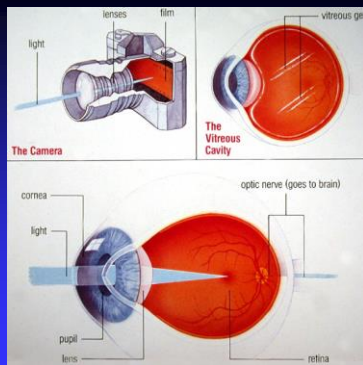


## Eye Findings in Alström syndrome

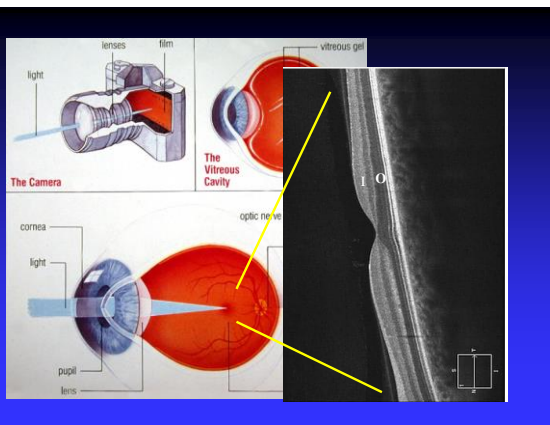
Alex V. Levin, MD, MHSc, FRCSC  
 Chief, Pediatric Ophthalmology and Ocular Genetics  
 Flaum Eye Institute and Golisano Children's Hospital  
 Chief, Clinical Genetics  
 University of Rochester, New York

It's call about the retina!



## The retina

- cones and rods  
= outer retina
- Inner retina  
= transmission pathway to the brain



## Alström Syndrome: multisystem disease



## Cone-Rod Dystrophy

- Shaky eyes (nystagmus)
- Photophobia
- Vision loss

## Alström Syndrome

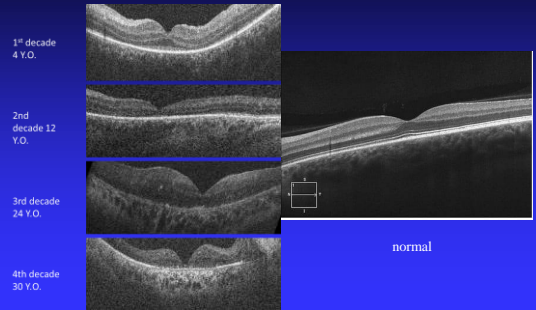
- Prevalence of less than one per million in the general population  
= Sample size challenges

THANK YOU!!!!

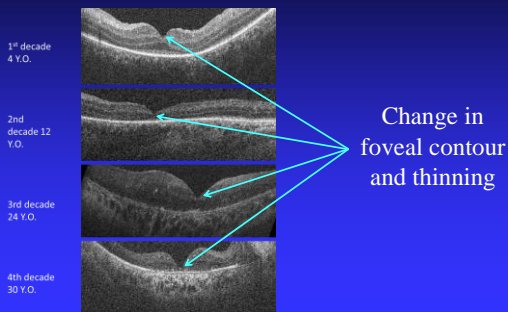
Dotan G, Khetan V, Marshall JD, Affel E, Armiger-George D, Naggert JK, Collin GB, Levin AV: Spectral-domain optical coherence tomography findings in Alström syndrome. *Ophthalmic Genet* 2017;38(5):440–445



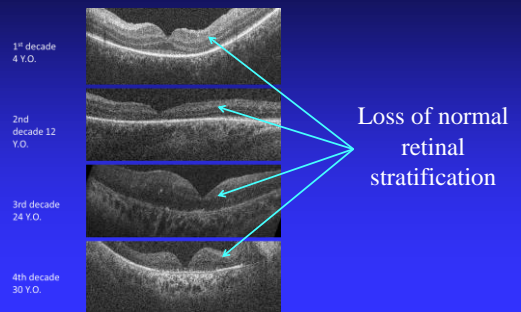
## Fovea Morphology by Decade



## Fovea Morphology by Decade



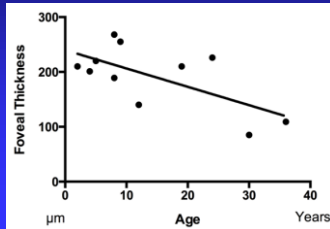
## Fovea Morphology by Decade



## Correlation of Foveal Thickness and Age

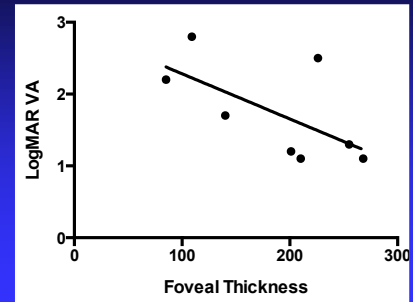
- Foveal thickness decreased by 3.3  $\mu\text{m}$  per year (95% confidence interval, 0.4 to 6.2  $\mu\text{m}$ )

$r=-0.65$   
 $P=0.028$



## Correlation of Foveal Thickness and Visual Acuity

$r=-0.62$   
 $P=0.095$



## Eye Findings in Alström Syndrome

Yiyun Zhou, MD, PhD, MBA, Antonie D. Kline, MD, Mary L. Collins, MD, Marcia Ferguson, MGC, Jennifer Billiet, MGC, Janet Sunness, MD, Michelle Bianchi OT, Sharon Payne OTMS, Alex V. Levin, MD, MHSc, FRCSC

## Current study design

- Objective: quantify the common ocular findings of Alström syndrome
- Design: Case series data, Semiannual Multidisciplinary Alström Syndrome Clinics (2015-2023) at GBMC, organized by Alström Syndrome International (ASI)

## Often misdiagnosed/delayed diagnosis

mostly at the end of the first decade of life

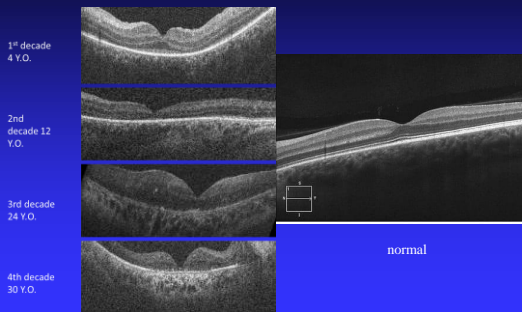
frequent misdiagnosis: Bardet-Biedl or achromatopsia or cone dystrophy

Early recognition of subtle signs is critical to early diagnosis

## Remarkable differences between adult and young children

- Marked tendency to lose vision with age
- Retinal findings subtle early = when gene therapy better

## Fovea Morphology by Decade



## Loss of photoreceptors

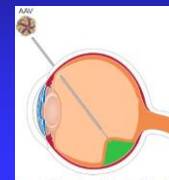
= loss gene therapy opportunity

What is “gene therapy”?

Is it science fiction?

Will there be treatment for  
Alstrom?

Is Gene Therapy possible?



## Luxturna

- Approved by FDA Jan 2018
- biallelic *RPE65*
- $\geq 1$  year old

## *Is this success?*

- RPE65 = 1 gene
- 20 years
- maybe 250 eligible people
- only works on some
- < 10 centers
- \$425,000 per eye!!!

## What if...

- Open access
- Mass production
- Low cost treatment
- Nonprofit
- No person left behind

## It's happening now

- Ed Stone at Iowa
- Iowa-Rochester collaboration

## How much does it really cost?

- Gene therapy \$20,000

## HOW??????

- philanthropy

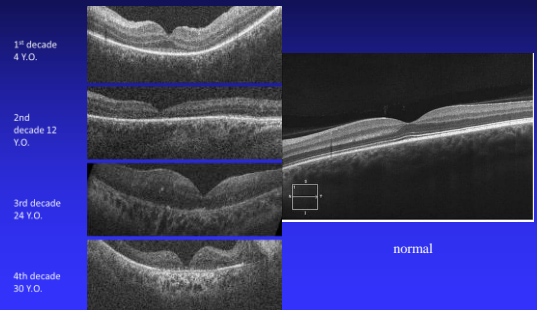
## ALMS1 Gene Therapy

- Technology is there
- Program is there
- Gene is small
- Need early intervention!
  - Diagnostic challenges
  - Ethical and surgical challenges

stopping progression vs reversal?

Plan B?

## Fovea Morphology by Decade

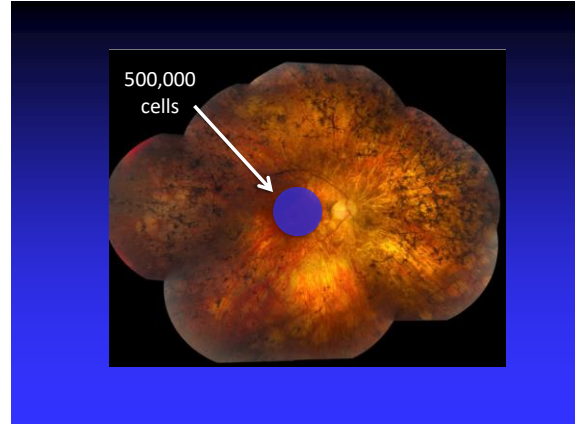
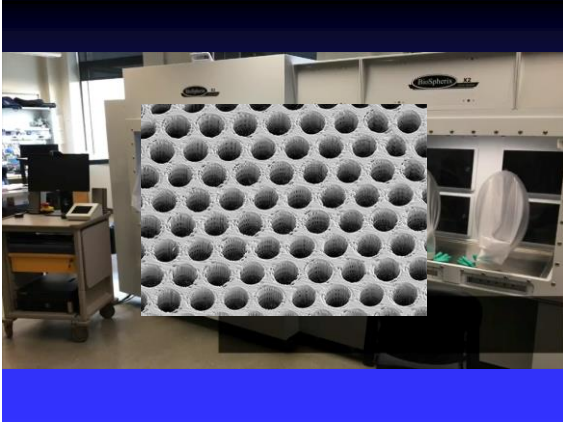


## Stem cells

= cells that become new retina  
from embryos  
from self

## Stem cell

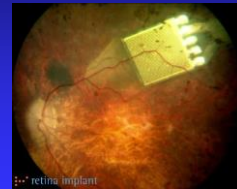
3mm piece of skin  
convert skin cells to stem cells  
to cone cells  
fix the ALMS1 gene  
reimplant under your retina



Plan C, D...?

## “Bionic Eyes”

retinal microchips



## Retinal chips



increasing quality of vision  
 studies underway  
 retinitis pigmentosa (RP)  
 macular degeneration (ARMD)  
 others...

## Other options?

- Gene agnostic
  - lots of trials
  - gene therapy
  - stem cell
  - drugs (eg Antabuse)

## Other options?

eyeball transplant  
still very much experimental  
artificial vision



**There will be treatment!**

## Why does it take so long?

Trial phases  
Money  
Competing diseases  
It's hard!

But progress is huge (and so is dedication)

## What can I do now?

Gene testing (accurate diagnosis)  
Don't smoke  
Sunglasses (rose, orange, yellow)  
Fish  
Vitamins/diet changes?  
    vitamin A, omega 3, lutein...

**There will be treatment!**