Best Evidence Statement (BESt)

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Screening for Retinopathy of Prematurity (ROP)

Clinical Question

P (population/problem):	In premature infants
O (outcome)	to achieve best outcomes related to retinopathy of prematurity
I (intervention)	what is the optimal screening protocol for ROP?

Target Population:

Premature infants who either:

- weigh 1500 gm or less at birth, or
- weigh 1501 to 2000 gm at birth, and are gestational age 32 weeks or less

Additional infants whose actual birthweight is large for gestational age, or for whom actual gestational age is in question may be considered for ROP screening at the discretion of the neonatologist.

Recommendations

Initial referral and screening

1. It is recommended that infants in the target population
   - be identified at birth by the inpatient unit,
   - be re-identified if transferred to another hospital or unit, and
   - be referred for screening for ROP *(AAP 2006 [S,E])*.

   Note 1: Timely identification and treatment of ROP reduces the risk of visual loss *(AAP 2006 [S,E])*.
   Note 2: Among infants weighing less than 1250 gm at birth born in Cincinnati, the incidence of ROP warranting surgery is 11.1% *(Yang 2006 [D])*.

2. It is recommended that initial screening for ROP be performed at postmenstrual age 32 weeks or 5 weeks after birth, whichever comes later *(Yang 2006 abstract [D], Local Consensus [E])*.

   Note 1: Infants are at small risk for apnea, bradycardia or cyanosis during screening eye exams and may need assisted ventilation *(Local Consensus [E])*.
   Note 2: Simultaneously using both chronological age and postmenstrual age reliably identifies ROP with fewer unnecessary screenings than either method alone *(Hutchinson 1998 [D])*.
   Note 3: Infants in the target population at greatest risk for missed screening include those who are discharged from the neonatal intensive care unit (NICU) prior to an initial screening *(Attar 2005 [D])*.

3. It is recommended that appropriate ongoing parent education be initiated and documented, to include:
   - awareness of the screenings
   - notification and subsequent updates if the infant is diagnosed with ROP
   - information about ROP
   - possible consequences of serious ROP if screenings were to be missed or if a significant risk of poor visual outcome develops

   (AAP 2006 [S,E]).

   Note: A standard process which includes role responsibility for each member of the care team for communication to caregivers regarding ROP information, examination findings and timing for next screening will improve reliability of the provision of appropriate education *(Menke 2006 [E])*.

Follow up screening schedule

4. It is recommended that the timing of follow-up exams be performed based on initial findings *(AAP 2006 [S,E], AAP 2001 [S,E])*. See Table 1 for schedule of follow-up exams *(Yang 2007 abstract [D], Yang 2006 abstract [D], Wallace 1998 [D], AAP 2006 [S,E])*.

   Note 1: Infants are at small risk for apnea, bradycardia or cyanosis during screening eye exams and may need assisted ventilation *(Local Consensus [E])*.

   Note 2: The sequential nature of ROP progression is observed by follow-up retinal examinations. An ideal follow-up schedule would minimize unnecessary examinations, minimize the risk of missing progression of ROP to a severity warranting surgery, and minimize unnecessary surgery for ROP which would otherwise spontaneously regress *(AAP 2006 [S,E])*.

Table 1: Schedule for ROP screening frequency or treatment based on examination findings*

Zone	Stage / other findings	*Plus*** or No plus	Timing for follow up, treatment, or termination
Zone I	Stage 3 ROP	*Plus*	Treat
		No plus	Treat
	Stage 2 ROP (with or without popcorn)	*Plus*	Treat
		No plus	≤ 1 week
	Stage 1 ROP	*Plus*	Treat
		No plus	≤ 1 week
	immature vascularization, no ROP	question of plus	Reconfirm within 48 hours
		No plus	1 to 2 weeks
Zone II	Stage 3 ROP	*Plus*	≤ 1 week or Treat
		No plus	≤ 1 week
	Stage 2 ROP (with or without popcorn)	*Plus*	≤ 1 week or Treat
	Stage 2 ROP (new onset popcorn)	No plus	≤ 1 week
	Stage 2 ROP (without popcorn, or with old popcorn unchanging)	No plus	2 weeks
	Stage 1 ROP		
	regressing ROP (with or without popcorn)		
	immature vascularization, no ROP	No plus	2 to 3 weeks
	suspected chronic peripheral avascularity	No plus	4 to 6 weeks
	at least 45 weeks PMA with less than prethreshold ROP	No plus	Terminate follow up
Zone III	Stage 3 ROP	*Plus*	≤ 1 week or Treat
		No plus	≤ 1 week
	Stage 2 ROP (new popcorn)	No plus	≤ 1 week
	Stage 2 ROP (old popcorn or no popcorn)	No plus	2 to 3 weeks
	Stage 1 ROP	No plus	2 to 6 weeks
	regressing ROP	No plus	2 to 3 weeks
	suspected chronic peripheral avascularity	No plus	4 to 6 weeks
	immature vascularization with previous ROP	No plus	2 to 6 weeks
	immature vascularization without previous ROP and less than 35 weeks PMA		
	immature vascularization without previous ROP and at least 35 weeks PMA	No plus	Terminate follow up
	at least 45 weeks PMA with Stage 2 or less ROP		
All	full retinal vascularization	No plus	Terminate follow up
	regression of ROP or consistent evidence of chronic peripheral avascularity		
	if treated with surgery	NA	Comply with postoperative follow up per treating surgeon

*See Appendix for basic glossary of terms related to the management of retinopathy of prematurity.
**Plus disease is defined as a degree of dilation and tortuosity of the posterior retinal blood vessels as defined by a standard photograph.
(Yang 2007 abstract [D], Yang 2006 abstract [D], Wallace 1998 [D], AAP 2006 [S,E], Local Consensus [E])

5. It is recommended that effective processes be developed and implemented by the neonatal intensive care unit for initial and follow-up screenings for infants who are:
   - hospitalized on the unit
   - transferred to another institution
   - discharged to home

   (AAP 2006 [S,E]).

   Note 1: A safety-net protocol developed by the Ophthalmic Mutual Insurance Company identified three critical points for safety-net attention. These are a hospital tracking system to document the infant's ROP screening and care during inpatient stay and at disposition, a program of family education, and a program to assure appropriate follow-up care after discharge or transfer. A sample task-assignment chart may be found in their protocol *(Menke 2006 [E])*.

   Note 2: Infants in the target population at greatest risk for missed screening include those who are:
   - discharged from the neonatal intensive care unit (NICU) prior to an initial screening
   - discharged to home and do not have a follow-up appointment arranged at the time of discharge
   - discharged to home and do not have a follow-up plan recommended in the discharge summary

   (Attar 2005 [D]).

6. It is recommended that an integrated aggressive and rigid process be developed and implemented at all levels of ophthalmology clinic access (e.g. phone triage, office reception, appointment scheduling, nursing, technical, medical) to assure appropriate follow up for ambulatory patients who miss, or attempt to cancel or reschedule appointments *(AAP 2006 [S,E])*. See Table 2 to determine appropriate follow-up interval for these patients.

Table 2: Determination of urgency of follow up for missed or rescheduled appointments

Originally scheduled interval for follow-up screening	Required timeframe, from originally scheduled date, for rescheduled appointment
1 week or less	within 48 hours
2 weeks	within 4 days
3 to 6 weeks	within 7 days

(Local Consensus [E])

Initiation of treatment or termination of screenings

7. It is recommended that peripheral ablation be considered based on examination findings *(Yang 2007 abstract [D], Yang 2006 abstract [D], AAP 2006 [S,E])*. See Table 1 for treatment schedule *(Yang 2007 abstract [D], Yang 2006 abstract [D], AAP 2006 [S,E])*.

8. It is recommended that termination of screenings be considered based on examination findings *(Yang 2007 abstract [D], Yang 2006 abstract [D], AAP 2006 [S,E])*. See Table 1 for schedule for termination of screenings *(Yang 2007 abstract [D], Yang 2006 abstract [D], AAP 2006 [S,E])*.

9. It is recommended that post-acute-phase screenings for untreated infants with birth weight 1250 gm or less
   - be conducted following the last acute-phase screening, and
   - be terminated if:
     - the six months to one year post-acute phase screening is normal,
     - the infant never developed stage 3 ROP or higher, and
     - the infant has no risk factors for strabismus

   (Cryotherapy for ROP Cooperative Group 1990 [A], Quinn 1992 [C], Local Consensus [E]).

   Note: There are no studies related to appropriate post-acute-phase screenings of infants greater than 1250 gm..

References (see grading scale following references)

When using the electronic version of this document "_____☜" refers to journal articles that have a hyperlink to the PubMed abstract. A second hyperlink http://xxxxxxxxxxxxxxxxxxxxxxxxxx below the reference will access a PDF of the full article for those who have access to the CCHMC network.

1. **AAP:** American Academy of Pediatrics, Section on Ophthalmology, American Academy of Ophthalmology, American Association for Pediatric Ophthalmology and Strabismus, Screening examination of premature infants for retinopathy of prematurity.[erratum appears in Pediatrics. 2006 Sep;118(3):1324]. *Pediatrics*, 117(2): 572-6, 2006, *[S,E]* _____☜ http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthAAP2006ROPScreening.pdf.
2. **AAP:** American Academy of Pediatrics, Section on Ophthalmology, Screening examination of premature infants for retinopathy of prematurity. *Pediatrics*, 108(3): 809-11, 2001, *[S,E]* _____☜ http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthAAP2001ROPScreening.pdf.
3. **Attar, M. A.; Gates, M. R.; Iatrow, A. M.; Lang, S. W.; and Bratton, S. L.:** Barriers to screening infants for retinopathy of prematurity after discharge or transfer from a neonatal intensive care unit. *J Perinatol*, 25(1): 36-40, 2005, *[D]* _____☜ http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthAttar2005.pdf.
4. **Cryotherapy for ROP Cooperative Group:** Multicenter trial of cryotherapy for retinopathy of prematurity. One-year outcome--structure and function. Cryotherapy for Retinopathy of Prematurity Cooperative Group. *Arch Ophthalmol*, 108(10): 1408-16, 1990, *[A]* _____☜ http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthCryoROP1990.pdf.
5. **Cryotherapy for ROP Cooperative Group:** Multicenter trial of cryotherapy for retinopathy of prematurity: preliminary results. Cryotherapy for Retinopathy of Prematurity Cooperative Group. *Pediatrics*, 81(5): 697-706, 1988, *[A]* _____☜ http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthCryoROP1988.pdf.
6. **Early Treatment for ROP Cooperative Group:** Revised Indications for the Treatment of Retinopathy of Prematurity. *Arch Ophthalmol*, 121: 1684-1696, 2003, *[A]* _____☜ http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthEarlyTreatment2003ROP.pdf.
7. **Hutchinson, A. K.; Saunders, R. A.; O'Neil, J. W.; Lovering, A.; and Wilson, M. E.:** Timing of initial screening examinations for retinopathy of prematurity. *Arch Ophthalmol*, 116(5): 608-12, 1998, *[D]* _____☜ http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthHutchinson1998.pdf.
8. **ICROP:** The International Classification of Retinopathy of Prematurity revisited. *Arch Ophthalmol*, 123(7): 991-9, 2005, *[E]* _____☜ http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthICROP2005.pdf.
9. **Local Consensus:** During recommendation development timeframe. *[E]* ☜.
10. **Menke, A. M.:** Retinopathy of Prematuriy: Creating a Safety Net. *Ophthalmic Mutual Insurance Company*, 2006, *[E]* _____☜ http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthMenke2006OMIC.rtf.
11. **Quinn, G. E.; Dobson, V.; Repka, M. X.; Reynolds, J.; Kivlin, J.; Davis, B.; Buckley, E.; Flynn, J. T.; and Palmer, E. A.:** Development of myopia in infants with birth weights less than 1251 grams. The Cryotherapy for Retinopathy of Prematurity Cooperative Group. *Ophthalmology*, 99(3): 329-40, 1992, *[C]* _____☜ http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthQuinn1992.pdf.
12. **Wallace, D. K.; Kylstra, J. A.; Greenman, D. B.; and Freedman, S. F.:** Significance of isolated neovascular tufts ("popcorn") in retinopathy of prematurity. *J AAPOS*, 2(1): 52-6, 1998, *[D]* _____☜ http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthWallace1998.pdf.
13. **Yang, M. B.:** Risk-Stratification and an Alternative Screening Protocol for Reduction of ROP Screening to Detect Type 1 or Threshold ROP. *abstract*, 2007, *[D]* ☜ http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthYang2007ARVO.pdf.
14. **Yang, M. B.:** Risk Analysis and Alternative Protocols for Reduction of ROP Screening. *abstract*, 2006, *[D]* ☜ http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthYang2006ARVO.pdf.
15. **Yang, M. B.; Donovan, E. F.; and Wagge, J. R.:** Race, gender, and clinical risk index for babies (CRIB) score as predictors of severe retinopathy of prematurity. *J AAPOS*, 10(3): 253-61, 2006, *[D]* _____☜ http://groups/p2/EBC_Files/Articles_Cited_in_EPIC_Ophth/OphthYang2006.pdf.

CCHMC Evidence Grading Scale			
M	Meta-analysis or Systematic Review	O	Other evidence
A	Randomized controlled trial: large sample	S	Review article
B	Randomized controlled trial: small sample	E	Expert opinion or consensus
C	Prospective trial or large case series	F	Basic Laboratory Research
D	Retrospective analysis	Q	Decision analysis

Appendix: Basic Glossary of Terms Related to the Management of Retinopathy of Prematurity

chronic peripheral avascularity	A condition in which the outer retinal area does not grow any blood vessels over a long period of time.
plus disease	A form of ROP when the blood vessels of the retina have become enlarged and twisted, indicating a worsening of the disease *(Cryotherapy for ROP Cooperative Group 1988 [A], ICROP 2005 [E]).*
PMA (postmenstrual age)	Gestational age at birth plus chronologic age *(AAP 2006 [S,E]).* EXAMPLE: an infant born at 28 weeks of pregnancy and who is now 2 weeks old, is 30 weeks PMA
popcorn	Small isolated tufts of new blood vessels, also called isolated neovascular tufts, sometimes observed during the growth of new blood vessels in the retina of the premature infant *(Wallace 1998 [D], ICROP 2005 [E]).* This is not equivalent to stage 3 ROP.
prethreshold	A definition established by the Cryotherapy for ROP studies of the 1980's and 1990's to guide decisions regarding treatment. Prethreshold ROP is less serious than threshold ROP and includes any of the following: zone I, any stage ROP zone II, stage 2 ROP with plus disease zone II, stage 3 ROP *(Cryotherapy for ROP Cooperative Group 1988 [A]).*
regression of ROP	Spontaneous (untreated) return of the retina from ROP to normal vascularization *(AAP 2006 [S,E], ICROP 2005 [E]).*
retinal vascularization	Normal blood vessel growth in the retina of the premature infant ▪ full: growth of the blood vessels in the retina is complete; there is no more risk of ROP ▪ immature: growth of the blood vessels is not complete; development is monitored with follow-up examinations
ROP	Retinopathy of prematurity; also known as retrolental fibroplasia ▪ a condition seen only in premature infants ▪ frequent examinations are required to determine if the eyes are getting worse or better ▪ untreated severe cases are somewhat likely to go blind; surgery in severe cases often prevents blindness ▪ most cases are not severe and get better without surgery
stage 1, 2, 3	The first three stages of retinopathy of prematurity stage 1: mild stage 2: moderate stage 3: severe *(ICROP 2005 [E]).*
surgery ablation (cryotherapy, laser)	Surgical removal of the outer retinal area by cryotherapy or laser coagulation to stop progression of ROP.
threshold	A definition established by the Cryotherapy for ROP studies of the 1980's and 1990's to guide decisions regarding treatment. Threshold is a level of severity of ROP at which the risk of blindness is predicted to approach 50% *(Cryotherapy for ROP Cooperative Group 1988 [A]).*
type 1 ROP	A definition established by the Early Treatment for ROP studies of the 2000's to guide decisions regarding treatment. Type 1 ROP is more serious than type 2 and includes any of the following: zone I, any stage ROP with plus disease zone I, stage 3 ROP without plus disease zone II, stage 2 or 3 ROP with plus disease *(Early Treatment for ROP Cooperative Group 2003 [A]).*
type 2 ROP	A definition established by the Early Treatment for ROP studies of the 2000's to guide decisions regarding treatment. Type 2 ROP is less serious than type 1 and includes any of the following: Zone I, stage 1 or stage 2 ROP without plus disease Zone II, stage 3 ROP without plus disease *(Early Treatment for ROP Cooperative Group 2003 [A]).*
zone I, II, III	Areas of the retina symmetrically surrounding the optic nerve head. Zone I is the zone closest to the optic nerve. For schema drawing see *(AAP 2006 [S,E]).*

Supporting information

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Search strategy

1. Initial Search

OVID DATABASES
- MEDLINE – OVID
- Cochrane Database for Systematic Reviews (CDSR) – OVID

OVID SEARCH TERMS & MeSH TERMS
- ROP / Retinopathy of Prematurity / Retrolental Fibroplasia

OVID FILTERS
- Children
- Human
- Guidelines, Systematic Reviews, and Meta-Analyses (1996 to present)
  OR diagnosis/screening (2005 to present) [to identify articles published subsequent to

Website search of all known ophthalmology related websites – for guidelines related to ROP

2. Additional articles identified by clinicians

3. Additional articles identified from references lists of reviewed articles

Applicability issues

Outcomes that are planned to be measured include:
Of patients in the target population:
- Percent who had peripheral or total retinal detachment during the ROP screening period
- Percent who completed screening protocol
- Percent transitioning from NICU who had their first outpatient ROP check in the recommended follow-up time period
- Percent who had at least one ambulatory visit and are within the recommended follow-up time period for the next ROP check
- Percent treated within 72 hours of referral for ablation surgery for ROP

Complete operational definitions are on file.

Note

This Best Evidence Statement addresses only key points of care for the target population; it is not intended to be a comprehensive practice guideline. These recommendations result from review of literature and practices current at the time of their formulation. This Best Evidence Statement does not preclude using care modalities proven efficacious in studies published subsequent to the current revision of this document. This document is not intended to impose standards of care preventing selective variances from the recommendations to meet the specific and unique requirements of individual patients. Adherence to this Statement is voluntary. The clinician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding the priority of any specific procedure.

Reviewed by Clinical Effectiveness