Retinopathy of Prematurity

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Disclaimer and Acknowledgements

No proprietary interests

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Roadmap of Today’s Talk...

• Why is ROP important?
• Overview of disease process
• What are Risk factors?
  • Race/ethnicity
• Classification
• Screening guidelines
• Brief overview of Tx
• How to avoid legal pitfalls?
• Future directions
Why is ROP Important?

- 3-10% of blindness in children
- 600 children blinded in US annually
  - Translates to 30,000 life-years of blindness
- 2100 infants with cicatricial sequellae
- Malpractice liability

Don’t just take my word for it…

$20M Award to Boy Blinded by Hospital

$11M Settlement—Failure to Diagnose Neonatal Eye Disorder

S. Cal. 2006

$6.8M Failure to Screen for ROP

Scott vs. Hillyard

Orange County Superior Court

$4.6 million verdict in Hudson County NJ, 2004

$3.375M Lost in 2006 Lawsuit in S. Carolina

$3M Settlement U of Chicago Hospital

Treatment Delays in ROP 2002

ROP: Overview of Disease

- Normal Retinal Development:
  - Vascularization proceeds from optic nerve to periphery
  - Temporal retina last to vascularize (normally just at or after full term birth)
  - Premature exposure to atmospheric PO2 arrests normal vascularization
  - Differentiation of retina increases O2 demand, resulting in ischemia and neovascularization
ROP: Classification

- Based upon 3 findings:
  - Location
  - Stage
  - Vascular dilation

Stage 1: Demarcation line

Stage 2: Line with Height
Stage 3: Neovascular ridge

Stage 4a: Focal Detachment
Stage 4b: Macula Off Detachment

Vascular dilation="Plus Disease"

• Normal retina
ROP: Demographics/Risk factors

- Gest Age
- Gender
- Oxygen
- Race/Ethnicity

Incidence of ROP by Gest Age

Need for ROP Surgery by Gest Age
ROP risk factors - Gender/Race

- Yang et al., JAAPOS 2006
  n= 596, looked at race/gender relative to CRIB score

<table>
<thead>
<tr>
<th>Incidence of eyes warranting surgery for ROP</th>
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<tbody>
<tr>
<td>Black</td>
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<tr>
<td>Male</td>
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<tr>
<td>Female</td>
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<td>Total by Race</td>
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ROP risk factors - Ethnicity

  - Severe vision threatening ROP:
    - 7.4 white infants
    - 3.2% black infants
- Elisaon et. al J AAPOS 2007 epub
  - ROP similar incidence in white and hispanic infants
- Sabri, Can J Ophth 2007
  - No diff Caucasian vs. SE Asian babies

Risk Factors for ROP Genetics

- Bizzarro et. al. Pediatrics 2006;118;1858-1863
  - Retrospective analysis 63 MZ and 137 DZ premie twins
  - Mixed effects logistic regression analysis controlling for gest age and supp O2
  - 70% of variance due to genetic factors
ROP risk factors: Oxygen Tx

- O2 one of many ROP risk factors
- Optimal O2 levels controversial
- **Chow and Wright** - Pediatrics 2003
  - Avoiding episodes of HYPEROXIA and swings in O2 sats
    - Decreased stage 3 or 4 ROP 12.5% to 4.5%
    - NO babies needed Laser
- **VanderVeen et. Al** - AAPOS 2006
  - O2 sat alarm limits: lower limit lowered from 87% to 85% and upper limit lowered from 97% to 93%
  - Decreased prethreshold ROP 17% vs. 5.6%

Revised AAP ROP Screening Guidelines

- **Infants <BW 1500 gms or**
- **Gest Age <= 30 weeks or**
- "Selected infants 1500-2000 gms or >30 wks gest age believed by their attending pediatrician or neonatologist to have high risk"
  - Such as very unstable course with h/o requirement of cardiorespiratory support

ROP Screening Guidelines

- **NOT 32 weeks gestation**
- **Should be 30 weeks!**
Timing of 1st ROP exam:

<table>
<thead>
<tr>
<th>Gestational Age at Birth</th>
<th>Age at Initial Examination, wk</th>
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Note: Table includes reference to ROP with high confidence, usual with follow-up examination.

Timing of ROP Exams

- Window of opportunity!
- LAWSUITS from failure to f/u on time:
  - Failure of discharge planning communication to ophthalmologist
  - Last name of baby changes
  - Parents “no show” - claim lack of knowledge

Tracking ROP patients
ROP TREATMENT OPTIONS

- Supplemental O2 after ROP develops
- Ablation of avascular retina
  - Laser
  - Cryo
- Future: Vascular endothelial growth factor inhibitors

STOP-ROP

- Supplemental therapeutic O2 given AFTER development of ROP
  - Theoretically to reduce hypoxia
  - Raising O2 sats to 96-99% range after ROP developed did NOT reduce need for ablative Tx
    - Subgroup w/prethreshold w/out plus may have benefit
    - Increased risk of adverse pulmonary events

ROP Treatment

- Ablate peripheral avascular retina
  - Cryo ROP Study
    - 10 yr f/u:
      - Unfavorable visual outcome reduced from 62% to 44%
      - Only 13% better than 20/40
  - Laser (Landers 1990 AJO)
    - Connolly Opth 1998
      - N= 52, 5.8 yr f/u
      - better outcomes, less myopia
ROP Treatment

- Early Tx Prethreshold ROP Study (ETROP) Conclusions TREAT:
  - Zone I any stage with "PLUS" dz
  - Zone I Stage 3 w/out "PLUS" dz
  - Zone II Stage 2 or 3 with "PLUS" dz

ROP Time-lapse

- courtesy of Anna Ells, MD

Future directions

- Screening- RetCam
  - Quantitative processing of images
  - May allow non ophthalmologist to acquire data
  - ?med legal implications
  - $$$
- Treatment- Vascular Endothelial Growth Factor (VEGF) inhibitors eg. Avastin, Lucentis
  - Promising early results
  - ? Effect on other developing organs?
Summary: Take Home Messages

• ROP is important preventable cause of blindness
• Evaluated by stage and location of dz
• Timing of screening and treatment crucial
• Med legal landmine: Bullet-proof tracking system essential
• Laser current Tx of choice
• Future hope for anti-VEGF agents