LONG TERM RESULTS OF PLANNED PRETERM DELIVERY AND TREATMENT OF NORRIE DISEASE

Robert A. Sisk, MD, FACS

Virginia M. Utz, MD

Terry L. Schwartz, MD

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DISCLOSURES

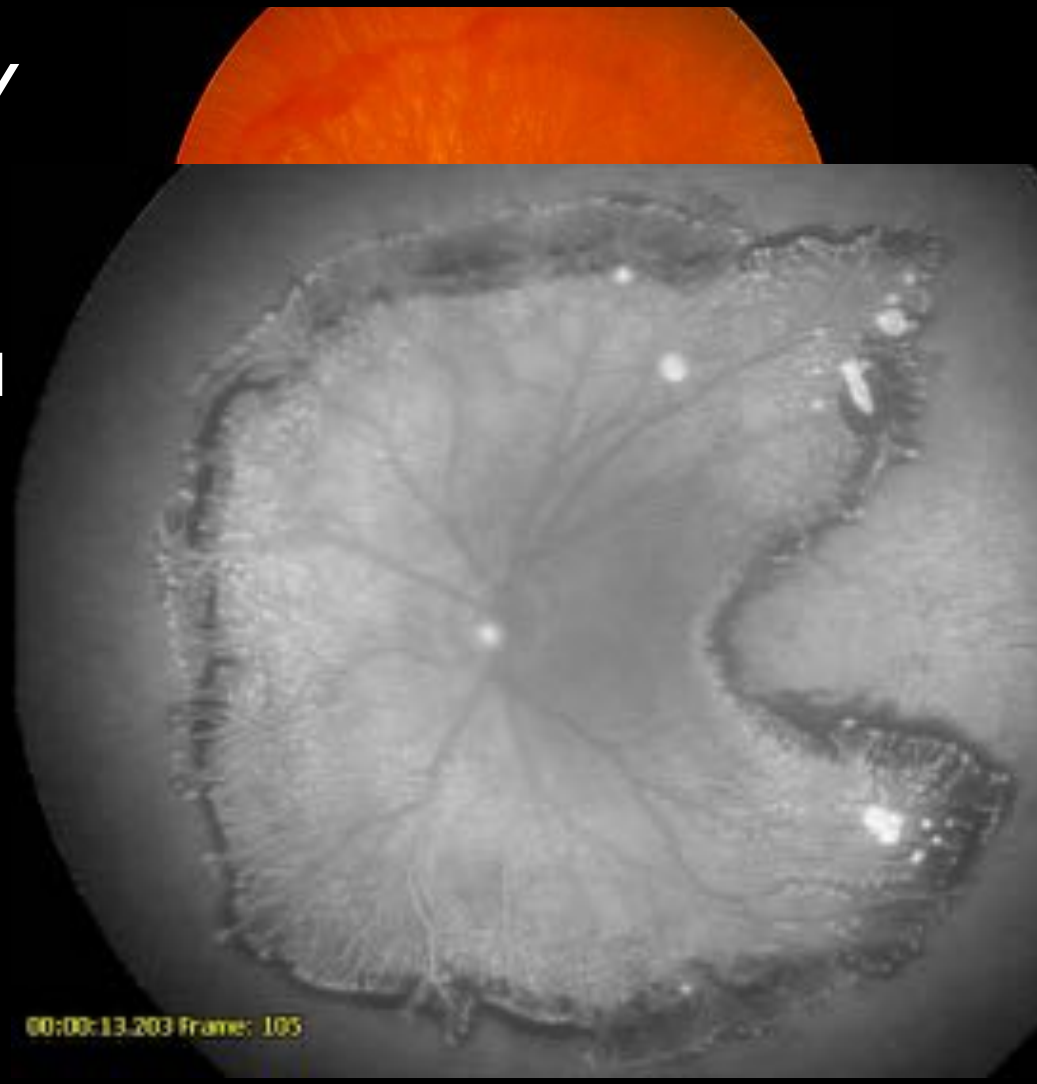
- Robert Sisk, MD
  - Leica (C)
  - Gyroscope (C)
  - AGTC (A, C)
- Virginia Utz, MD – Retrophin (R)
- Terry Schwartz, MD - None

SUMMARY

- There were no late sequelae or developmental delay after planned preterm delivery and ablative laser treatment for Norrie disease
- The retinas remained attached and no further treatment was required beyond the first year of life
- Despite no neurovascular development of the fovea at birth, visual function gradually improved over the first few years of life

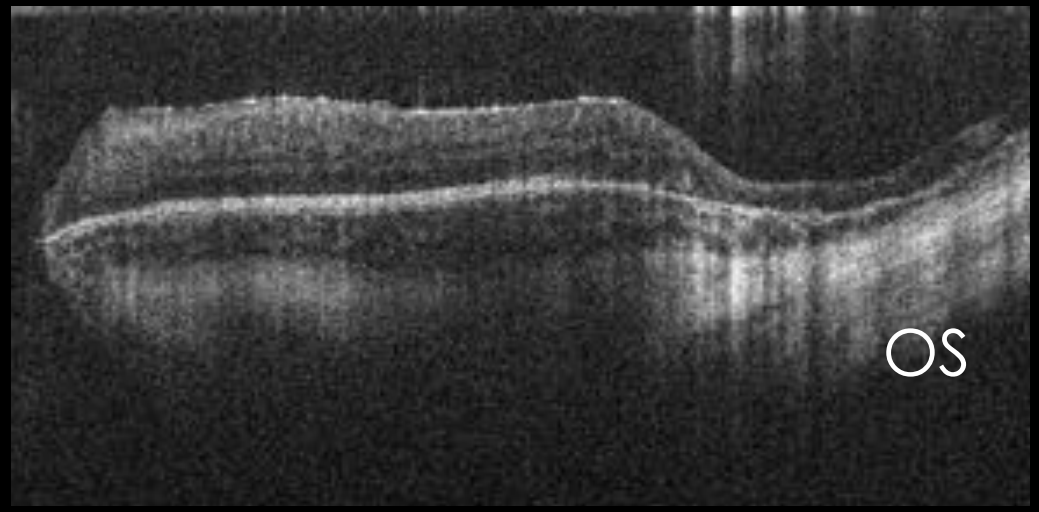
REVIEW OF PAST HISTORY

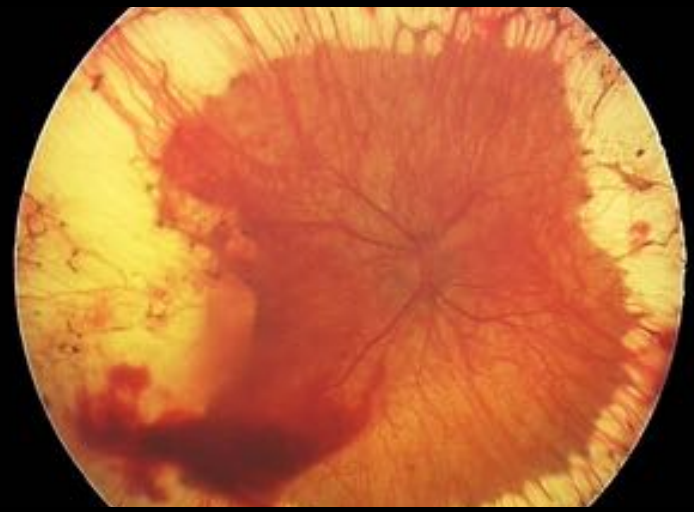
- +FamHx Norrie disease (Older brother and maternal uncle blind at birth from TRD OU) and +NDP, +LRP5 by amniocentesis
- Delivered at 34 weeks GA with EUA; 2 days later, laser ablation of avascular retina, and intravitreal bevacizumab (IVA) OS
- Zone 1 ROP/PFV phenotype OU with severe FEVR-like capillary abnormalities and preretinal neovascularization

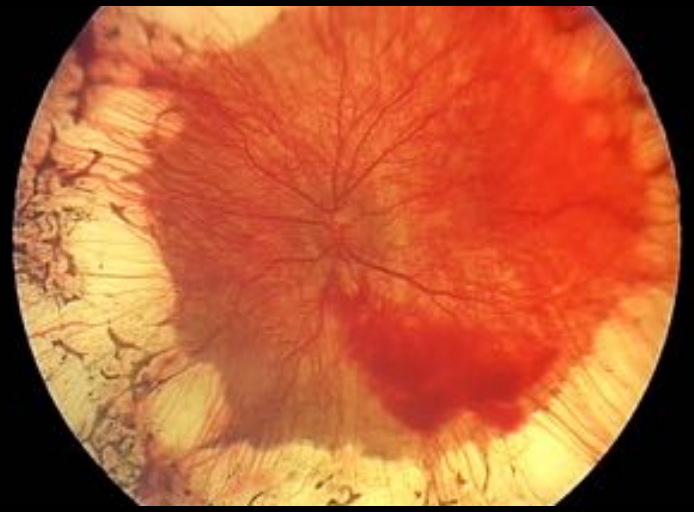


REVIEW OF PAST HISTORY

- At 20 weeks postnatal, limited vitreous hemorrhage OU from hyaloid artery regression was treated with repeat IVA OU
- OCT demonstrated no foveal architecture at birth or during first year of life







NDP/NORRIN FUNCTIONS TO:

- Stimulate retinal angiogenesis and capillary development from the superficial vascular plexus from the astrocytic framework
- Regress hyaloid vascular system
- Promote retinal ganglion cell survival

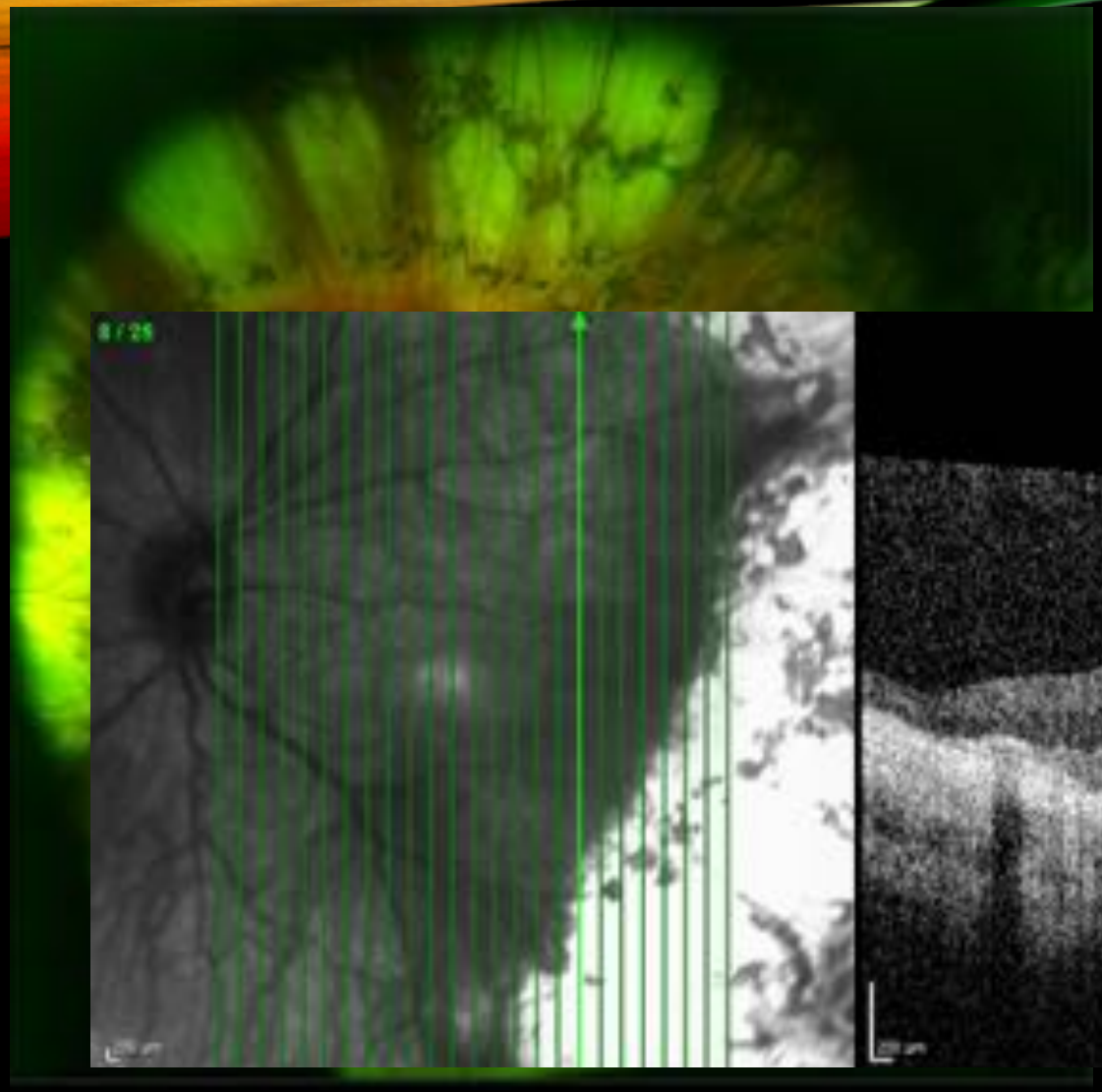
WITHOUT NORRIN:

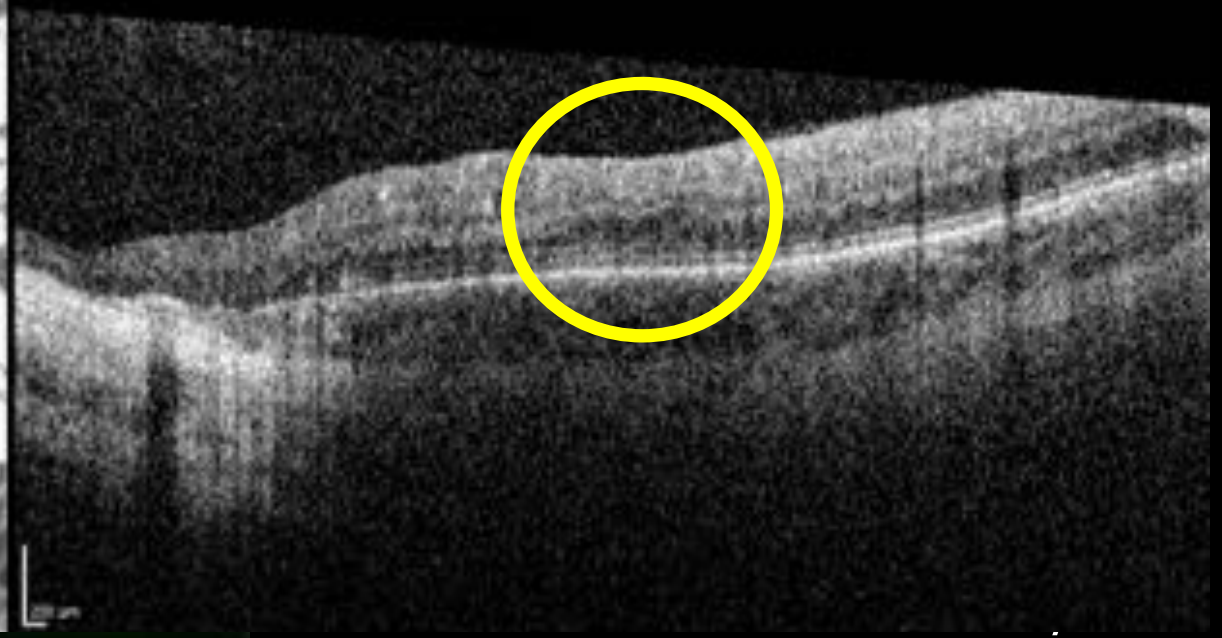
- Angiogenesis beyond vasculogenesis does not occur, including lack of deep retinal vessels
- Creates relative ischemia, even in portions of the retina with larger vessels coursing through them
- Hypoxia upregulates VEGF-A, HIF-1a, and Angiopoeitin 2, which promote retinal neovascularization
- Fibrosis, tractional retinal detachment, and pseudoglioma formation with secondary microphthalmia from RD/tethering by hyaloid system that failed to regress

FUNCTIONAL OUTCOMES: FIRST YEAR OF LIFE

Age	Binocular Visual Acuity (Teller)	Refractive Error	Other Findings
3 mos	20/540 (38 cm)	-9.50+1.00x100 -8.00+3.75x097	-Horizontal right jerk nystagmus - Alternating XT
5 mos	20/360 (38 cm)	-8.50+3.00x080 -8.00+5.00x 100	Horizontal right jerk nystagmus - Alternating XT
9 mos	20/360 (38 cm)	-8.50+3.00x080 -8.00+5.00x 100	Horizontal right jerk nystagmus (improved) X(T)
12 mos	20/190 (38 cm)	-8.50+3.00x080 -8.00+4.75x100	Horizontal right jerk nystagmus (improved) X(T) (well-controlled)

5 YEARS LATER:

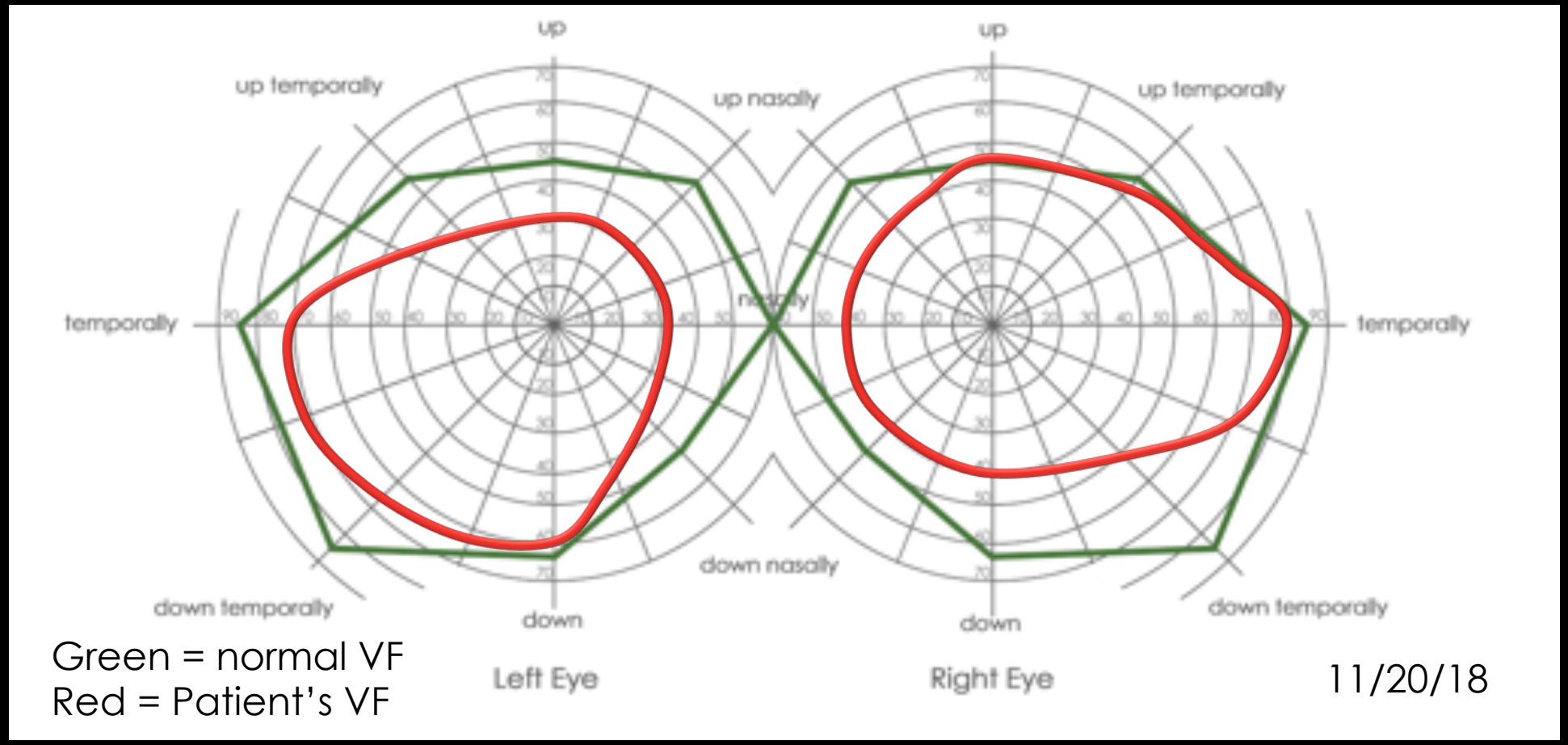




Near = 20/40 with +4.00

Nystagmus – intermittent, dampens with convergence, and small left face turn

VISUAL FIELD BY ARC PERIMETRY



Green = normal VF
Red = Patient's VF

11/20/18

1cm round stimulus, 100% contrast against white background

DISCUSSION

- Patient has functional real-world vision - drives dirt bikes, plays baseball, and attends regular school with help from low vision aids
- Foveal vascularization never progressed beyond pattern observed at birth, even in eye not initially treated with bevacizumab
- Visual acuity improvement over time may relate to foveal differentiation or cortical development (visual maturation)
- Recurrent retinal neovascularization or secondary vitreoretinal traction was not observed beyond the first year of life

CONCLUSIONS

- The onset of RD in Norrie disease is unknown. Prenatal genetic confirmation and preterm delivery affords the opportunity to prevent lifelong blindness by ablative laser and intravitreal bevacizumab
- Visual acuity improved despite foveal hypoplasia and incomplete retinal vascular development, and the patient achieved a highly functional visual outcome