Text in pink = 2021 iCROP3 changes

Text in yellow = 2018 Policy Statement**[[1]](#footnote-1)** (PS) changes

Text in green = Key PS changes

* **Follow-up after anti-VEGF injection**
* **End-of-screening criteria**
	+ **45 weeks postmenstrual age (PMA) if no Type I ROP**
	+ **65 weeks PMA if treated with anti-VEGF medication**

# [**Table 1. Which infants need an ROP screening examination**](#Table_1)

Infants meeting any of the following criteria need an exam:

* Birth weight of ≤ 1500 g (3 lbs., 4 oz.)
* Gestational age of 30 weeks or less (as defined by the attending neonatologist)
* Selected infants with a birth weight between 1500 and 2000 g (from 3 lbs., 4 oz. to 4lbs, 6 oz.) or gestational age of more than 30 weeks who are believed by their attending pediatrician or neonatologist to be at risk for ROP (such as infants with hypotension requiring inotropic support, infants who received oxygen supplementation for more than a few days, or infants who received oxygen without saturation monitoring).

**REFERENCE: ROP Screening Policy Statement # 1**. Based on Recchia, Franco and Capone, Antonio, Contemporary Understanding and Management of Retinopathy of Prematurity, *Retina* 2004; 24:283-92.

# **[Table 2. When to start ROP screening](#Table_2)**

The onset of serious ROP correlates better with postmenstrual age (gestational age at birth plus chronological age) than with postnatal age. This protocol bases the initial eye examination on postmenstrual age and chronological age. The initial eye examination should be conducted:

* By 31 weeks postmenstrual age if gestational age < 27 weeks
* At 4 weeks chronological age if gestational age ≥ 27 weeks

 **Age in weeks at initial exam**

|  |  |  |
| --- | --- | --- |
| **Gestational age at birth**  | **Postmenstrual age** | **Chronologic age** |
| 22a\* | 31 | 9 |
| 23a\* | 31 | 8 |
| 24\* | 31 | 7 |
| 25\* | 31 | 6 |
| 26 | 31 | 5 |
| 27 | 31 | 4 |
| 28 | 32 | 4 |
| 29 | 33 | 4 |
| 30 or more | 34 | 4 |
|  |  |  |

a This guideline should be considered tentative rather than evidence-based for 22-to-23-week infants owing to the small number of survivors in these gestational age categories.

**\***Some practitioners have advocated for earlier screening on the basis of speculation that treatable aggressive ROP (A-ROP) could occur before 31 weeks postmenstrual age. A-ROP[[2]](#footnote-2) is a severe form of ROP that is characterized by rapid progression to advanced states in aggressive ROP.

**REFERENCE:ROP Screening Policy Statement #2.** Based upon Reynolds JD, Dobson V, Quinn GE, et al. CRYO-ROP and LIGHT-ROP Cooperative Groups. Evidence-Based Screening Criteria for Retinopathy of Prematurity: Natural History Data from the CRYO-ROP and LIGHT-ROP Studies. *Arch Ophthalmol.* 2002; 120 (11): 1470-1476.

# **[Table 3. Follow-up schedule for ROP exams](#Table_3)**

The examining ophthalmologist should use retinal findings as classified by ICROP[[3]](#footnote-3),[[4]](#footnote-4) to determine the timing of the follow-up examinations.

* 1 week or less
	+ Zone I: Immature vascularization, no ROP
	+ Zone I: Stage 1 or 2 ROP
		- **NOTE IN PS:** Zone I, Stage 3 requires treatment, not observation
	+ Immature retina extends into posterior zone I, near the boundary of zone –zone II.
	+ Suspected presence of A-ROP (aggressive ROP)
	+ After laser photocoagulation or anti-VEGF injection to ensure that there is no need for additional laser treatment in areas where ablative treatment was not complete or additional anti-VEGF injection.
* 1 to 2 weeks
	+ Posterior zone II: Immature vascularization
	+ Zone II, Stage 2 ROP
	+ Zone I: Unequivocally regressing ROP
* 2 weeks
	+ Zone II: Stage 1 ROP
	+ Zone II: no ROP, immature vascularization
	+ Zone II: Unequivocally regressing ROP
* 2 to 3 weeks
	+ Zone III: Stage 1 or 2 ROP
	+ Zone III: Regressing ROP

**REFERENCE**:**ROP Screening Policy Statement #4**. Based on Reynolds JD, Dobson V, Quinn GE, et al. CRYO-ROP and LIGHT-ROP Cooperative Groups. Evidence-Based Screening Criteria for Retinopathy of Prematurity: Natural History Data from the CRYO-ROP and LIGHT-ROP Studies. *Arch Ophthalmol.* 2002; 120 (11): 1470-1476.

# **Table 4. When to treat ROP**

* The presence of plus disease in zones I or II suggests that peripheral ablation, rather than observation, is appropriate.\*
	+ Plus and Preplus disease[[5]](#footnote-5) “is defined by the appearance of dilation and tortuosity of retinal vessels, and preplus disease is defined by abnormal vascular dilation, tortuosity insufficient for plus disease or both.”
	+ “These changes should be assessed by vessels within zone 1, rather than from only vessels within the field of narrow-angle photographs and rather than from the number of quadrants of abnormality.”
* Treatment should be initiated for the following retinal findings that characterize Type 1 ROP:
	+ Zone I ROP: any stage with plus disease
	+ Zone I ROP: stage 3, no plus disease
	+ Zone II ROP: stage 2 or 3 with plus disease
* Treatment should generally be accomplished, when possible, within 72 hours of determination of treatable disease to minimize the risk of retinal detachment.
* Consideration may be given to treatment of infants with zone I stage 3+ ROP with intravitreal injection of bevacizumab.#
	+ Bevacizumab and other anti-VEGF substances are not approved by the US Food and Drug Administration for the treatment of ROP.
	+ Treatment should only be administered after obtaining detailed informed consent, because there remain unanswered questions involving dosage, timing, safety, and visual and systemic outcomes. Studies have yielded contrary findings on the increased incidence of neurodevelopmental problems, including severe cerebral palsy, hearing loss, and bilateral blindness.
	+ Infants treated with bevacizumab should be monitored closelyuntil at least 65 weeks postmenstrual age
	+ Longer follow-up is required because recurrence occurs considerably later (16 ± 4.6 weeks vs 6.2 ± 5.7 weeks) than after laser therapy. There are reports of recurrence requiring retreatment as late as 65 to 70 weeks postmenstrual age.
	+ The timeframe of highest disease reactivation is between 45 and 55 weeks.
* Follow up is recommended in 3 to 7 days after laser photocoagulation or anti-VEGF injection to ensure that there is no need for additional laser treatment in areas where ablative treatment was not complete or for additional anti-VEGF injection.

**REFERENCE:ROP Screening Policy Statement #4 based upon:**

\* Early Treatment for Retinopathy of Prematurity Cooperative Group. Revised Indications for the Treatment of Retinopathy of Prematurity. Results of the Early Treatment for Retinopathy of Prematurity Randomized Trial. *Arch Ophthalmol.* 2003; 121:1684-1694.

* # Mintz-Hittner HA, Kennedy KA, Chuang AZ; BEAT-ROP Cooperative Group. Efficacy of intravitreal bevacizumab for stage 3+ retinopathy of prematurity. *N Engl J Med*. 2011; 364(7):603–615.

# **Table 5. When to stop ROP screening**

**Per the Policy Statement, one exam is sufficient only if it unequivocally shows the retina to be fully vascularized in both eyes.**

The conclusion of acute-retinal-screening examinations should be based on age and retinal ophthalmoscopic findings. Findings that suggest that examinations can be terminated include:

* Full retinal vascularization in close proximity to the ora serrata for 360°--that is, the normal distance found in mature retina between the end of vascularization and the ora serrata.
* Zone III retinal vascularization attained without previous zone I or II ROP
	+ If there is examiner doubt about the zone or if the postmenstrual age is less than 35 weeks, confirmatory examinations may be warranted.
* Postmenstrual age of 45 weeks: No type 1 ROP or worse is present, and no anti-VEGF treatment
	+ Type 1 ROP disease (previously called “pretheshold”) defined as:
		- Stage 3 ROP in zone II
		- Any ROP in zone I
* Postmenstrual age of 65 weeks: Infants treated with anti-VEGF
	+ Follow closely until at least 65 weeks postmenstrual age
	+ Particularly close follow-up is needed during the time of highest risk for disease reactivation (45 to 55 weeks PMA)
	+ Care must be taken to be sure that there is no abnormal vascular tissue present that is capable of reactivation and progression in Zone II or III
	+ Full retinal vascularization should be the criterion for all infants treated solely with anti-VEGF medication.
	+ Full retinal vascularization is not always achieved in infants treated with anti-VEGF alone.
	+ If there is not full retinal vascularization at 65 weeks PMA, rely upon prolonged observation, clinical judgment, and evolving criteria for termination of exams or a need for further treatment.
* Regression of ROP (see ICROP)[[6]](#footnote-6)
	+ Care must be taken to be sure that there is no abnormal vascular tissue present that is capable of reactivation and progression in zone II or III.
	+ Anti-VEGF has presented new challenges. Updated definitions of regression and reactivation exist.
	+ “Regression can be complete or incomplete. Location and extent of peripheral avascular retina (PAR) should be documented.”

**REFERENCE:ROP Screening Policy Statement # 4.** Based upon Reynolds JD, Dobson V, Quinn GE, et al. CRYO-ROP and LIGHT-ROP Cooperative Groups. Evidence-Based Screening Criteria for Retinopathy of Prematurity: Natural History Data From the CRYO-ROP and LIGHT-ROP.*Arch Ophthalmol.* 2002; 120 (11): 1470-1476.

1. Fierson WM. “Screening Examination of Premature Infants for Retinopathy of Prematurity.” Policy Statement (PS) issued by the American Academy of Pediatrics (AAP) Section on Ophthalmology, the American Association for Pediatric Ophthalmology and Strabismus (AAPOS), and the American Association of Certified Orthoptists. Originally issued in 1997 and updated in 2001, 2005, 2006, and 2018; current version published in *Pediatrics* (Volume 142, Number 6, 2018, at <http://pediatrics.aappublications.org/content/early/2018/11/21/peds.2018-3061>. This document refers to recommendations based upon the numbers assigned to them in the PS. [↑](#footnote-ref-1)
2. Chang MF, Quinn GE, Fielder AR, Wu WC, Zhao P, Zin A, *et al*. International Classification of Retinopathy of Prematurity, Third Edition. *Ophthalmology*. 2021;128(10):E51-E68. Available at: <https://doi.org/10.1016/j.ophtha.2021.05.031> (Accessed: 3/10/22) [↑](#footnote-ref-2)
3. Chang MF, Quinn GE, Fielder AR, Wu WC, Zhao P, Zin A, *et al*. International Classification of Retinopathy of Prematurity, Third Edition. *Ophthalmology*. 2021;128(10):E51-E68. Available at: <https://doi.org/10.1016/j.ophtha.2021.05.031> (Accessed: 3/10/22) [↑](#footnote-ref-3)
4. The International Classification of Retinopathy of Prematurity Revisited. International Committee for the Classification of Retinopathy of Prematurity. *Arch Ophthalmol* 2005. 123: 991-999. Available at <https://jamanetwork.com/journals/jamaophthalmology/fullarticle/417157>. [↑](#footnote-ref-4)
5. Chang MF, Quinn GE, Fielder AR, Wu WC, Zhao P, Zin A, *et al*. International Classification of Retinopathy of Prematurity, Third Edition. *Ophthalmology*. 2021;128(10):E51-E68. Available at: <https://doi.org/10.1016/j.ophtha.2021.05.031>(Accessed: 3/10/22) [↑](#footnote-ref-5)
6. Chang MF, Quinn GE, Fielder AR, Wu WC, Zhao P, Zin A, *et al*. International Classification of Retinopathy of Prematurity, Third Edition. *Ophthalmology*. 2021;128(10):E51-E68. Available at: <https://doi.org/10.1016/j.ophtha.2021.05.031> (Accessed: 3/10/22) [↑](#footnote-ref-6)