GUIDELINES FOR THE
SCREENING AND MANAGEMENT
OF RETINOPATHY OF PREMATURITY
IN KENYA
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ACKNOWLEDGEMENTS

These guidelines have been developed through an elaborate and participatory process involving technical experts, partners and end-users of the guidelines in the public, private and faith-based health services in Kenya.

The Technical Working Group for developing ROP guidelines, led by Dr Sarah Sitati, was composed of individuals with considerable experience in their areas of expertise, and also with keen interest and commitment to this task. The members of the TWG are listed in the list of contributors. This guideline is evidence of their valuable contribution to the reduction of the risk of blindness for premature babies in the country. The work done by this team, and by implication the contribution of the institutions they work for, is especially commended.

The guideline is written in a clear and accessible style, and the evidence base of the recommendations is also provided. We thank the team for collating the evidence, adapting it to our local setup and articulating the practical application of this evidence. The team has made every effort to acknowledge the sources of the evidence and illustrations correctly, and any omissions that may be noted will be corrected in the next edition.

The preparation of the guidelines has been supported by the College of Ophthalmology of Eastern, Central and Southern Africa (COESCSA), The Fred Hollows Foundation, Sightsavers, Light for the World and CBM. The Ministry of Health recognizes the financial and non-financial contribution of these partners.

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FOREWORD

Clinical guidelines are fundamental tools to enhance implementation of effective and evidence-based interventions. This is the first edition of the national guidelines for screening and management of retinopathy of prematurity (ROP) and it has been developed in recognition of the rising magnitude of ROP. The guidelines are designed to contribute to significant improvement in the quality of care provided to premature infants and to prevent avoidable blindness. This is in line with the Constitution of Kenya 2010, and the Kenya Health policy Framework 2014-2030. It is evidence of the health sector’s commitment, under the government’s stewardship, to ensuring that the health care is responsive to the needs of the population, and that all citizens can attain the highest possible standards of health.

These guidelines are comprehensive, easy to read and embrace the principles of prevention, screening and management. The scope and depth of all the sections of the guidelines is extensive and provides very specific and practical recommendations. It will therefore provide a ready reference to its target users, who are nurses, paediatricians, ophthalmologists, health care managers and policy-makers.

A critical aspect of control of ROP is the need to recognise inter-related and inter-disciplinary aspects of care. The guidelines recommend close collaboration between neonatal and eye care services, and also note the role of obstetric services. The specific roles of the different actors have been outlined in the document, but beyond these, each actor will also need to work to establish networks with other stakeholders.

There is need to raise awareness regarding retinopathy of prematurity among health workers and parents of premature babies. The recommendations of these guidelines need to be fully understood, owned and implemented by the various stakeholders in ROP care in public, private and faith-based services. It is my hope that all the actors will rally around these guidelines to ensure that the objectives of the guidelines are achieved.

I am glad to note that the guidelines come with other outputs to be used at the point of care, including decision algorithms and ROP evaluation cards. This is expected to make implementation of the recommendations practical and feasible. As the guidelines are intended to improve quality of care for those at risk of ROP, it will be important to implement the monitoring and evaluation framework and share the lessons learnt from the implementation.

DR JACKSON K. KIOKO, MBS
DIRECTOR OF MEDICAL SERVICES
## DEFINITIONS OF TERMS

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<th>Term</th>
<th>Definition</th>
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<tr>
<td>Preterm</td>
<td>An infant born before 37 weeks of pregnancy</td>
</tr>
<tr>
<td>Aggressive Posterior ROP</td>
<td>An uncommon, rapidly progressing, severe form of ROP characterised by its posterior location, prominence of plus disease and the ill-defined nature of the retinopathy</td>
</tr>
<tr>
<td>Plus Disease</td>
<td>Increased venous dilatation and arteriolar tortuosity of the posterior retinal vessels in at least two quadrants of the eye</td>
</tr>
<tr>
<td>Pre-Plus Disease</td>
<td>Vascular abnormalities of the posterior pole which signify the presence of ROP, but which are insufficient for the diagnosis of plus disease</td>
</tr>
<tr>
<td>Regression/Involution</td>
<td>The process of ROP changing from active, progressive disease to inactive disease</td>
</tr>
<tr>
<td>Sight-Threatening ROP</td>
<td>Presence of stage 3 disease as defined in ICROP classification, type 1 or type 2 disease as defined below</td>
</tr>
<tr>
<td>Type 1 disease</td>
<td>Zone I, any Stage ROP with plus disease</td>
</tr>
<tr>
<td>Type 2 disease</td>
<td>Zone I, Stage 1 or 2 ROP without plus disease</td>
</tr>
<tr>
<td>Zone</td>
<td>The areas of the retina used to describe the location of ROP</td>
</tr>
<tr>
<td>Zone</td>
<td>The areas of the retina used to describe the location of ROP</td>
</tr>
</tbody>
</table>
# ABBREVIATIONS AND ACRONYMS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>AGREE</td>
<td>Appraisal of Guidelines, Research and Evaluation</td>
</tr>
<tr>
<td>AP-ROP</td>
<td>Aggressive posterior retinopathy of prematurity</td>
</tr>
<tr>
<td>BIO</td>
<td>Binocular Indirect Ophthalmoscopy</td>
</tr>
<tr>
<td>BW</td>
<td>Birth Weight</td>
</tr>
<tr>
<td>COECSA</td>
<td>College of Ophthalmology of Eastern, Central and Southern Africa</td>
</tr>
<tr>
<td>CRYO-ROP</td>
<td>Cryotherapy for Retinopathy of Prematurity Trial</td>
</tr>
<tr>
<td>ETROP</td>
<td>Early Treatment of Retinopathy of Prematurity trial</td>
</tr>
<tr>
<td>FAE</td>
<td>Fluid Air Exchange</td>
</tr>
<tr>
<td>GA</td>
<td>Gestational Age</td>
</tr>
<tr>
<td>ICROP</td>
<td>International Committee for Classification of Retinopathy of Prematurity</td>
</tr>
<tr>
<td>PPV</td>
<td>Pars plana Vitrectomy</td>
</tr>
<tr>
<td>PMA</td>
<td>Post menstural age</td>
</tr>
<tr>
<td>ROP</td>
<td>Retinopathy of Prematurity</td>
</tr>
<tr>
<td>SpO2</td>
<td>Oxygen saturation</td>
</tr>
<tr>
<td>TWG</td>
<td>Technical Working Group</td>
</tr>
<tr>
<td>VEGF</td>
<td>Vascular Endothelial Growth Factors</td>
</tr>
<tr>
<td>VI</td>
<td>Visual Impairment</td>
</tr>
<tr>
<td>VLBW</td>
<td>Very Low Birth Weight</td>
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</table>
INTRODUCTION

Retinopathy of prematurity (ROP), previously known as retrolental fibroplasia, is a serious vascular disorder affecting the retina in preterm infants and very low birthweight infants. It is one of the major morbidities associated with prematurity. Although ROP is both preventable and treatable, severe ROP that is not appropriately treated is associated with adverse visual outcomes. Over the last two decades, ROP has been recognized as a leading cause of avoidable childhood visual impairment (VI) and blindness of global concern. A recent study found the prevalence of ROP among premature infants who had undergone screening in one hospital in Nairobi to be 41.7%. Of those with ROP, 20.9% had vision-threatening ROP.

The incidence of ROP is increasing in low and middle income countries. This is associated with increasing survival of preterm infants; lack of clinical guidelines for prevention, screening and treatment; and insufficient resources for monitoring of newborn care. In low resource settings, managing patients with ROP has unique challenges. Insufficient awareness, infrastructure, staffing, expertise and budgets constitute barriers to good ROP care. Persistent efforts to support effective and accessible care are needed in order to preserve the vision of infants. Such efforts must pay attention to these barriers.

A guideline is a document containing evidence based recommendations about health interventions, which may include clinical, public health or policy recommendations. Guidelines aim to streamline care processes and provide best practices to improve the quality of the care. This is the first national guideline for the prevention, screening, treatment and follow-up of ROP.

Scope and rationale for the guidelines

The elimination of preventable blindness attributable to ROP is an important agenda for both Ophthalmology and Neonatology teams. Infants with poor visual outcomes due to ROP are reported to have a lower health-related quality of life than those infants who do not develop severe visual impairment. Globally and nationally, concerns exist about availability, access, and outcomes of ROP care. This concern has provided the impetus for developing national guidelines, whose goal is to reduce the incidence of VI and blindness from ROP.

The scope of the guideline includes all aspects of prevention, screening, treatment and follow-up of ROP. These are the key areas where change in practice is considered a priority and where implementation on a national scale is feasible. The comprehensive management of low vision and blindness associated with ROP (rehabilitative aspects of care) is however beyond the scope of the guideline.

The main clinical question the guideline development seeks to address is ‘How can sight loss from ROP be prevented?’ A PIPOH (Population, Intervention, Professionals targeted, Outcomes and Health care setting for the implementation) summary is provided below:

Table 1: PIPOH summary of the ROP guidelines

<table>
<thead>
<tr>
<th>PIPOH summary</th>
<th>Neonates at risk of ROP</th>
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<tr>
<td>Population of interest</td>
<td>1. Prevention of the risk factors for ROP</td>
</tr>
<tr>
<td></td>
<td>2. Retinal screening</td>
</tr>
<tr>
<td></td>
<td>3. Timely treatment of ROP</td>
</tr>
<tr>
<td>Intervention</td>
<td>1. Nurses (Neonatal and Ophthalmic nurses)</td>
</tr>
<tr>
<td></td>
<td>2. Paediatricians (Neonatologists and General Paediatricians)</td>
</tr>
<tr>
<td></td>
<td>3. Ophthalmologists (Paediatric Ophthalmologists, General Ophthalmologists and Vitreo-retinal surgeons)</td>
</tr>
<tr>
<td></td>
<td>4. Health care managers</td>
</tr>
<tr>
<td></td>
<td>5. Policy-makers for health care</td>
</tr>
<tr>
<td>Professionals targeted</td>
<td>1. ROP is prevented</td>
</tr>
<tr>
<td></td>
<td>2. All newborns at risk are screened</td>
</tr>
<tr>
<td></td>
<td>3. ROP is identified and timely treatment provided</td>
</tr>
<tr>
<td></td>
<td>4. Childhood visual impairment (VI) and blindness from ROP is prevented</td>
</tr>
<tr>
<td>Outcome of interest</td>
<td>All newborn units in all hospitals in Kenya</td>
</tr>
<tr>
<td>Health care setting</td>
<td>All newborn units in all hospitals in Kenya</td>
</tr>
</tbody>
</table>
Methodology of guideline development

A multi-disciplinary technical working group for ROP was convened in 2016. This consisted of technical experts (Neonatologists, Ophthalmologists, Paediatric Ophthalmologists, Vitreoretinal surgeons, Paediatricians), methodologists and implementers of the guidelines drawn from clinical practice, academia and programs. The implementers included representatives of the College of Ophthalmology of Eastern, Central and Southern Africa (COECSA), neonatal nurses and program managers. Following an extensive consultation phase, consensus was reached regarding the recommendations set in the guideline.

The process involved guideline adaptation from existing guidelines\(^5-9\) rather than de novo development of new guidelines, with consideration for availability and access to different interventions in the local context. The guidelines reviewed were found to be similar in most aspects, only differing in the upper limits of gestational age and birth weight beyond which screening is not necessary. The Appraisal of Guidelines, Research and Evaluation (AGREE II)\(^10\) process of quality assurance in guideline development was followed.

Once the final guidelines are ready, a pilot implementation will be conducted in selected high volume facilities. This will inform the final version of the document.

Risk factors for ROP

Since it was first described in the 1940s, the burden of ROP has been increasing in tandem with the increased survival of premature infants across the world, which has resulted from increased access to neonatal care. Low gestational age (GA) and low birth weight (BW) are the main determinants of risk of ROP. Both the incidence and severity of ROP increase with decreasing gestational age and birth weight.

Although these are the main independent risk factors, ROP is a multifactorial disease and many other factors influence its incidence.

Pathophysiology of ROP

Normal vascularization of the retina in the fetus begins at the optic nerve head in the 16th week of gestation. It proceeds anteriorly towards the ora serrata and is completed by the 36th to 40th week. ROP represents an interruption in this process of vasculogenesis, and it only occurs in immature retinal tissue. In the case of preterm birth, the infant is born before the retinal vessels are fully formed. As the vascular development is incomplete, the vessels do not reach the anterior edge of the retina, leaving an anterior avascular zone.

Within the first few weeks of extra-uterine life, the retina experiences relative hyperoxia, due to exposure to ambient or supplemental oxygen. This provokes vasoconstriction of retinal vessels, cessation of vascular growth and retinal hypoxia. Abnormal vascular development at the junction of the vascularized and avascular retina leads to formation of a visible line or a ridge.

Compensatory mechanisms lead to vasoproliferative changes, where blood vessels grow abnormally. This neovascularization is mediated by vascular endothelial growth factor (VEGF). These abnormal blood vessels are fragile and can leak or bleed. Severe fibroproliferative changes result in traction of the retina. Retinal detachment is the main cause of VI and blindness in ROP.

The features of abnormal vascular development (visible line, ridge and proliferating blood vessels) and retinal detachment are all signs of ROP. Mild ROP resolves spontaneously without visual sequelae. However in some infants the ROP is progressive. Severe untreated ROP leads to permanent ocular complications, which lead to visual impairment and blindness. It is critical that severe ROP should be detected and treated in time.

Classification of ROP

The International Committee for Classification for Retinopathy of Prematurity\(^11\) has recommended that classification should be based on the following criteria:

- The anterior-posterior location by zone (I-III)
- The stage (six stages; 1, 2, 3, 4a, 4b, 5)
- The extent (by clock hours): number of 30-degree sectors or clock hours of retinopathy along the circumference of the vascularized retina
- The presence or absence of plus disease
The schema of the retina below shows the zones of the retina and clock hours used to show the location and extent of ROP.

![Figure 1: Schema of the retina of both eyes showing the zones and clock hours used to describe ROP (reproduced from the Committee for Classification of Retinopathy of Prematurity)](image)

The severity of ROP is indicated by the stage and presence of aggressive posterior ROP (AP-ROP).

The stages of ROP describe the ophthalmoscopic findings at the junction between the vascularized and avascular retina:

<table>
<thead>
<tr>
<th>Stage</th>
<th>Retinal findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A demarcation line between vascularised posterior retina and avascular anterior retina</td>
</tr>
<tr>
<td>2</td>
<td>An elevated ridge between vascularised and avascular retina</td>
</tr>
<tr>
<td>3</td>
<td>A ridge with extraretinal fibrovascular tissue proliferating into vitreous cavity</td>
</tr>
<tr>
<td>4</td>
<td>Subtotal retinal detachment</td>
</tr>
<tr>
<td>4a</td>
<td>Extrafoveal detachment</td>
</tr>
<tr>
<td>4b</td>
<td>Foveal detachment</td>
</tr>
<tr>
<td>5</td>
<td>Total retinal detachment</td>
</tr>
</tbody>
</table>

*Stage 1 and 2 are considered mild, stage 3-5 are severe, while stage 4b and 5 are sight-threatening.*
Stage 1: Demarcation line

Stage 2: Ridge
Stage 3: Extra-retinal fibrovascular tissue

Stage 4: Subtotal detachment of the retina
Plus disease

Pre-plus disease

Aggressive ROP

Figure 2: Staging of ROP. (Photo credit: The International Classification of Retinopathy of Prematurity Revisited11 Arch Ophthalmol. 2005;123(7):991-999. doi:10.1001/archopht.123.7.991)

Aggressive posterior ROP is characterised by:
- Severe dilatation and tortuosity of posterior pole vessels
- Difficult to distinguish ROP at the junction between vascularised and avascular retina
- May occur in zone I or II
- Rapid progression
Plus or Preplus disease describe the posterior pole vascular abnormalities:
- **Plus disease** refers to significant vascular dilation and tortuosity of the retinal vessels at the posterior pole, present in two or more quadrants. It may be present at any stage and reflects the increased blood flow through the retina.
- **Preplus disease** refers to abnormal vascular dilation and tortuosity that is insufficient for the diagnosis of Plus disease.

Control of ROP

ROP is a disorder of both clinical and public health importance because of the huge impact of a lifetime of blindness.

The main pillars of control of ROP are:
- Prevention of the risk factors, especially through good neonatal care
- Early detection and timely treatment of ROP requiring treatment, mainly through neonatal screening programs
- Surgical interventions in advanced retinopathy

The program for control of ROP therefore requires a multi-pronged approach that includes all these strategies, and involves Parents, Nurses, Paediatricians, Ophthalmologists and other actors.

*Figure 3: The risk of blindness from ROP can be reduced through a combination of strategies such as timely screening and treatment (Photo credit: Dr Sarah Sitati)*
RECOMMENDATIONS FOR THE PREVENTION OF RISK FACTORS OF ROP

Obstetric care
The main risk factor for ROP is prematurity. The more preterm the neonate, the greater the risk of ROP. The most effective intervention would be to reduce premature births. Although this is difficult to achieve, good obstetric care helps to minimise or detect the risk of preterm birth. The following interventions are recommended:

- **Antenatal corticosteroids** for preterm births (< 35 weeks’ gestation) reduces the severity of respiratory distress and other complications, and may help prevent ROP

- **Delay the clamping the umbilical cord** by 30–60 seconds in vigorous preterm infants

Neonatal care
Poor neonatal care increases the risk of ROP, even in less premature babies. Best practices in neonatal care can reduce the risk.

Clinical teams who are monitoring the preterm infants should be aware of:
- The presence of the additional risk factors for developing ROP (besides GA and BW)
- The importance of the consideration of the clinical course as a factor for screening
- The need for meticulous newborn care

The POINTS of care strategy is a set of interventions that would reduce the incidence of ROP, by addressing common risk factors for ROP. Such risk factors include:
- Anything that makes babies unstable: pain, poor temperature control and not keeping the baby comfortable and supported in the cot or incubator.
- Infection during the first few weeks.
- Inadequate nutrition with poor weight gain during the first few weeks of life.

Table 2: POINTS of care for newborn infants

<table>
<thead>
<tr>
<th>Pain control</th>
<th>Pain makes babies unstable and should be assessed and controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Strategies to prevent painful episodes include:</td>
</tr>
<tr>
<td></td>
<td>Reduce unnecessary painful procedures (such as taking blood samples, fixing drips, inserting nasogastric tubes)</td>
</tr>
<tr>
<td></td>
<td>Anticipate pain and assess babies for pain</td>
</tr>
<tr>
<td></td>
<td>Take parent’s perception of pain into consideration</td>
</tr>
<tr>
<td></td>
<td>Prevent pain by swaddling, use of oral sucrose/glucose, use of a pacifier</td>
</tr>
<tr>
<td></td>
<td>Systemic analgesics can be used in very painful procedures</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Oxygen management</th>
<th>Judicious use of ventilation and supplemental oxygen therapy is a crucial strategy. Both hypoxia and hyperoxia are undesirable. Oxygen saturation (SpO2) should be monitored by pulse oximetry and maintained between 91% and 95%.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>There is need for enough equipment to safely deliver and monitor oxygen therapy.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infection control</th>
<th>Apply infection control procedures, including:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Hand washing by all persons entering NBU, before and after handling baby</td>
</tr>
<tr>
<td></td>
<td>- Careful skin preparation before procedures such as taking blood samples</td>
</tr>
<tr>
<td></td>
<td>- Avoid sharing equipment between babies to prevent cross-contamination</td>
</tr>
</tbody>
</table>

| Good Nutrition               | Exclusive breastfeeding is recommended                                                                                               |
Temperature

Keep preterm babies warm. Use a plastic bag or occlusive wrapping. Maintaining normal temperature (36.5–37.2 °C) reduces the risk of severe ROP and other complications.

Supportive care

Keep babies comfortable and stable, through:
- Kangaroo care
- Good positioning of the baby in an incubator or cot
- Minimise noise and bright lights
- Minimise blood transfusions

Figure 4: A newborn unit: Good neonatal care is fundamental to the prevention of ROP (Photo credit: Dr Oscar Onyango)
RECOMMENDATIONS FOR SCREENING

ROP screening is an important aspect of delivering high quality care to neonates. The natural history of ROP is well understood, and the appropriate timing of the screening examination has been elucidated. The clinical benefits of appropriate and accurate periodic retinal screening to establish the presence of treatable ROP have been well documented through the use of well-controlled multi-centre studies\textsuperscript{14-17}. Bedside binocular indirect ophthalmoscopy (BIO) with pupillary dilatation has been the standard technique for retinal evaluation in premature infants.\textsuperscript{18}

Who should be screened (inclusion criteria)?
The key parameters to be considered are established by birth weight (<1,501g), gestational age (<=32 weeks) and unstable neonatal clinical course.\textsuperscript{19}

The following categories of neonates should be screened:

1. All new-borns with BW <1501g
2. All new-borns with GA <= 32 weeks (as determined by the postmenstrual age). Because ROP takes longest to develop in very immature infants, timing of the first examination should be based on postmenstrual age rather than postnatal age.
3. Neonates with BW 1501g - 2000g (inclusive), and/or GA >32 - 35 weeks (inclusive) if they have comorbidities (see list of comorbidities below)
4. Any baby whose clinical course is unstable and, in the opinion of the Neonatologist/Paediatrician has a risk for developing ROP

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>- High/prolonged oxygen supplementation</td>
<td>- Apnea</td>
</tr>
<tr>
<td>- Respiratory distress syndrome (RDS)</td>
<td>- Neonatal acidosis</td>
</tr>
<tr>
<td>- Sepsis</td>
<td>- Multiple births</td>
</tr>
<tr>
<td>- Hyperbilirubinaemia/Jaundice/ need for phototherapy</td>
<td>- Necrotizing enterocolitis</td>
</tr>
<tr>
<td>- Extended assisted ventilation</td>
<td>- Cardiac defects</td>
</tr>
<tr>
<td>- Intraventricular haemorrhage III-IV</td>
<td>- Intercurrent surgical interventions</td>
</tr>
<tr>
<td>- Poor postnatal weight gain</td>
<td>- Poor postnatal weight gain</td>
</tr>
</tbody>
</table>

The screening examination

Before the screening examination:

1. The newborn unit Nurse will list the new-borns that are scheduled for screening each week (initial or follow up), counsel the parents, take informed consent, and inform the Paediatrician.
2. Data that will need to be available to the ophthalmologist:
   - Date of birth, GA, BW, oxygen therapy exposure time, comorbidities (sepsis, HIV, enterocolitis and others)
3. The comfort of the infant must be maintained:
   - Avoid hypothermia
   - Position the infant comfortably
   - Topical analgesic/anaesthetics, pacifiers, swaddling and sucrose should be available and used to reduce discomfort.
4. The Nurse will administer mydriatics (1% Tropicamide combined with 2.5% Phenylephrine, or 0.5% - 1% Cyclopentolate eye drops combined with 2.5% Phenylephrine); use the minimum effective dose to prevent side-effects.
   - Mydriatics can be administered by trained nurses.
   - The dilating drops should be sufficient to allow adequate dilatation for examination of the fundi
   - Avoid instilling multiple drops if the pupil fails to dilate, since poor pupillary dilation can occur in advanced ROP, and administering multiple doses of dilating drops can adversely affect the systemic status of the infant.

During the examination

5. Screening will be conducted in the new-born unit
6. The Ophthalmologist must have the appropriate competency and sufficient time to conduct the screening
7. Screening will utilise binocular indirect ophthalmoscopy with mydriasis, with a +20D lens. RetCam (specialized digital retinal photography) can also be used.
8. It is important that the periphery of the retina can be seen and this may be facilitated by the use of an eyelid speculum and scleral indenter, which should be autoclave sterilized before each use.

9. Infection control practices need to be observed, especially hand washing.

Timing of first screening
ROP is not present at birth. The recommendations for the timing of the first screening are informed by an understanding of the natural history of ROP from two large clinical trials – the Multicenter Trial of Cryotherapy for ROP and the Effects of Light Reduction on ROP.

The recommendations are:
- Screen neonates born at GA < 30 weeks within three weeks after delivery
- Screen all other newborns within 4-6 weeks after delivery

Timing of follow up screening
The follow up date for each infant will be determined by the Ophthalmologist based on the following table:

Table 3: Follow up after screening

<table>
<thead>
<tr>
<th>ZONE 1</th>
<th>ZONE 2</th>
<th>ZONE 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>STAGE 3</td>
<td>Treatment</td>
<td>≤ 1 week</td>
</tr>
<tr>
<td>STAGE 2</td>
<td>≤ 1 week</td>
<td>1-2 weeks</td>
</tr>
<tr>
<td>STAGE 1</td>
<td>≤ 1 week</td>
<td>2 weeks</td>
</tr>
<tr>
<td>NO ROP (Immature retina)</td>
<td>1-2 weeks</td>
<td>2-3 weeks</td>
</tr>
<tr>
<td>Regressing ROP</td>
<td>1-2 weeks</td>
<td>2 weeks</td>
</tr>
</tbody>
</table>

Release from screening
Ocular fundus evaluations can be suspended when the following conditions are met:
- Complete retinal neovascularization up to zone III
- Post-menstrual age > 45 weeks and the absence of pre-threshold disease
- ROP regression with non-reactivation certainty (although patients with post-menstrual age > 43 weeks generally stabilize, relapses can occur in association with surgical interventions, general anaesthesia, sepsis or deterioration of clinical status). These babies need follow up screening examinations till 6-9 months of age, especially if they have been on anti-VEGF treatment.

Long term follow up
Babies with ROP and babies with BA < 1501g are at risk of developing other ocular conditions, such as high refractive error, strabismus, anisometropia, amblyopia, glaucoma and cataract. They need long term follow up. It is recommended that after discharge they should be followed up for at least 9-12 months, to assess for these conditions. Further follow up is also necessary and the schedule will depend on the ocular findings.
Information for parents and guardians

You can participate in the care of your baby in the following ways:
- Continue to provide the day-to-day parental care of the baby, such as changing diapers and feeding
- Give Kangaroo care for the baby, it has benefits for both baby and caregiver. This will require your presence in the newborn unit from time to time
- Ask the care provider for information about ROP, and its possible effects on visual function
- Ask the paediatrician if your baby needs screening for ROP
- Ask the eye doctor about results of the screening and the need for urgent treatment, if required
- Enquire about the risks of treatment from the eye doctor
- Your baby will need follow up care after treatment for ROP. Be sure to ask the eye doctor about the schedule for follow-up visits

Information for health workers

1. Preterm babies can have serious vision loss from retinopathy of prematurity (ROP), which may not be externally visible.
2. All preterm babies with a birth weight of less than 1.5Kg or born at 32 weeks of gestation or less (1 month or more before EDD) need a complete eye examination (dilated retina examination) between 20-30 days after birth.
3. Follow up is needed every 1-2 weeks if ROP is present, or every 2-3 weeks if ROP is absent but the retina is immature until the retina matures fully.
4. Very urgent laser or Anti-Vascular Endothelial Growth Factor (Anti-VEGF) treatment is needed if abnormal blood vessels are seen on examination of the retina (back side of the eye).
5. All normal and preterm newborns should undergo an eye examination for Red Reflex and torch light examination within a few hours of birth and thereafter every month until 6 months of age.
Efficacy and safety of treatment

ROP can often be effectively treated with cryotherapy or laser retinal ablative surgery or intravitreal anti-VEGF injections when diagnosed early. Cryotherapy and laser have been used for a long period and their safety profile is known. However they require expertise, equipment and infrastructure that is not available in many facilities that have a newborn unit. This means that treatment with laser is not accessible to most patients, a barrier that can contribute to development of blinding ROP. Anti-VEGF treatment is a more recent advancement and may be more feasibly implemented in most facilities with a newborn unit. Although studies have shown the effectiveness of anti-VEGF, the safety of these drugs in preterm babies still needs to be monitored.

Indications for Treatment

Not all infants with ROP require treatment. The following findings necessitate treatment:

1. Type 1 ROP
   a. Zone I, any Stage of ROP in the presence of plus disease
   b. Zone I, Stage 3 without plus disease
   c. Zone II, Stage 2 or 3 with plus disease
2. Aggressive posterior ROP

Timing of the treatment

Treatment for severe ROP is urgent; should be given in the strict time window of 24-48 hours following diagnosis of ROP requiring treatment. Aggressive posterior ROP should be treated immediately or within 24 hours.

Treatment methods

The treatment options are tabulated below. The mainstay of treatment for severe ROP is peripheral retinal photocoagulation, delivered by transpupillary laser. Only the avascular retinal periphery should be treated. The laser burns should be light and almost confluent. Laser treatment requires a trained and highly skilled ophthalmologist.

Agents which block vascular endothelial growth factor (anti-VEGF), which are given by intravitreal injection, can give rapid short-term resolution of ROP. A longer period of follow-up and closer monitoring is required when using anti-VEGF therapy.

Table 4: Treatment options

<table>
<thead>
<tr>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Anti-Vascular Endothelial Growth Factor (Anti-VEGF agents)</td>
</tr>
<tr>
<td>Bevacizumab 0.625mg in 0.025ml</td>
</tr>
<tr>
<td>Ranibizumab 0.25mg in 0.025ml</td>
</tr>
<tr>
<td>b. Laser</td>
</tr>
<tr>
<td>Indirect Retinal photocoagulation. (810 diode laser or 532 FD ND-YAG Laser)</td>
</tr>
<tr>
<td>c. Cryotherapy</td>
</tr>
<tr>
<td>d. Indirect Laser then Parsplana Vitrectomy (PPV) + Fluid Air Exchange (FAE)</td>
</tr>
</tbody>
</table>

Applying the treatment options

Criteria for treatment

a. Immature retina, No ROP: Review in 3 weeks
b. Type 1 ROP: Treat
   Zone I, any stage with plus disease
   Zone I, stage 3 without plus disease
   Zone II, stage 2-3 with plus disease
c. Type 2 ROP: Observe
   Zone I, stage 1-2 without plus disease
   Zone II, stage 3 without plus disease

Choice of treatment mode

Zone 1
- Recommended Anti-VEGF
- Laser if Anti-VEGF is unavailable

Zone 2 & 3
- Anti-VEGF or Laser or Cryotherapy according to surgeon’s discretion/availability of modality

Stage 4
- Indirect Laser then Parsplana Vitrectomy (PPV) + Fluid Air Exchange (FAE)

Stage 5
- PPV+FAE
Figure 7: Plus disease-standard reference photograph

![Stage 2 zone II](image)
![Stage 3 zone II](image)
![Stage 3](image)
![Plus disease](image)
![Stage 4B](image)
![Stage 5](image)

Figure 8: Treatment decisions depend on stage of ROP (Photo credit-Dr Oscar Onyango)

**Delivering the treatment**
Treatment for ROP is a specialised procedure that should be carried out by ophthalmologists after consideration of the recommended treatment options and counselling the parent or caregiver. Treatment can be provided in the newborn unit or in theatre, but the environment should be safe for the laser treatment or intravitreal injections. Mydriasis is required. The infant should be in a warm comfortable environment during treatment, and should be appropriately monitored by the Paediatrician or Neonatal Nurse.
The treatment is painful, hence pain monitoring and management are important during treatment. Topical anaesthesia should be given. Sedation and/or general anaesthesia are recommended where necessary, which requires the presence of an anaesthesiologist.

The procedure for administering anti-VEGF involves:
- Give the injection under sterile conditions
- Prepare the peri-orbital skin with 5% povidone-iodine
- Instil a drop of 2.5% povidone–iodine ophthalmic solution into the conjunctival sac for 1 minute; remove the excess using a sterile cotton tip applicator from the temporal lid margin
- Use callipers to determine the injection site, which is 1.5mm posterior to the limbus
- Administer the drug in a 30-32 gauge needle and 0.3ml syringe. The needle should be aimed towards the optic nerve, and the needle advanced about two thirds its length before emptying the drug
- After the injection, 2.5% povidone–iodine is placed into the conjunctival sac for 1 minute with the excess removed by a sterile cotton tip applicator from the temporal lid margin.
- The speculum is then removed from between the lids. The same procedure is repeated for the other eye.
- After the procedure, antibiotic eye drops are administered for prophylaxis for 3-4 days
- Serial eye check-ups should be done in 24 hours and then on a weekly basis.
- Indirect ophthalmoscopy is useful to identify complications of the procedure such injury to the lens, retinal tears or vitreous haemorrhage.

Follow up after treatment
Babies should be followed up regularly after any ROP treatment to check that ROP is regressing. Retreatment is indicated if there is no regression. For those that have received laser, check that treatment of the peripheral retina is complete (no skip areas / laser scars are sufficiently confluent).

The table below shows the recommended follow up schedule after treatment:

### Table 5: Follow-up after treatment

<table>
<thead>
<tr>
<th>Finding</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immature retina</td>
<td>2 weekly till maturation to zone III or 45 weeks post-menstrual age (PMA)</td>
</tr>
<tr>
<td>Type 1 ROP</td>
<td>Treat then follow up 1-2 weekly up to 45 weeks PMA or full retinal vascularization</td>
</tr>
<tr>
<td>Type 2 ROP</td>
<td>Follow up 2 weekly</td>
</tr>
<tr>
<td>APROP</td>
<td>Treat then alternate day follow up and/or further treatment.</td>
</tr>
</tbody>
</table>

Outcomes
Treatment of severe ROP is associated with better long-term visual and structural outcomes. However, in a small but significant proportion of preterm infants, the disease progresses despite treatment. In addition, treatment carries a risk of both short- and long-term ophthalmic complications.
IMPLEMENTATION OF THE GUIDELINES

The ROP screening and management team will be composed mainly of the following cadres, with the following responsibilities

**Table 6: Responsibilities of each cadre**

1. **Nurses (Neonatal nurses and Ophthalmic nurses)**
   - Prepare lists of all babies requiring ROP screening and inform the paediatrician (for babies in NBU) or the ophthalmologist (for babies in the eye clinic)
   - Counsel parents and take informed consent
   - Ensure that babies are comfortable during screening or treatment
   - Instill mydriatic eye drops as needed

2. **Neonatologist/General Paediatrician**
   - Ensure that preterm babies receive the best neonatal care to prevent ROP
   - Ensure that a clear process is in place to identify infants who require ROP screening and that the ophthalmologist is informed
   - When treatment is required, ensure that transfer or other arrangements occur in a timely manner
   - When planning hospital discharge or transfer of baby at a time when ROP screening is ongoing, communicate with the screening ophthalmologist to determine current ROP status and when the next eye examination is needed
   - Work with the Ophthalmologist to provide clinical governance for the ROP program, training, referral and implement the monitoring and evaluation framework

3. **Paediatric ophthalmologist/ VR surgeon/ General Ophthalmologist**
   - Document the findings of each retinal examination and the decision regarding treatment/further examination/appropriate timing of the action or discontinuation of screening exam
   - Schedule future contact times for ROP care
   - Ensure that a clear system is in place for the follow-up examinations of infants that need further screening or treatment at the eye clinic
   - Arrange for any longer term ophthalmic follow-up that may be required after discharge from the ROP screening program
   - Inform parents on the treatment for ROP, the risks involved and the possible outcomes, and document these discussions
   - Make timely arrangements for treatment
   - Work with the Paediatrician to provide clinical governance for the ROP program, training, referral and implement the monitoring and evaluation framework

Optimal compliance with the guidelines calls for engagement with the unique health system issues at the facility, county and country level, such as personnel and equipment challenges. There is need for advocacy for:

**New-born units:**
- Sufficient nurses to man new-born units,
- Equipment for quality new-born care (pulse oximeters, oxygen delivery system, thermal control, infection control)

**Eye care services:**
- Sufficient ophthalmologists
- Equipment for screening (BIO, scleral indenters)
- Equipment for delivering treatment (lasers, sterile facilities for anti-VEGF treatment)

**Additional interventions required are:**
- Creating awareness/training the front line health workers
- Improving obstetric care to reduce the risk of preterm birth
- Reducing the baby to nurse ratio
- Providing the necessary equipment/infrastructure to provide/monitor neonatal care
- Providing clinical guidelines and protocols
- Creating awareness among parents of preterm babies
- Engage in advocacy to address any barriers to these interventions
- Constant surveillance to ensure that no babies are missed in screening
- Close coordination between paediatric and ophthalmology teams

Dissemination of the guidelines
The guidelines will be disseminated through:
- Stakeholder consensus meetings
- Official public launch
- Print copies will be distributed to neonatal units and eye clinics
- Training workshops for the cadres involved in ROP care
- Decision algorithms posted in the newborn unit
- Electronic copies will be available for downloading on the Ministry of Health website
- Posters and fliers
- Social media
- Mass media publicity
- Publications

Monitoring and Evaluation
The main question to be addressed in the monitoring and evaluation process is ‘How well do newborn units adhere to the guidelines?’

The main process indicators are:
1. Completeness of screening programme (screening rates)
   - proportion of babies <=32 weeks GA or <1501g birthweight who receive at least one ROP eye examination
2. ROP Treatment
   - proportion of babies with any zone 1 ROP who receive treatment
3. Timing of treatment
   - proportion of babies needing ROP treatment for their ROP who are treated within 48 hours of the decision to treat being made.

The main input indicators are:
- Nurse to baby ratio in new-born units
- Number of training workshops for health workers (on the guidelines)
- Number of health workers trained
- Number of guidelines printed and disseminated

The main outcome indicators will be the visual outcome of babies with ROP, and the incidence of any adverse event.

This data will be collected monthly by a member of the care team appointed by the ophthalmologist and the paediatrician, and used to inform decision-making at the facility level and county level. At the national level the Ophthalmic Services Unit will collect quarterly data and will use it to inform the program.

Implications for future research
Local data to inform the ROP program is required, preferably before the revision of the guidelines is due. The research questions include:
- Are these screening criteria locally relevant and evidence-based?
- What is the cost of implementing the guidelines?
- How does the use of telemedicine and RetCam compare with the use of BIO in this population?
- What are the factors associated with missed screening?

Implications for policy
The main policy outputs that implementation of the guidelines will improve are access to ROP care and quality of ROP care. The demand for ROP care will also increase in the medium term as a result of the guidelines. For this reason, it is important to put in measures to increase availability of ROP services, as these are currently insufficient. Timely interventions such as staffing, training, advocacy and provision of the necessary equipment are imperative.

Revision of the guidelines
These guidelines will be reviewed within five years after the official launch.
REFERENCES


