

**Drug toxicity surveillance in children**

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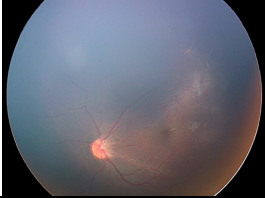
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**4-month-old referred for nystagmus**

<p><b>RIGHT EYE</b></p> <p>Closed funnel retinal detachment, Dysplastic retina, vascular stalk centrally Optic nerve obscured by retinal detachment</p>	<p><b>LEFT EYE</b></p> <p>Retinal blood vessels straightened, pulled temporally Slightly dysplastic optic nerve peripheral retinal nonperfusion seen 360°</p> 
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**Assessment and Plan**

- 4-month-old child with bilateral peripheral retinal vasculopathy
  - *Right eye: complete retinal detachment, poor prognosis*
  - *Left eye: peripheral vasculopathy and optic nerve dysplasia*
- Proceed with prophylactic laser photocoagulation, left eye
- TORCH workup, MRI
- Refer to genetics for further workup

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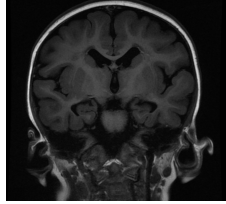
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### Clinical Course

- **MRI Brain:** Abnormal periventricular white matter and mild diffuse cerebral parenchymal loss
- New developmental delay and autism
- Diagnosed with infantile spasms, started on vigabatrin
- EyeGene testing negative for FEVR variant
- Found to have *heterozygous mutation in the NR2E3 gene (c.265 A>G, p. Met89Val)*



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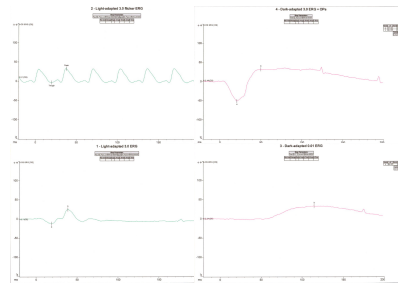
### Repeat EUA with ERG

Left eye only:

Reduced rod-mediated responses

Reduced mixed rod and cone-mediated a-wave and b-waves

Severely reduced oscillatory responses



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### Summary and Clinical Course

- 2-year-old with developmental delay, autism, infantile spasms on vigabatrin, retinal dystrophy, and genetic variant of uncertain significance presenting with an abnormal ERG after starting vigabatrin
- Vigabatrin discontinued at age 3
- Repeat ERG (age 5) was normal

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**Major Article**

**Ocular examinations, findings, and toxicity in children taking vigabatrin**

Yvette Schein, BA,<sup>1</sup> Keith D. Miller, BS,<sup>1</sup> Ying Han, MD, PhD,<sup>1</sup> Yixi Yu, MS,<sup>1</sup> Alejandra G. de Alba Campomanes, MD, MPH,<sup>2</sup> Gil Binenbaum, MD, MSCE,<sup>2</sup> and Julius T. Oatts, MD<sup>1</sup>

- 1,281 assessments of 284 children (mean age, 2.09 years)
- Two children (0.7%) had definite vigabatrin-related ocular toxicity

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**Vigabatrin**

**Clinical concern:** concentric peripheral VF loss  
**Recommended dose:** 50-100 mg/kg/day

**Baseline exam (prior to initiating):** complete eye exam, visual field testing

**Follow-up exam:** ideally every 3 months\*  
▪ Serial fundus exams (thinning of nasal RNFL, macular RPE changes), OCT, visual field testing

\*Most children on vigabatrin are young, nonverbal, and unable to cooperate with examination and/or visual field testing

*Adapted from AAPOS Vigabatrin: The Problem of Monitoring for Peripheral Vision Loss in Children (2017)*

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**Hydroxychloroquine**

Consider discontinuation after any sign of maculopathy or VF defect

**Clinical concern:** toxic maculopathy  
**Early manifestations:** paracentral relative scotomas  
**Recommended dose:** daily max 5.0 mg/kg real weight

**Baseline exam (within 1 year of initiating):** VA, Amsler grid, DFE  
▪ Consider color vision (pseudo-isochromatic plates), SD-OCT, HVF 10-2\*, fundus photo depending on level of concern

**Follow-up exam:** SD-OCT, HVF (+/- FAF, mfERG)  
▪ Annual screening after 5 years on acceptable dose  
▪ Increase risk in patients w/ renal disease or on tamoxifen (consider dose adjustment or more frequent screening)

*Adapted from AAO Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy - 2016*

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**Ethambutol**

Consider discontinuation after any sign of loss of VA/color vision or VF defect

**Clinical concern:** toxic optic neuropathy

**Early manifestations:** loss of visual acuity or color vision, central scotoma

**Baseline exam:** VA, color vision, DFE/optic nerve exam, VF

**Monthly exams for dose >15mg/kg/day**

(No standard for frequency of exams with doses <15mg/kg/day)

**\*Consider OCT RNFL or contrast sensitivity testing**

*Adapted from AAO Drug-Related Adverse Effects of Clinical Importance to the Ophthalmologist (2014)*

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**Panel discussion**

- Do you currently screen for Vigabatrin toxicity?
- What are the indications for Vigabatrin screening?
- What diagnostics do you perform, if any?

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**Panel Discussion**

- How do you handle referrals for medications with potential ocular side effects? Does this change for clinical trial patients?
- How do you define clinically significant toxicity?
- How do these principles apply to other medications such as MEK inhibitors or hydroxychloroquine?
- Adult versus child diagnostics: What works and what doesn't?

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**Take home points**

- Screening diagnostics and schedules based on adult patients may not apply to children
- Assessment of toxicity is not without risk and ultimately may not change management

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