% 1 drop QDS for 1 week

Intravitreal injections

Treatment with intravitreal anti-VEGF agents (Bevacizumab, Ranibizumab) is indicated in aggressive posterior ROP (AP-ROP) and disease is in zone I. Laser would lead to poor structural and visual outcomes given proximity to macula and therefore there is a likelihood of better visual outcomes through using anti-VEGF agents as the initial treatment in zone I disease.

Anti-VEGF agents inhibit the action of vascular endothelial growth factor (VEGF), a key regulator of new vessel formation in foetal life. Animal studies had shown significant reduction in the endovascular response following injection of anti-VEGF antibodies into the vitreous cavity of the eyes ('intravitreal' therapy).

Anti-VEGF agents may also be recommended when laser is not possible due to media opacities. Furthermore, anti-VEGF agents may be recommended in exceptional circumstances when a baby is not medically stable enough to undergo the prolonged sedation required for laser.

The safety data and recommendations for use of Bevacizumab together with dose delivered have been reviewed with the DTC at the Royal Derby Hospital.

Parents will be counselled regarding the use of unlicensed medications and given information [appendix 4], potential for unknown systemic and neuro-developmental effects. The rationale for use and consent will be documented in the medical notes.

Prior to treatment with Bevacizumab, parents must have read through the information leaflet, and signed the consent form [appendix 2].

Post injection eye drops:- Chloramphenicol eye drops 1 drop QDS for 5 days

4.0 Post Treatment Review

When should infants treated for ROP be reviewed and what are the indications for retreatment of ROP?

Laser:
The first examination should take place 5-9 days after treatment and should initially continue weekly to assess for signs of regression or for any signs that re-treatment may be required. From 7-14 days start to consider re-treatment with laser if disease regression is inadequate and untreated retinal areas are identified. Rescue treatment with an anti-VEGF agent should be considered from 14 days if disease regression is inadequate and laser treatment has been optimal.

Anti-VEGF:
The first examinations should take place 1-2 days and 5-7 days after treatment to detect adverse effects of treatment. Following partial or complete disease regression, regular examinations should be maintained to detect disease reactivation: weekly for 4 weeks, 2 weekly for a further 12 weeks and then 4-weekly for at least a further 8 weeks (total of 24 weeks) and up to 32 weeks in eyes treated for A-ROP with bevacizumab).

Disease reactivation in the form of plus disease and / or extraretinal new vessels should be treated with transpupillary laser, to produce near-confluent ablation of the entire avascular retina.

Anti-VEGF agents may be used for retreatment but require more intensive follow up and carry a higher rate of further disease reactivation, requiring further retreatment.

Anti-VEGF agents differ. The above follow up schedule was used in the RAINBOW trial of ranibizumab. Longer follow up may be needed following bevacizumab (follow up to 65 weeks postmenstrual age has been recommended).

Follow up in OPD:

Paediatric Ophthalmologist will decide which babies need follow up in the children's outpatient department.

Audit

- Number of eligible babies who are screened for ROP
- Appropriate timing of ROP screening
- Number of infants requiring treatment for ROP
  Above audit data to be collated from NNAP.

5.0 References (including any links to NICE Guidance etc.)

- Guideline for the Screening and Treatment of Retinopathy of Prematurity May 2022. RCO, RCPCH, BAPM, BLISS
- University Hospitals of Leicester, Retinopathy of Prematurity: Screening and Treatment, October 2021, available online: Guidelines for prophylaxis against thromboembolic disease following caesarean section (leicestershospitals.nhs.uk)

6.0 Documentation Controls

Reference Number From Library and Knowledge Service Manager	**Version:** V002		**Status** Final	
Version / Amendment History	Version	Date	Author	Reason
	V001	April 18	Bala Subramaniam	Guideline required
	V002	May 2022	Harriet Hughes/Shavani Kasbekar	Joint guideline required for Derby and Burton
Intended Recipients: The guidelines is aimed at neonatal consultants and ophthalmologists and nurses				
Training and Dissemination: The guideline will be circulated to all neonatal consultants and Ophthalmologists at UHDB. All training can be provided in house.				
Development of Guideline: Harriet Hughes/ Shivani Kasbekar (Ophthalmologist) **Job Title: Advanced Pharmacist/Ophthalmology consultant**				
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Appendices below

Appendix 1: Information for Parents on the use of anti-VEGF drugs to treat Retinopathy of Prematurity [Print pages 12-15]

Introduction

Retinopathy of prematurity (ROP) is one of the leading causes of blindness and visual disability in children worldwide.

The causes of retinopathy of prematurity are now reasonably well understood. The hormone vascular endothelial growth factor (VEGF) plays a central role in causing the disease. A number of drugs that block the action of VEGF have been developed and have a wide range of accepted uses in clinical medicine in particular in the treatment of age related macular degeneration in adults.

Over the past several years there have been a number of reports and case series describing the use of anti-VEGF drugs in the treatment of retinopathy of prematurity. The two most commonly used drugs are Bevacizumab (Avastin) and Ranibizumab (Lucentis).

There has only been one good trial looking at the risks and benefits of using anti-VEGF drugs in ROP in premature babies. The study was called BEAT-ROP which stands for the Bevacizumab Eliminates the Angiogenic Threat of Retinopathy of Prematurity. The results of this trial were published in 2011 in the New England Journal of Medicine (the most respected medical scientific journal in the world).

This trial compared the use of the new treatment (injections of Avastin a common anti-VEGF drug) and the standard care of laser treatment. The study suggested that the new anti-VEGF drug treatment was better than standard laser treatment for very severe ROP and that there was no difference in outcomes for moderate ROP. Babies with Mild ROP were not enrolled in the trial.

There are however continued concerns about the risks of using anti-VEGF drugs in premature babies. Anti-VEGF drugs work by stopping the growth of new blood vessels. In premature babies there are many important organs (such as the brain, kidneys, heart, liver and lungs) that need new blood vessels to grow and develop normally to allow the organ to work properly when the baby is older.

This information document discusses some of the concerns and uncertainties about the use of anti-VEGF drugs for ROP in premature babies.

Will screening finish before my baby goes home?

Your baby will be discharged as soon as they are well enough to go home. This might be before the last eye screening. If this is the case, staff should arrange an out-patient appointment before you take your baby home.

It is very important that you bring your baby back for his/her eyes to be checked if you are asked to. When you are ready to take your baby home ask the staff if you need to bring him/her back and when. They will also write to remind you about the appointment.

Where can I get more information?

Please contact the following member of staff:

Name.....Tel.....

For further information and support, you can contact BLISS - the premature baby charity. BLISS is dedicated to working for premature and sick babies and their families and can put you in touch with other parents who have been through similar experiences.

Family Support Helpline: FREEPHONE 0500 618 140
enquiries@bliss.org.uk
www.bliss.org.uk

About this leaflet

This leaflet has been produced to accompany a guideline for the screening and treatment of the ROP developed by the Royal College of Paediatrics and Child Health, the British Association of Perinatal Medicine and the Royal College of Ophthalmologists. Parents and professionals have helped to write the leaflet. The main guideline contains recommendations for health professionals informed by research evidence. The full guideline and further copies of this leaflet can be obtained from www.rcpch.ac.uk/ROP

will need only one examination although most babies need at least two.

What happens during screening?

About an hour before the examination, eye drops are put in the eye to make the pupil open widely so the retina can be seen. The ophthalmologist examines the retina using an ophthalmoscope (or sometimes a camera) placed gently on the surface of your baby's eye. They may also use a speculum (to hold the eyelid open) and an indentor (to rotate the eye) to enable a better view of the retina.

Is the examination painful?

Eye examinations can be uncomfortable even for adults and babies sometimes cry or show signs of distress when their eyes are examined. The ophthalmologist will make the examination as quick as possible although they do need enough time to see the retina properly. If a speculum, indentor or a camera are used then anaesthetic eye drops should be used to minimise the discomfort to your baby.

Research has also suggested that wrapping your baby firmly or giving sucrose drops can help to keep babies calm during the eye examination. The nurses on the unit will have a lot of experience in preparing babies for the eye examination and will be able to explain what their practice is and involve you as much as possible.

What happens if my baby is ill when the eye examination is due?

There is no evidence that ROP screening is harmful for babies but the doctors may decide to postpone the examination for a short while until your baby is stronger. However, screening must not be postponed so long that the opportunity for treatment is missed.

What happens if ROP is found?

This depends on how serious it is.

- If ROP is mild, there will need to be a follow-up examination 1 to 2 weeks later. If the follow-up examination shows it has not become worse, the ROP will settle on its own.
- More severe ROP will require an earlier re-examination, usually in a week.
- In a very few cases the ROP may be severe enough to require treatment. If your baby requires treatment at any stage the ophthalmologist will talk to you to explain exactly what will happen.
- We have produced a separate leaflet with more information called 'Treatment for ROP'. Your unit should have a copy. Copies can also be downloaded from the internet www.rcpch.ac.uk/ROP

What are the possible benefits of intravitreal bevacizumab in the treatment of ROP?

Anti-VEGF drugs are accepted as safe and effective drugs in the treatment of eye diseases in adults where the hormone VEGF plays a major cause (as it does in ROP). It is therefore not unreasonable to hope that it may be useful in the treatment of similar eye diseases in children as well.

The BEAT-ROP showed better short term structural eye results for severe ROP compared to conventional laser treatment. It is well known from other studies that results of laser treatment for severe ROP are worse compared to those for milder forms of ROP. Anti-VEGF drugs therefore in the future are likely to be the first line and most recommended treatment for severe forms of ROP.

Laser treatment of severe ROP has higher rates of complications to the eye (field loss, short-sightedness, corneal scars, raised pressure in the eye and cataract) compared to anti-VEGF drug injections. Laser treatment, very importantly, also leads to greater stress for the baby at the time of treatment. This is because the prolonged handling, sedation and general anaesthetic needed to do the laser treatment can worsen lung and heart conditions that premature babies often have. This may increase the need for lung and heart treatments following laser treatment and in some rare cases lead to the death of the baby.

Injections into the eye of a baby with anti-VEGF drugs are technically easier than laser treatment. It certainly would be much easier and safer in an unwell and unstable infant as it does not require a general anaesthetic and prolonged handling. Laser treatment normally lasts 1 hour while anti-VEGF injections would normally take only 5 minutes. The shorter time for treatment would be less stressful for the infant and reduce the chance of the baby becoming sicker or even dying from any after effects.

Laser treatment is by its nature destructive to normal retina while anti-VEGF injections are almost certainly not. This is highly likely to mean that when the baby is older the edges of the visual field will still work as the edges of the retina will not have been destroyed by the anti-VEGF treatment.

What are the potential risks of anti-VEGF treatment?

The risks of anti-VEGF therapy can be discussed as eye and whole body (systemic). Both contain known and unfortunately unknown areas of risk.

Known eye risks are uncommon, but include a small risk of infection in the eye. In adults the risk of infection in the eye from an injection of anti-VEGF are around 1in 500. The risks in a baby maybe slightly higher as their immature immune systems may not be able to fight

infection so well. Damage to other parts of the eye may also occur rarely including lens damage (cataract) bleeding into the eye and retinal detachment all of which can cause loss of vision. All these possible complications can be treated by further surgery but can still lead to loss of vision despite treatment.

Unknown eye risks include possible long-term effects of anti-VEGF treatment to the developing eye tissues in particular the retina and nerve of sight. There is no evidence that anti-VEGF drugs damage adult eye tissues but we do not know if this would also be the case in developing and growing eye tissues.

Whole body risks are still largely unknown. There are possible increased risks of damaging organs and causing death in premature babies using anti-VEGF drugs as they are designed to stop normal new blood vessel growth. The current information that we have does not tell us about the possible long-term whole body outcomes of inside the eye injections of anti-VEGF drugs in premature babies. The BEAT-ROP study was too small to spot any differences in long-term outcomes on organ and eye development.

Very premature babies sadly don't always survive and some of the babies treated for ROP die not long afterwards, though it is hard to know how much the ROP treatment contributes to these deaths. It was noted in the BEAT-ROP study from 2011 that the death rate in the anti-VEGF treated group was larger than that in the conventional laser treatment group (five deaths compared with two respectively). It is possible that inside the eye injections of anti-VEGF drugs may result in poor wound healing in unwell babies who have undergone recent surgical procedures.

The possible effects of anti-VEGF treatment on new blood vessel growth elsewhere in the body of developing infants is of concern. This may affect the brain and cause the growing child to miss developmental mile stones leading to learning difficulties and cerebral palsy (difficulty moving the arms and legs). Lung development is also a particular concern, particularly in children who already have significant prematurity-related lung disease. Other organs undergoing important growth at this time may also be at risk, including the kidneys, heart, bones, muscles and reproductive organs.

When Avastin is given to patients adults with metastatic colorectal cancer, some patients experience serious and sometimes life-threatening complications such as, gastrointestinal perforations or wound healing complications, haemorrhage, arterial thromboembolic events (such as stroke or heart attack), hypertension, proteinuria (protein in your urine) and congestive heart failure. Patients who experience these complications not only had metastatic colon cancer but were also given 400 times the does you will be given, at more frequent intervals and in a way (through an intravenous infusion) that spreads the drug throughout their bodies.

Strategies to reduce risk associated with inside the eye anti-VEGF injections

If the baby's eye is very small we reduce the dose and the volume accordingly to minimise both systemic effects and the effects from the volume of the drug.

A sterile technique is used when giving the injection. We use a povidone-iodine solution to clean the eye and skin around the eye to kill any bugs that might cause infection. Antibiotic drops will also be given for 5 days after the injections to reduce the chance of infection.

Local anaesthetic drops are used to numb the eye so as the injection is as pain-free as possible. Sedation may also be necessary if a baby cannot lie still enough for the injections.

How can we monitor for side effects?

After treatment for the first few weeks there will be regular eye examinations to monitor the response of the ROP to the actual treatment and any possible complications such as infection, retinal detachment and cataract.

In the long term there is the possibility for both eye and whole body side-effects from anti-VEGF treatment. As all the current known information has only reported the short-term outcomes babies will be followed up for both eye and whole body assessment for several years afterwards.

Is anti-VEGF treatment licensed?

Currently Avastin is licensed for the treatment of eye conditions in adults. In order to obtain a license drugs must be thoroughly investigated and be shown to be safe to the satisfaction of the Medicines and Healthcare products Regulatory Agency (MHRA) which is the government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe.

Avastin is not licensed for treatment of Retinopathy of Prematurity – and the proposed use is described as being an "off-license" use of a licensed drug. This reflects the fact that in order to obtain a license the manufacturers have been obliged to demonstrate that a number of safety and manufacturing safe guards are in place – this is something that is not the case with some "unlicensed" drugs.

Appendix 2: Consent form for parents [Intravitreal Bevacizumab]

NHS
University Hospitals of Derby and Burton
NHS Foundation Trust

Consent form: Use of anti-VEGF drug Avastin (bevacizumab) to treat Retinopathy of Prematurity

Patient Identification Sticker

Please initial box

We / I confirm that we / I have read and understand the information sheet for the use of Avastin in the treatment of Retinopathy of Prematurity.	☐
We / I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
We / I understand that Avastin (bevacizumab) is not licensed for the treatment of Retinopathy of Prematurity.	☐
We / I understand that long-term effects are unknown and that our child will continue to require follow-up for longer than she/he might otherwise do.	☐
We / I agree to our child's GP or other care professional being informed of the use of Avastin (bevacizumab)	☐
We / I agree on behalf of our child to proceed with this treatment	☐

Name of Parent(s)	Date	Signature(s)

Name of Person witnessing consent	Date	Signature

Appendix 3: <u>Prescription for:</u> INTRAVITREAL bevacizumab (Avastin) Injection

[Unlicensed]

Patient identification sticker	Consultant Ophthalmologist: _____ Date of procedure: ____/____/____
Allergies:	

Has consent been gained and documented? Yes / No – ***ONLY*** *PROCEED IF YES*

Drug	**Bevacizumab**
Presentation	25mg in 1mL Pre-filled Syringe 1.25mg in 0.05mL
Storage	Fridge (2-8 degrees)
Route	**INTRAVITREAL**
Indication	Treatment of Retinopathy of Prematurity (ROP)

CHECK CONCENTRATION OF DRUG BEFORE ADMINISTERING

Note that syringe may contain more volume than is required to be administered

INTRAVITREAL	**Left** eye	Dose and Volume to be administered*	☐ 0.32mg [0.013mL] ☐ 0.625mg [0.025mL]	Prescribed by _____	Date __/__/__
	Right eye	Dose and Volume to be administered*	☐ 0.32mg [0.013mL] ☐ 0.625mg [0.025mL]	Prescribed by _____	Date __/__/__

Procedure undertaken by:_____ (Consultant Ophthalmologist) on ___/___/___

Observed by: _____ (Neonatologist)
_____ (Neonatal Nurse)
_____ (Ophthalmology Nurse)

Appendix 4: ROP Screening Examination Record Form

Retinopathy of Prematurity Examination Record

Name:

Hospital No:

DoB: **Male/Female**

Gestational age (wks):

Birth Weight (g):

Previous screening? Y/N **Hospital**:

Previous treatment? Y/N **Type**:

Stage 1 **Stage 2** **Stage 3** **Stage 4/5** **Laser**

Date of examination:

Name of examiner:

Postmenstrual age:

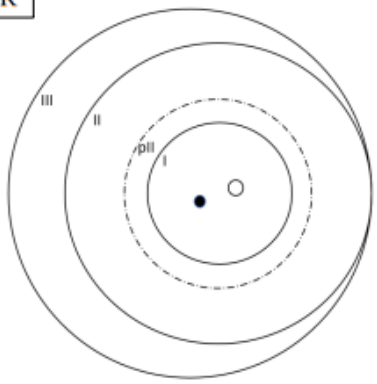
Findings:

Progression ☐
Regression ☐
No change ☐

Follow up:

Refer: Y/N

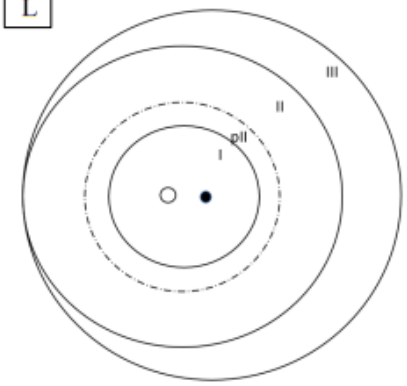
R



Zone: Stage: A-ROP: Y/N

Zone I/posterior zone II due to temporal notch: Y/N Plus: Y/N Pre-plus: Y/N

L



Zone: Stage: A-ROP: Y/N

Zone I/posterior zone II due to temporal notch: Y/N Plus: Y/N Pre-plus: Y/N

Comments:

Date of examination:

Name of examiner:

Postmenstrual age:

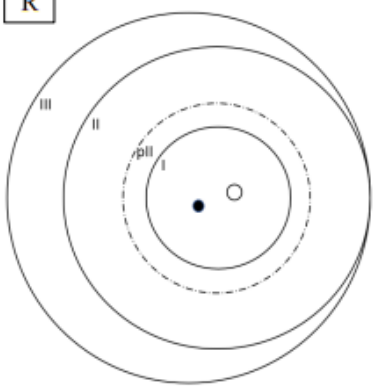
Findings:

Progression ☐
Regression ☐
No change ☐

Follow up:

Refer: Y/N

R



Zone: Stage: A-ROP: Y/N

Zone I/posterior zone II due to temporal notch: Y/N Plus: Y/N Pre-plus: Y/N

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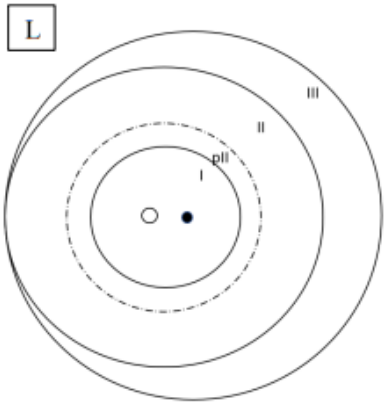


Zone: Stage: A-ROP: Y/N

Zone I/posterior zone II due to temporal notch: Y/N Plus: Y/N Pre-plus: Y/N

Comments:

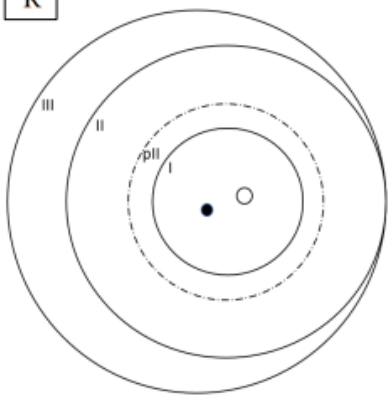
Stage 1	Stage 2	Stage 3	Stage 4/5	Laser

Date of examination:

Name of examiner:

Postmenstrual age:

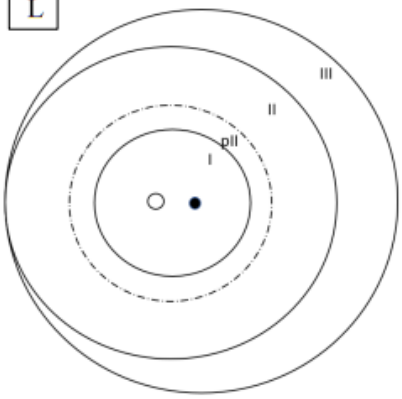
R



Zone: Stage: A-ROP: Y/N

Zone I/posterior zone II due to temporal notch: Y/N Plus: Y/N Pre-plus: Y/N

L



Zone: Stage: A-ROP: Y/N

Zone I/posterior zone II due to temporal notch: Y/N Plus: Y/N Pre-plus: Y/N

Findings:

Progression ☐
Regression ☐
No change ☐

Follow up:

Refer: Y/N

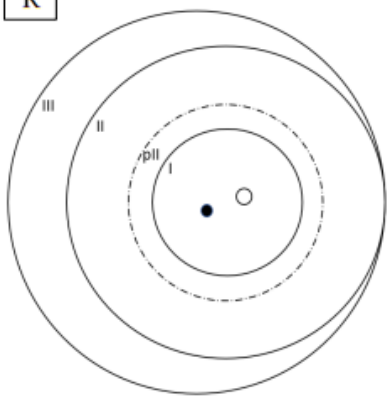
Comments:

Date of examination:

Name of examiner:

Postmenstrual age:

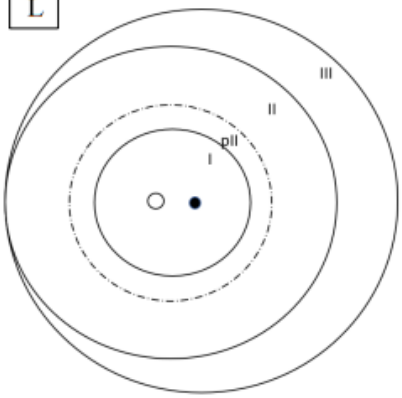
R



Zone: Stage: A-ROP: Y/N

Zone I/posterior zone II due to temporal notch: Y/N Plus: Y/N Pre-plus: Y/N

L



Zone: Stage: A-ROP: Y/N

Zone I/posterior zone II due to temporal notch: Y/N Plus: Y/N Pre-plus: Y/N

Findings:

Progression ☐
Regression ☐
No change ☐

Follow up:

Refer: Y/N

Comments:

Appendix Information leaflet for parents on ROP Screening

(Can also be printed from [Screening of retinopathy of prematurity (ROP) - clinical guideline | RCPCH](#)**)**

Screening for retinopathy of prematurity

Information for parents and carers

The Royal College of Ophthalmologists · British Association of Perinatal Medicine · Bliss for babies born premature or sick · RCPCH Royal College of Paediatrics and Child Health

You have been given this leaflet because your baby was born at less than 31 weeks of pregnancy (very premature birth) or had a birthweight under 1501 grams and is at risk of developing retinopathy of prematurity (ROP). ROP is a condition which affects your baby's eyes and can cause severe problems with vision.

Most babies will not develop ROP or will have a mild condition which will usually go away by itself. The only way to see if your baby has ROP and to see if it will need treating is to look at the back of their eyes with special equipment. This is called screening for ROP.

This leaflet will:

- give you more information about ROP
- clarify what happens during screening, and how you can support your baby
- explain what happens after screening.

As well as reading this information, the medical team looking after your baby will talk to you about screening for ROP. You will be able to discuss any questions or concerns you have with them.

What is ROP?

ROP is a condition that affects blood vessels (which carry blood around the body) in a part of the eye called the retina. The retina is at the back of the eye – it detects light which allows us to see. After a very premature birth, these blood vessels can start growing abnormally, resulting in ROP.

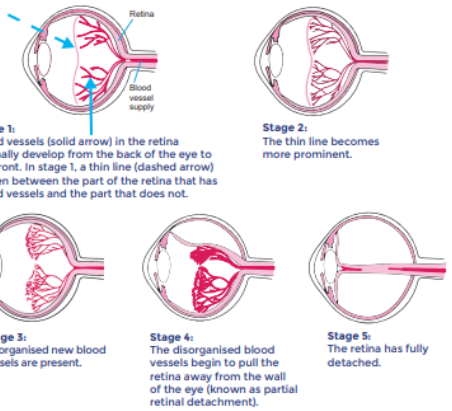
The main cause of ROP is a very premature birth. Other health problems associated with a very premature birth may also affect whether your baby will develop ROP, or if it will become severe.

In most babies, ROP is mild and will get better by itself, but for a small number (around one in twenty) of very premature babies, it may become severe. This can lead to partial or total loss of sight (blindness).

As it is not possible to tell if your baby has ROP from looking at the outside of the eye, we need to regularly look at the retinas of all babies who are at risk of ROP to find out if it is developing. Finding and treating ROP before it becomes severe can reduce the risk of sight loss. ROP is classified by numbered stages which are shown in the diagram below.

What does ROP look like?

The diagrams show the stages of ROP. Mild ROP of stages 1 and 2 is very common and usually settles on its own. Only a small proportion of babies develop stage 3, which is more serious and may need treatment. By screening for ROP and providing treatment if needed, the most serious stages (4 and 5) can usually be prevented.



Stage 1: Blood vessels (solid arrow) in the retina normally develop from the back of the eye to the front. In stage 1, a thin line (dashed arrow) is seen between the part of the retina that has blood vessels and the part that does not.

Stage 2: The thin line becomes more prominent.

Stage 3: Disorganised new blood vessels are present.

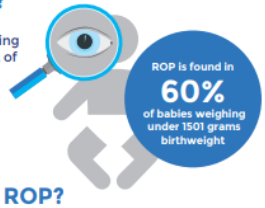
Stage 4: The disorganised blood vessels begin to pull the retina away from the wall of the eye (known as partial retinal detachment).

Stage 5: The retina has fully detached.

We acknowledge Prof Rebeccah Slater and Ms Sarah Chamberlain, Paediatric Neuroimaging Group, Department of Paediatrics and National Perinatal Epidemiology Unit (NPEU), University of Oxford for providing these diagrams.

How common is ROP?

ROP is found in 60% of babies weighing less than 1501 grams at birth; in most of these babies, the ROP is only mild.



What is screening for ROP?

ROP screening is an eye examination that looks for signs of ROP. The examination is done at the cotside. A headlight and lens or a special camera are used so the retina can be seen. About an hour before the examination, eye drops will be put in each eye – this is to make the pupils open widely so the retinas can be seen. Instruments called a speculum (to hold the eyelid open) and an indentor (to roll the eye) may also be used to help see the retina more clearly.

We know these eye examinations are uncomfortable for your baby and your baby is likely to cry and show signs of distress. Your baby's comfort is important to us and there are things we can do to make your baby as comfortable as possible before and during screening. These may include:

- putting anaesthetic drops in their eyes to numb any pain
- swaddling your baby in a blanket to help them feel secure and calm
- giving them small amounts of milk or sugar drops.

After the procedure your baby might be more unsettled, and their eyes may be a bit red and puffy. This should improve within a few hours after the examination. Even if no ROP is found, most babies will need to be examined more than once.

What can I do as a parent/carer?

The nurses on the unit are experienced in getting babies ready for the eye examination and supporting them during it. They will be able to explain how they do this and will involve you as much as possible.

If you choose to be present, you may be able to comfort your baby before or after the examination. Being present will also give you another opportunity to ask any questions that you may have.

What happens if my baby is too unwell for an eye examination?

If your baby is very unwell, senior doctors may decide to delay the examination. It will be rescheduled as soon as possible to make sure that no changes to your baby's eyes are missed. Screening must not be delayed so long that ROP is missed.

What happens if ROP is found?

If ROP is found, the eyes will be re-examined one to two weeks later. In a small number of cases, the ROP may be severe enough to need treatment. If your baby needs treatment, the ophthalmologist (a specialist eye doctor) will explain what will happen.

The Royal College of Ophthalmologists have produced a separate leaflet with more information on the treatment for ROP. Copies can be downloaded from www.rcpch.ac.uk/ROP.

Will screening finish before my baby goes home?

Your baby will be discharged as soon as they are well enough to go home. This might be before the first or last eye examination. If this is the case, staff should arrange an outpatient appointment for ROP screening before you take your baby home. More than one ROP screening appointment might be needed as an outpatient.

It is very important that you bring your baby back for their outpatient eye appointment if they have one.

How can ROP affect my baby's vision?

If the ROP is mild, your baby's eyes and vision are unlikely to be affected. If the ROP is more severe, problems such as short-sightedness and a squint could develop as your baby grows older, and your child might need to wear glasses.

If your baby is not being seen as an outpatient in the hospital, their eyes and vision will be examined at routine health checks for children that are performed by GPs and health visitors during early childhood. Your child's eyes and vision will also be checked when they start school.

If you have concerns about your baby's eyesight or the presence of a squint, please talk to your doctor – either your GP or when your baby is seen for follow-up as an outpatient in the hospital.

Any other questions?

If you have any further questions about your baby, please ask the nurses or doctors in charge of your baby's care.

Where can I get more information?

Please contact the following member of staff:

Name..... Tel.....

Please scan this QR code to visit the RCPCH webpage, www.rcpch.ac.uk/ROP, for further information and for a digital copy of this leaflet.

About this leaflet

This leaflet has been produced to accompany a guideline for the screening of ROP developed by the Royal College of Paediatrics and Child Health. Parents and professionals have helped to write this leaflet. The main guideline contains recommendations for health professionals informed by research evidence. The full guideline and further copies of this leaflet can be obtained from www.rcpch.ac.uk/ROP.

Screening for Retinopathy of Prematurity
Information for parents and carers

Other sources of support

Bliss: for babies born premature or sick.
Bliss's vision is for every baby born premature or sick to have the best chance of survival and quality of life. They offer a wide range of services to support parents and families who have experienced neonatal care.
Email: hello@bliss.org.uk
www.bliss.org.uk

RNIB (Royal National Institute of Blind People) Helpline
Tel: 0303 123 9999
Email: helpline@rnib.org.uk
www.rnib.org.uk/children

The Royal College of Paediatrics and Child Health
www.rcpch.ac.uk/ROP

The Royal College of Ophthalmologists
www.rcophth.ac.uk