Q

- Patients with a PDA are at increased risk of ROP
Patients with a PDA are at increased risk of ROP True

Birth weight is a greater predictor for ROP than O2 exposure True; LBW is #1 risk factor

Exposure to ambient light has a small but significant effect on ROP development False; the Light-ROP study found no relationship

Infants with a R→L cardiac shunt (and subsequent low O2 sat) are protected from ROP False, and this provides strong evidence that excess PaO2 is not causative

Whites have a greater risk of ROP than blacks True

The sexes have roughly equal ROP incidence rates False; ROP is significantly more common in males

Once the ROP process starts, it usually progresses to an advanced level False; roughly 80% of ROP arrests spontaneously, without significant sequelae
Patients with a **PDA** are at increased risk of ROP **True**

*Why would a Personal Digital Assistant put someone at increased risk of ROP?*

In this context, PDA stands for **quack**
Patients with a PDA are at increased risk of ROP True

Why would a Personal Digital Assistant put someone at increased risk of ROP? In this context, PDA stands for patent ductus arteriosus
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(low birth weight)
Q

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ROP: True or false
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Note the pattern…
Q

- Patients with a PDA are at increased risk of ROP True
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OK, but which variable is the best predictor of when an infant will develop significant ROP?
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Can you be more specific? That is, which age is the best predictor--postmenstrual, gestational or chronologic? (And what are these different ages anyway?)
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**Q/A**

**ROP: True or false**

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Infant age

*Can you be more specific? That is, which age is the best predictor--postmenstrual, gestational or chronologic? (And what are these different ages anyway?)*

Development of significant ROP correlates best with the infant’s postmenstrual age.

Postmenstrual age equals one way of measuring infant age + another age.
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Postmenstrual age equals gestational age at birth + chronologic (postnatal) age. Research indicates that infants rarely develop significant ROP before postmenstrual age **31 weeks**. Thus, screening exams before this age have very low yield, and needlessly stress the infant.

*What does this indicate about the relationship between timing of ROP development and an infant’s chronologic age?*

It indicates that **younger preemies take longer to develop significant ROP than do older preemies.**
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**What does the term Everest in utero have to do with ROP?**

The term highlights the fact that the gestational environment is profoundly hypoxic compared to life ex utero. Oxygen levels in utero are about what they are at the 26,000 ft level on Everest—the so-called 'death zone.' It is under these $O_2$ conditions that the retinal vasculature is supposed to develop. What does this suggest about premature birth and the pathophysiology of ROP? When the preemie experiences atmospheric $O_2$ levels, further development of the retinal vasculature is impaired. This leaves more peripheral retinal areas with inadequate oxygenation. As they mature, these hypoxic retinal cells do what hypoxic retinal cells tend to do—they produce VEGF. The result is the now-familiar cascade of neovascularization, bleeding, and tractional retinal detachment.
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\textit{What does this suggest about premature birth and the pathophysiology of ROP?}

When the preemie experiences normal ex utero O₂ levels, further development of the retinal vasculature is suppressed. This leaves more peripheral retinal areas with inadequate oxygenation. As they mature, these hypoxic retinal cells do what hypoxic retinal cells tend to do—they produce VEGF. The result is the now-familiar cascade of neovascularization, bleeding, and tractional retinal detachment.
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In other words, ROP is a **biphasic disease:**

(What happens first?)

strong evidence that excess $P_a O_2$ is not causative

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In other words, ROP is a biphasic disease:
--First, premature birth (+/- supplemental $O_2$) exposes the immature retina to vastly higher-than-normal O2 levels, leading to downregulation of VEGF. This causes the immature retinal vascular tree to stop proliferating.

What happens later?)

strong evidence that excess $P_aO_2$ is not causative

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In other words, ROP is a **biphasic disease**:
--First, premature birth (+/- supplemental O₂) exposes the immature retina to vastly higher-than-normal O₂ levels, leading to **downregulation of** VEGF. This causes the immature retinal vascular tree to **stop proliferating**.
--Later, the (unvascularized) peripheral retina becomes metabolically active. The lack of vascularization renders the peripheral retina hypoxic, leading to **upregulation of** VEGF. This causes the vascular tree to **start proliferating again**.

What does the term **Everest in utero** have to do with ROP?
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ROP classification: Based on pathology (called... criterion), another criterion (called... criterion), and another criterion (two words) status:
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
  - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
  - Zone 3: Residual crescent anterior to Zone 2

- **Appearance**
  - Stage 1: Demarcation line
  - Stage 2: Elevated line ('ridge') +/- small tufts of neo
  - Stage 3: Ridge with extensive neo growing through ILM
  - Stage 4: Subtotal RD
  - Stage 5: Total RD
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - Zone 1:
  - Zone 2
  - Zone 3
**ROP classification**: Based on pathology **location** (zone), **appearance** (stage), and **plus** disease status:

- **Location**
  - **Zone 1**: Circle around ONH w/ radius 2x disc-fovea distance
  - **Zone 2**
  - **Zone 3**

(ONH = optic nerve head)
**ROP classification**: Based on pathology location, appearance, and plus disease status:

- **Location**
  - **Zone 1**: Circle around ONH w/ radius 2x disc-fovea distance
  - **Zone 2**: 
  - **Zone 3**

- **Stage 1**: Demarcation line
- **Stage 2**: Elevated line ('ridge') +/- small tufts of neo
- **Stage 3**: Ridge with extensive neo growing through ILM
- **Stage 4**: Subtotal RD
- **Stage 5**: Total RD
• **ROP classification**: Based on pathology **location** (zone), **appearance** (stage), and **plus disease** status:

  - **Location**
    - **Zone 1**: Circle around ONH w/ radius 2x disc-fovea distance
    - **Zone 2**: Edge of Zone 1 to nasal ora, and around temporally
    - **Zone 3**
ROP classification: Based on pathology **location** (zone), **appearance** (stage), and **plus disease** status:

- **Location**
  - **Zone 1:** Circle around ONH w/ radius 2x disc-fovea distance
  - **Zone 2:** Edge of Zone 1 to nasal ora, and around temporally
  - **Zone 3:**

![Diagram of ROP classification zones](image-url)
• **ROP classification**: Based on pathology **location** (zone), **appearance** (stage), and **plus disease** status:

  - **Location**
    - **Zone 1**: Circle around ONH w/ radius 2x disc-fovea distance
    - **Zone 2**: Edge of Zone 1 to nasal ora, and around temporally
    - **Zone 3**: Residual crescent anterior to Zone 2
**ROP classification**: Based on pathology **location (zone)**, **appearance (stage)**, and **plus disease** status:

**Location**
- **Zone 1**: Circle around ONH w/ radius 2x disc-fovea distance
- **Zone 2**: Edge of Zone 1 to nasal ora, and around temporally
- **Zone 3**: Residual crescent anterior to Zone 2

**Appearance**
- **Stage 1**
- **Stage 2**
- **Stage 3**
- **Stage 4**
- **Stage 5**
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - **Zone 1**: Circle around ONH w/ radius 2x disc-fovea distance
  - **Zone 2**: Edge of Zone 1 to nasal ora, and around temporally
  - **Zone 3**: Residual crescent anterior to Zone 2

- **Appearance**
  - **Stage 1**: Demarcation line
  - **Stage 2**
  - **Stage 3**
  - **Stage 4**
  - **Stage 5**
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - *Zone 1*: Circle around ONH w/ radius 2x disc-fovea distance
  - *Zone 2*: Edge of Zone 1 to nasal ora, and around temporally
  - *Zone 3*: Residual crescent anterior to Zone 2

- **Appearance**
  - *Stage 1*: Demarcation line
  - *Stage 2*
  - *Stage 3*
  - *Stage 4*
  - *Stage 5*
**ROP classification**: Based on pathology **location** (zone), **appearance** (stage), and **plus disease** status:

- **Location**
  - **Zone 1**: Circle around ONH w/ radius 2x disc-fovea distance
  - **Zone 2**: Edge of Zone 1 to nasal ora, and around temporally
  - **Zone 3**: Residual crescent anterior to Zone 2

- **Appearance**
  - **Stage 1**: Demarcation line
  - **Stage 2**: Elevated line (‘ridge’) +/- small tufts of neo
  - **Stage 3**: Ridge with extensive neo growing through ILM
  - **Stage 4**: Subtotal RD
  - **Stage 5**: Total RD

(neo = short for ‘neovascularization’)

[Images of retinal images are shown, with one labeled CRYO-ROP and the other labeled Processed Image.]
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
  - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
  - Zone 3: Residual crescent anterior to Zone 2

- **Appearance**
  - Stage 1: Demarcation line
  - Stage 2: Elevated line (‘ridge’) +/- small tufts of neo
  - Stage 3: Ridge with extensive neo growing through ILM
  - Stage 4
  - Stage 5
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
  - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
  - Zone 3: Residual crescent anterior to Zone 2

- **Appearance**
  - Stage 1: Demarcation line
  - Stage 2: Elevated line (‘ridge’) +/- small tufts of neo
  - Stage 3: Ridge with extensive neo growing through ILM

(ILM = internal limiting membrane)
**ROP classification**: Based on pathology **location** (zone), **appearance** (stage), and **plus disease** status:

- **Location**
  - **Zone 1**: Circle around ONH w/ radius 2x disc-fovea distance
  - **Zone 2**: Edge of Zone 1 to nasal ora, and around temporally
  - **Zone 3**: Residual crescent anterior to Zone 2

- **Appearance**
  - **Stage 1**: Demarcation line
  - **Stage 2**: Elevated line ('ridge') +/- small tufts of neo
  - **Stage 3**: Ridge with extensive neo growing through ILM
  - **Stage 4**: 
  - **Stage 5**
**ROP classification**: Based on pathology **location (zone)**, **appearance (stage)**, and **plus disease status**:

- **Location**
  - **Zone 1**: Circle around ONH w/ radius 2x disc-fovea distance
  - **Zone 2**: Edge of Zone 1 to nasal ora, and around temporally
  - **Zone 3**: Residual crescent anterior to Zone 2

- **Appearance**
  - **Stage 1**: Demarcation line
  - **Stage 2**: Elevated line (‘ridge’) +/- small tufts of neo
  - **Stage 3**: Ridge with extensive neo growing through ILM
  - **Stage 4**: Subtotal RD
  - **Stage 5**: (RD = retinal detachment)
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

### Location
- **Zone 1**: Circle around ONH w/ radius 2x disc-fovea distance
- **Zone 2**: Edge of Zone 1 to nasal ora, and around temporally
- **Zone 3**: Residual crescent anterior to Zone 2

### Appearance
- **Stage 1**: Demarcation line
- **Stage 2**: Elevated line (‘ridge’) +/- small tufts of neo
- **Stage 3**: Ridge with extensive neo growing through ILM
- **Stage 4**: Subtotal RD
- **Stage 5**

Stage 4 is divided into two substages:
4a: RD with macula…
4b: RD with macula…
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
  - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
  - Zone 3: Residual crescent anterior to Zone 2

- **Appearance**
  - Stage 1: Demarcation line
  - Stage 2: Elevated line (‘ridge’) +/- small tufts of neo
  - Stage 3: Ridge with extensive neo growing through ILM
  - Stage 4: Subtotal RD
  - Stage 5

Stage 4 is divided into two substages:
- 4a: RD with macula…on
- 4b: RD with macula…off
**ROP classification**: Based on pathology location, appearance, and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
  - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
  - Zone 3: Residual crescent anterior to Zone 2

- **Appearance**
  - Stage 1: Demarcation line
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  - Stage 4: Subtotal RD
  - Stage 5: Total RD
**ROP classification**: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - **Zone 1**: Circle around ONH w/ radius 2x disc-fovea distance
  - **Zone 2**: Edge of Zone 1 to nasal ora, and around temporally
  - **Zone 3**: Residual crescent anterior to Zone 2

- **Appearance**
  - **Stage 1**: Demarcation line
  - **Stage 2**: Elevated line (‘ridge’) +/- small tufts of neo
  - **Stage 3**: Ridge with extensive neo growing through ILM
  - **Stage 4**: Subtotal RD
  - **Stage 5**: Total RD
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

Location
- Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
- Zone 2: Edge of Zone 1 to nasal ora, and around temporally
- Zone 3: Residual crescent anterior to Zone 2

Appearance
- Stage 1: Demarcation line
- Stage 2: Elevated line (‘ridge’) +/- small tufts of neo
- Stage 3: Ridge with extensive neo growing through ILM
- Stage 4: Subtotal RD
- Stage 5: Total RD

What description is usually applied to the Stage 5 total RD?
**ROP classification**: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
  - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
  - Zone 3: Residual crescent anterior to Zone 2

- **Appearance**
  - Stage 1: Demarcation line
  - Stage 2: Elevated line (‘ridge’) +/- small tufts of neo
  - Stage 3: Ridge with extensive neo growing through ILM
  - Stage 4: Subtotal RD
  - Stage 5: **Total RD**

**What description is usually applied to the Stage 5 total RD?**
*It is described as a ‘funnel’ RD*
ROP stages
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
  - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
  - Zone 3: Residual crescent anterior to Zone 2

- **Appearance**
  - Stage 1: Demarcation line
  - Stage 2: Elevated line (‘ridge’) +/- small tufts of neo
  - Stage 3: Ridge with extensive neo growing through ILM
  - Stage 4: Subtotal RD
  - Stage 5: Total RD

What are the three basic types of retinal detachment (generally speaking; not specific to ROP)?
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
  - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
  - Zone 3: Residual crescent anterior to Zone 2

- **Appearance**
  - Stage 1: Demarcation line
  - Stage 2: Elevated line ('ridge') +/- small tufts of neo
  - Stage 3: Ridge with extensive neo growing through ILM
  - Stage 4: Subtotal RD
  - Stage 5: Total RD

What are the three basic types of retinal detachment (generally speaking; not specific to ROP)?
Rhegmatogenous, exudative and tractional
ROP classification: Based on pathology location, appearance (stage), and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
  - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
  - Zone 3: Residual crescent anterior to Zone 2

- **Appearance**
  - Stage 1: Demarcation line
  - Stage 2: Elevated line (‘ridge’) +/- small tufts of neo
  - Stage 3: Ridge with extensive neo growing through ILM
  - Stage 4: Subtotal RD
  - Stage 5: Total RD

What are the three basic types of retinal detachment (generally speaking; not specific to ROP)?
Rhegmatogenous, exudative and tractional

Which sort of RD occurs in ROP?
Tractional RD (TRD)
**ROP classification**: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
  - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
  - Zone 3: Residual crescent anterior to Zone 2

- **Appearance**
  - Stage 1: Demarcation line
  - Stage 2: Elevated line (‘ridge’) +/- small tufts of neo
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What are the three basic types of retinal detachment (generally speaking; not specific to ROP)?
Rhegmatogenous, exudative and tractional

*Which sort of RD occurs in ROP?*
Tractional RD (TRD)
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

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  - Stage 3: Ridge with extensive neo growing through ILM
  - Stage 4: Subtotal RD
  - Stage 5: Total RD

- **Presence/absence of plus disease**
  - *Plus* disease = dilated/tortuous retinal vessels
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
  - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
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- **Appearance**
  - Stage 1: Demarcation line
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  - Stage 3: Ridge with extensive neo growing through ILM
  - Stage 4: Subtotal RD
  - Stage 5: Total RD

- **Presence/absence of plus disease**
  - Plus disease = Dilated/tortuous retinal vessels
ROP: *Plus* disease
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - **Zone 1**: Circle around ONH w/ radius 2x disc-fovea distance
  - **Zone 2**: Edge of Zone 1 to nasal ora, and around temporally
  - **Zone 3**: Residual crescent anterior to Zone 2

- **Appearance**
  - **Stage 1**: Demarcation line
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  - **Stage 3**: Ridge with extensive neo growing through ILM
  - **Stage 4**: Subtotal RD
  - **Stage 5**: Total RD

- **Presence/absence of plus disease**
  - *Plus disease* = Dilated/tortuous retinal vessels

**Q** How dilated/tortuous do the vessels need to be to qualify as plus disease?
**ROP classification**: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
  - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
  - Zone 3: Residual crescent anterior to Zone 2

- **Appearance**
  - Stage 1: Demarcation line
  - Stage 2: Elevated line (‘ridge’) +/- small tufts of neo
  - Stage 3: Ridge with extensive neo growing through ILM
  - Stage 4: Subtotal RD
  - Stage 5: Total RD

- **Presence/absence of plus disease**
  - *Plus* disease = **Dilated/tortuous** retinal vessels

*How dilated/tortuous do the vessels need to be to qualify as plus disease?*

*A standardized photo exists indicating the ‘official’ amount needed*
- **ROP classification**: Based on pathology location (zone), appearance (stage), and plus disease status:
  
  - **Location**
    - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
    - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
    - Zone 3: Residual crescent anterior to Zone 2
  
  - **Appearance**
    - Stage 1: Demarcation line
    - Stage 2: Elevated line (‘ridge’) +/- small tufts of neo
    - Stage 3: Ridge with extensive neo growing through ILM
    - Stage 4: Subtotal RD
    - Stage 5: Total RD
  
  - **Presence/absence of plus disease**
    - *Plus* disease = Dilated/tortuous retinal vessels

How dilated/tortuous do the vessels need to be to qualify as plus disease? A standardized photo exists indicating the ‘official’ amount needed

What if the vessels are definitely dilated/tortuous, but not to the extent indicated in the standardized photo?
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
  - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
  - Zone 3: Residual crescent anterior to Zone 2

- **Appearance**
  - Stage 1: Demarcation line
  - Stage 2: Elevated line (‘ridge’) +/- small tufts of neo
  - Stage 3: Ridge with extensive neo growing through ILM
  - Stage 4: Subtotal RD
  - Stage 5: Total RD

- **Presence/absence of plus disease**
  - *Plus* disease = Dilated/tortuous retinal vessels

How dilated/tortuous do the vessels need to be to qualify as plus disease?
A standardized photo exists indicating the ‘official’ amount needed

What if the vessels are definitely dilated/tortuous, but not to the extent indicated in the standardized photo? This is referred to as **Pre-Plus disease**
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
  - Zone 2: Edge of Zone 1 to nasal ora, and around temporally
  - Zone 3: Residual crescent anterior to Zone 2

- **Appearance**
  - Stage 1: Demarcation line
  - Stage 2: Elevated line (‘ridge’) +/- small tufts of neo
  - Stage 3: Ridge with extensive neo growing through ILM
  - Stage 4: Subtotal RD
  - Stage 5: Total RD

- **Presence/absence of plus disease**
  - Plus disease = Dilated/tortuous retinal vessels
    - Indicates arteriovenous shunting is taking place
**ROP classification**: Based on pathology **location (zone)**, **appearance (stage)**, and **plus disease** status:

- **Location**
  - **Zone 1**: Circle around ONH w/ radius 2x disc-fovea distance
  - **Zone 2**: Edge of Zone 1 to nasal ora, and around temporally
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- **Appearance**
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  - **Stage 4**: Subtotal RD
  - **Stage 5**: Total RD

- **Presence/absence of plus disease**
  - **Plus disease** = Dilated/tortuous retinal vessels
    - Indicates arteriovenous shunting is taking place
ROP classification: Based on pathology location (zone), appearance (stage), and plus disease status:

- **Location**
  - Zone 1: Circle around ONH w/ radius 2x disc-fovea distance
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  - Stage 3: Ridge with extensive neo growing through ILM
  - Stage 4: Subtotal RD
  - Stage 5: Total RD

- **Presence/absence of plus disease**
  - Plus disease = Dilated/tortuous retinal vessels
    - Indicates arteriovenous shunting is taking place
    - Strong indicator that disease is occurring
• **ROP classification:** Based on pathology **location (zone), appearance (stage),** and **plus disease** status:

  ● **Location**
    - **Zone 1:** Circle around ONH w/ radius 2x disc-fovea distance
    - **Zone 2:** Edge of Zone 1 to nasal ora, and around temporally
    - **Zone 3:** Residual crescent anterior to Zone 2

  ● **Appearance**
    - **Stage 1:** Demarcation line
    - **Stage 2:** Elevated line (‘ridge’) +/- small tufts of neo
    - **Stage 3:** Ridge with extensive neo growing through ILM
    - **Stage 4:** Subtotal RD
    - **Stage 5:** Total RD

  ● **Presence/absence of plus disease**
    - **Plus disease** = **Dilated/tortuous** retinal vessels
      - Indicates **arteriovenous shunting** is taking place
      - Strong indicator that disease **progression** is occurring
This is the **outdated** definition of when to treat ROP (so-called *Threshold disease*):

- 5 contiguous clock hours or 8 noncontiguous hours of Stage 3 disease (or worse) in Zone I or II, associated with *plus disease*
This is the *outdated* definition of when to treat ROP (so-called *Threshold disease*):

- 5 contiguous clock hours or 8 noncontiguous hours of Stage 3 disease (or worse) in Zone I or II, associated with *plus disease*

What was the name of the study from which these (now considered outdated) treatment guidelines were developed?
This is the **outdated** definition of when to treat ROP (so-called *Threshold disease*):

- 5 contiguous clock hours or 8 noncontiguous hours of Stage 3 disease (or worse) in Zone I or II, associated with **plus disease**

*What was the name of the study from which these (now considered outdated) treatment guidelines were developed?*

The **CRYO-ROP** study
This is the outdated definition of when to treat ROP (so-called Threshold disease):

- 5 contiguous clock hours or 8 noncontiguous hours of Stage 3 disease (or worse) in Zone I or II, associated with plus disease

What’s wrong with these criteria for treatment? Why don’t we use them anymore?
This is the *outdated* definition of when to treat ROP (so-called *Threshold disease*):

- 5 contiguous clock hours or 8 noncontiguous hours of Stage 3 disease (or worse) in Zone I or II, associated with plus disease

*What’s wrong with these criteria for treatment? Why don’t we use them anymore?* Research indicated that less than 13% of children treated via these criteria went on to have 20/40 or better vision in treated eyes! That’s not a very good outcome, so these criteria have been revised.
ROP: Treatment Considerations

- This is the **outdated** definition of when to treat ROP (so-called *Threshold disease*):
  - 5 contiguous clock hours or 8 noncontiguous hours of Stage 3 disease (or worse) in Zone I or II, associated with plus disease

*What’s wrong with these criteria for treatment? Why don’t we use them anymore?* 
Research indicated that less than 13% of children treated via these criteria went on to have 20/40 or better vision in treated eyes! That’s not a very good outcome, so these criteria have been revised.

*What are the new criteria?*
Treatment is indicated if the ROP meets one of three criteria:

1. or
2. or
3.
This is the **outdated** definition of when to treat ROP (so-called *Threshold disease*):
- 5 contiguous clock hours or 8 noncontiguous hours of Stage 3 disease (or worse) in Zone I or II, associated with plus disease

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*What’s wrong with these criteria for treatment? Why don’t we use them anymore?* Research indicated that less than 13% of children treated via these criteria went on to have 20/40 or better vision in treated eyes! That’s not a very good outcome, so these criteria have been revised.

*What are the new criteria?* Treatment is indicated if the ROP meets one of three criteria:

1. Zone 1, any Stage, with Plus disease
   *or*
2. Zone 1, Stage 3, with or without Plus disease
   *or*
3. Zone 2, Stage 2 or 3, with Plus disease
This is the outdated definition of when to treat ROP (so-called Threshold disease):
- 5 contiguous clock hours or 8 noncontiguous hours of Stage 3 disease (or worse) in Zone I or II, associated with plus disease

What’s wrong with these criteria for treatment? Why don’t we use them anymore? Research indicated that less than 13% of children treated via these criteria went on to have 20/40 or better vision in treated eyes! That’s not a very good outcome, so these criteria have been revised.

What are the new criteria?
Treatment is indicated if the ROP meets one of three criteria:

1. Zone 1, any Stage, with Plus disease
2. Zone 1, Stage 3, with or without Plus disease
3. Zone 2, Stage 2 or 3, with Plus disease

What was the name of the study from which these treatment guidelines were developed?
This is the *outdated* definition of when to treat ROP (so-called *Threshold disease*):

- 5 contiguous clock hours or 8 noncontiguous hours of Stage 3 disease (or worse) in Zone I or II, associated with plus disease.

What's wrong with these criteria for treatment? Why don't we use them anymore? Research indicated that less than 13% of children treated via these criteria went on to have 20/40 or better vision in treated eyes! That's not a very good outcome, so these criteria have been revised.

What are the new criteria?

**Treatment is indicated if the ROP meets one of three criteria:**

1. Zone 1, any Stage, with Plus disease  
   or  
2. Zone 1, Stage 3, with or without Plus disease  
   or  
3. Zone 2, Stage 2 or 3, with Plus disease

What was the name of the study from which these treatment guidelines were developed? The **ET-ROP** (Early Treatment of Retinopathy of Prematurity) study.
ROP: Treatment Considerations

This is the outdated definition of when to treat ROP (so-called Threshold disease):
- 5 contiguous clock hours or 8 noncontiguous hours of Stage 3 disease (or worse) in Zone I or II, associated with plus disease

The motivating factor behind the ET-ROP was to see whether earlier intervention could improve upon these dismal results.

What’s wrong with these criteria for treatment? Why don’t we use them anymore?
Research indicated that less than 13% of children treated via these criteria went on to have 20/40 or better vision in treated eyes! That’s not a very good outcome, so these criteria have been revised.

What are the new criteria?
Treatment is indicated if the ROP meets one of three criteria:

1. Zone 1, any Stage, with Plus disease (‘Rush disease’) or
2. Zone 1, Stage 3, with or without Plus disease or
3. Zone 2, Stage 2 or 3, with Plus disease
This is the *outdated* definition of when to treat ROP (so-called *Threshold disease*):

- 5 contiguous clock hours or 8 noncontiguous hours of Stage 3 disease (or worse) in Zone I or II, associated with plus disease.

What’s wrong with these criteria for treatment? Why don’t we use them anymore? Research indicated that less than 13% of children treated via these criteria went on to have 20/40 or better vision in treated eyes! That’s not a very good outcome, so these criteria have been revised.

What are the new criteria?

**Treatment is indicated if the ROP meets one of three criteria:**

1. Zone 1, any Stage, with Plus disease
   or
2. Zone 1, Stage 3, with or without Plus disease
   or
3. Zone 2, Stage 2 or 3, with Plus disease

*Per the ET-ROP, disease meeting these criteria are known as what ‘type’ of ROP?*
This is the outdated definition of when to treat ROP (so-called Threshold disease):
- 5 contiguous clock hours or 8 noncontiguous hours of Stage 3 disease (or worse) in Zone I or II, associated with plus disease

What’s wrong with these criteria for treatment? Why don’t we use them anymore? Research indicated that less than 13% of children treated via these criteria went on to have 20/40 or better vision in treated eyes! That’s not a very good outcome, so these criteria have been revised.

What are the new criteria?

**Treatment is indicated if the ROP meets one of three criteria:**

1. Zone 1, any Stage, with Plus disease
2. Zone 1, Stage 3, with or without Plus disease
3. Zone 2, Stage 2 or 3, with Plus disease

Per the ET-ROP, disease meeting these criteria are known as what ‘type’ of ROP?
Type I
This is the outdated definition of when to treat ROP (so-called Threshold disease):

- 5 contiguous clock hours or 8 noncontiguous hours of Stage 3 disease (or worse) in Zone I or II, associated with plus disease

Note that disease meeting ET-ROP criteria for treatment would not have met threshold under CRYO-ROP criteria. For this reason, the new criteria are sometimes referred to as ‘pre-threshold Type I ROP’

What are the new criteria?

Treatment is indicated if the ROP meets one of three criteria:

1. Zone 1, any Stage, with Plus disease
   or
2. Zone 1, Stage 3, with or without Plus disease
   or
3. Zone 2, Stage 2 or 3, with Plus disease

Per the ET-ROP, disease meeting these criteria are known as what ‘type’ of ROP?
Type I
What's wrong with these criteria for treatment? Why don't we use them anymore?

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By what special name is ‘Zone 1 + Plus disease’ known?

Rush disease

Why is it called Rush disease?

Because these eyes are at especially high risk of very rapid progression to TRD

Which infants are at particular risk for developing Rush disease?

Those weighing under 1000 grams
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Another term is used for aggressive posterior ROP--what is it?

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Another term is used for aggressive posterior ROP--what is it? It is called **Aggressive Posterior ROP (APROP)**

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**Is APROP simply another name for Rush disease?**
While the terms are sometimes used interchangeably, the clinical appearance and behavior of APROP can differ from that of Rush dz. APROP is characterized by the presence of neovascular fronds lying flat on the retinal surface (ie, without a ridge) in Zone 1 or posterior Zone 2. Active A-V shunting is the rule.

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1) Direct progression from Stage 1 to Stage 3 disease
2) Very rapid progression (Stage 1 to 3 or even 4 in a matter of days)
3) A proclivity to recur despite seemingly adequate treatment
4) A less-than-robust response to conventional laser treatment

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Ablation (via either cryo or laser) of the avascular retina

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Although it must be stressed that laser treatment is not wholly benign--issues with intra-operative apnea and/or adverse cardiac events have been reported, as have sequelae including cataract and glaucoma.

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What is the *UN*conventional treatment for ROP?

Intravitreal bevacizumab

What clinical trial evaluated intravitreal bevacizumab as a primary treatment for ROP?

The BEAT-ROP (Bevacizumab Eliminates Angiogenic Threat in ROP) trial

What is the conventional treatment for ROP?

Ablation (via either cryo or laser) of the avascular retina

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What sort of ROP was treated with bevacizumab in the BEAT-ROP?

Stage 3 in Zone 1 or posterior Zone 2--ie, Aggressive Posterior ROP

Why was APROP the target disease state?

As mentioned previously, APROP is notorious for its poor response to conventional laser tx (CLT)

What was the treatment protocol?

Pts received a single intravitreal injection of 0.625 mg bevacizumab. (Note that this is ½ the usual adult dose.)
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Another term is used for aggressive posterior ROP--what is it? It is called Aggressive Posterior ROP (APROP)

Is APROP simply another name for Rush disease?

While the terms are sometimes used interchangeably, the clinical appearance and behavior of APROP can differ from that of Rush dz. APROP is characterized by the presence of neovascular fronds lying flat on the retinal surface (ie, without a ridge) in Zone 1 or posterior Zone 2. Active A-V shunting is the rule. APROP is notorious for four unfortunate tendencies:

1) Progressing directly from Stage 1 to Stage 3 disease;
2) very rapid progression--Stage 1 to 3 (or even 4) in a matter of days;
3) a proclivity to recur despite seemingly adequate treatment; and
4) a less-than-robust response to conventional laser treatment

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- Length of follow-up
- Generalizability
- Functionality
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Q/A

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On the other hand, there is no reason to think CLT has any long-term effects outside the eye. Intravitreal bevacizumab was only 6%.

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What if the pt develops a TRD--how is that managed?

PPV and/or scleral buckle

Is it effective?

Not so much. Only 30% of cases achieve anatomic reattachment; of these, only 25% are still attached at 5 years, and only 10% have ambulatory vision.
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(PPV = Pars plana vitrectomy)
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Once a decision to treat has been made, how long can it be deferred? When possible, treatment should be initiated within 72 hours.
ROP screening

Who?

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  - …with a birth weight of less than \# \text{ gm}
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Who?

- Screen all infants...
  - ...with a birth weight of less than 1500 gm
ROP screening

Who?

- Screen all infants…
  - …with a birth weight of less than 1500 gm, and/or
  - …whose gestational age at birth was weeks or less
ROP screening

Who?

- Screen all infants…
  - …with a birth weight of less than 1500 gm, and/or
  - …whose gestational age at birth was 30 weeks or less
ROP screening

Who?

- Screen all infants…
  - …with a birth weight of less than 1500 gm, **and/or**
  - …whose gestational age at birth was **30** weeks or less

**What about infants >1500 gm and/or with gestational age >30 weeks? Should they be screened?**
ROP screening

Who?

- Screen all infants...
  - ...with a birth weight of less than 1500 gm, *and/or*
  - ...whose gestational age at birth was 30 weeks or less

What about infants >1500 gm and/or with gestational age >30 weeks? Should they be screened? Not as a general rule. However, the guidelines state that such infants should be screened if/when their neonatologist feels it is indicated.
ROP screening

Who?

- Screen all infants…
  - …with a birth weight of less than 1500 gm, and/or
  - …whose gestational age at birth was 30 weeks or less

When?

- Timing of first screen is a function of pt…
ROP screening

Who?

- Screen all infants...
  - with a birth weight of less than 1500 gm,
  - whose gestational age at birth was 30 weeks or less

When?

- Timing of first screen is a function of pt age (see table)

How Often?

- A single screening exam is sufficient if the retina is fully vascularized OU
- Otherwise, 1 - 3 week follow-up is indicated (depending upon exam findings)

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## ROP screening

### Who?
- Screen all infants... with a birth weight of less than 1500 gm, and/or... whose gestational age at birth was 30 weeks or less.

### When?
- Timing of first screen is a function of pt age (see table).
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### How Often?
- A single screening exam is sufficient if the retina is fully vascularized OU.
- Otherwise, 1 - 3 week follow-up is indicated (depending upon exam findings).

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Don’t try and memorize the table! Instead, here is first-screen timing in a nutshell:
**ROP screening**

**Who?**
- Screen all infants...
- ...with a birth weight of less than 1500 gm,
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**When?**
- Timing of first screen is a function of pt age (see table)
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**How Often?**
- A single screening exam is sufficient if the retina is fully vascularized OU
- Otherwise, 1 - 3 week follow-up is indicated (depending upon exam findings)

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**Table: ROP Screening and Follow-Up**

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*Don’t try and memorize the table! Instead, here is first-screen timing in a nutshell:*

If the infant’s gestational age at birth was 27 weeks or younger, perform first screen at *postmenstrual age 31 weeks,* or
**ROP screening**

**Who?**
- Screen all infants
  - with a birth weight of less than 1500 gm,
  - and/or
  - whose gestational age at birth was 30 weeks or less

**When?**
- Timing of first screen is a function of patient age
  - Serious ROP rare before postmenstrual age 31 weeks, so this is the youngest age that requires screening

**How Often?**
- A single screening exam is sufficient if the retina is fully vascularized OU
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*Don’t try and memorize the table! Instead, here is first-screen timing in a nutshell:*

- If the infant’s gestational age at birth was 27 weeks or younger, perform first screen at postmenstrual age **31 weeks**, or
- If the infant’s gestational age at birth was 28 weeks or older, perform first screen at chronologic age **4 weeks**
**ROP screening**

- **Who?**
  - Screen all infants…
    - …with a birth weight of less than 1500 gm, **and/or**
    - …whose gestational age at birth was **30** weeks or less

- **When?**
  - Timing of first screen is a function of pt **age** *(see table)*
    - Serious ROP rare before postmenstrual age **31** weeks, so this is the youngest age that requires screening

- **How Often?**
  - A single screening exam is sufficient if the retina is **three words**
**ROP screening**

**Who?**
- Screen all infants...
  - ...with a birth weight of less than **1500 gm**, *and/or*
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**When?**
- Timing of first screen is a function of pt **age** (*see table*)
  - Serious ROP rare before postmenstrual age **31 weeks**, so this is the youngest age that requires screening

**How Often?**
- A single screening exam is sufficient if the retina is **fully vascularized OU**
ROP screening

Who?
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**Long-term follow-up**: A child with ROP needs periodic follow-up beyond the newborn period because…
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  - Vitreoretinal traction can lead to RD in 1st or 2nd decade
Long-term follow-up: A child with ROP needs periodic follow-up beyond the newborn period because...

- Vitreoretinal traction can lead to RD in 1st or 2nd decade
- Amblyopia can result from refractive problem, macular pathology, and/or EOM problem
**Long-term follow-up**: A child with ROP needs periodic follow-up beyond the newborn period because…

- *Vitreoretinal traction* can lead to RD in 1\(^{st}\) or 2\(^{nd}\) decade
- Amblyopia can result from *high myopia*, macular dragging, and/or *strabismus*
ROP: Macular dragging
**Long-term follow-up**: A child with ROP needs periodic follow-up beyond the newborn period because...

- **Vitreoretinal traction** can lead to RD in the **1st or 2nd decade**.
- Amblyopia can result from **high myopia**, macular dragging, and/or **strabismus**.
- Macular dragging can produce a **pseudo EOM problem**.
**Long-term follow-up**: A child with ROP needs periodic follow-up beyond the newborn period because...

- **Vitreoretinal traction** can lead to RD in 1\textsuperscript{st} or 2\textsuperscript{nd} decade

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  - Macular dragging can produce **pseudostrabismus**
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- Amblyopia can result from **high myopia**, macular dragging, and/or **strabismus**.
  - Macular dragging can produce **pseudostrabismus**.
    - Will have positive angle kappa, but no shift on exam maneuver.

**Exam finding in pseudo-EOM problem**
**Long-term follow-up**: A child with ROP needs periodic follow-up beyond the newborn period because...

- **Vitreoretinal traction** can lead to RD in the 1st or 2nd decade.
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*Speaking of macular dragging…*
In addition to a dragged macula, ROP pts often have a dragged...
In addition to a dragged macula, ROP pts often have a dragged disc.
In addition to a dragged macula, ROP pts often have a dragged disc. What three other clinical entities can give a similar picture?

3 things that look like ROP:

1) ?
2) ?  Hints forthcoming…
3) ?
In addition to a dragged macula, ROP pts often have a dragged disc. What three other clinical entities can give a similar picture?

3 things that look like ROP:

1) **Hint: A phakomatosis (buzzterm: ‘Splashed paint’)**
2) ?
3) ?
In addition to a dragged macula, ROP pts often have a dragged disc. What three other clinical entities can give a similar picture?

3 things that look like ROP:

1) Incontinentia pigmenti
2) ?
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3 things that look like ROP:

1) Incontinentia pigmenti
2) Familial exudative vitreoretinopathy (FEVR)
3) ?

**Hint:** A dz of the vitreoretinal interface
In addition to a dragged macula, ROP pts often have a dragged disc. *What three other clinical entities can give a similar picture?*

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3 things that look like ROP:

1) Incontinentia pigmenti
2) Familial exudative vitreoretinopathy (FEVR)
3) Toxocara chorioretinitis

Hint: Can also look like Rb
In addition to a dragged macula, ROP pts often have a dragged disc. **What three other clinical entities can give a similar picture?**

3 things that look like ROP:

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What is the eponymous name for IP?

Bloch-Sulzberger syndrome

What is the inheritance pattern of IP?

X-linked dominant

What does this pattern portend for its demographics?

Males die in utero, so almost all cases will be females

We noted that IP is a phakomatosis. By what more on-the-nose term are phakomatoses known?

'Neurocutaneous syndromes.' Most present with multiple lesions in two or more organ systems, usually including the CNS and skin (hence the name).

To what does the buzzterm splashed paint refer?

The appearance of the infant's skin after erythema and bullae develop at age ~ 1 week
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Incontinentia pigmenti
A 4-month old girl with incontinentia pigmenti was admitted for seizures and intracranial hemorrhage. It may be difficult to appreciate the peripheral nonperfusion with RetCam photography alone (A-B), but the findings become clear with RetCam FA
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We noted that IP is a phakomatosis. By what more on-the-nose term are phakomatoses known? ‘Neurocutaneous syndromes.’ Most present with multiple lesions in two or more organ systems, usually including the CNS and skin (hence the name).

To what does the buzzterm splashed paint refer?
In addition to a dragged macula, ROP pts often have a dragged disc. What three other clinical entities can give a similar picture?

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Q/A

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Incontinentia pigmenti: Splashed-paint appearance
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In a nutshell, what sort of condition is FEVR?

A vitreoretinal dystrophy

What is the basic retinal problem in FEVR?

The temporal retina fails to vascularize

In what two ways will FEVR neonates differ from ROP neonates?

FEVR babies will be full-term, and have normal oxygenation status.
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FEVR: Fundus photo and FA
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What sort of bug is Toxocara?

A roundworm

What animals are the principal hosts?

Dogs and cats

How is the worm acquired by humans?

Usually via consumption of contaminated soil

What is the classic appearance of the ROP-like lesion?

A peripheral retinal mass connected by dense fibrous strands to the optic disc

What percent of ocular toxocariasis pts have the ROP-like presentation?

About half
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Mechanism(s) for disc/foveal dragging in each?

These two share a common mechanism
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Mechanism(s) for disc/foveal dragging in each?

Mechanism similar to ROP (peripheral neo→retinal traction)
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**Mechanism(s) for disc/foveal dragging in each?**

- **ROP:** Peripheral neo-retinal traction
- **Mechanism similar to ROP:** Peripheral neo-retinal traction
- **This one has a different mechanism:**
Patients s/p ROP often have a dragged fovea and/or dragged disc. **What three other clinical entities can give a similar picture?**

### Mechanism(s) for disc/foveal dragging in each?

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### 3 things that look like ROP:

- **Mechanism similar to ROP (peripheral neo→retinal traction)**
- **Disc/foveal dragging due to inflammatory granuloma**

**ROP: DDx**