Rodney Coe, MD, MS
SUNY Downstate Medical Center
April 2, 2009

Grand Rounds Presentation

Chief Complaint

39 yo African American woman with c/o difficulty seeing at night. Pt reports feeling "clumsy" and "bumping into things" more often.

History

PMH: denies
POH: denies
Fam Hx: “father has problems seeing”
Soc Hx: denies x3
All: NKDA
Meds: no gtt’s, no meds

Physical Examination

DVaSC	OD 20/25-2	OS 20/30-
MRx:		
OD	+1.75 sph	20/20-
OS	+0.50 -1.00 x15	20/20-

EOM: full OU

CVF: grossly constricted OU

Pupils: PERRL OU, no APD

Tapp: 13/11 @1:50pm

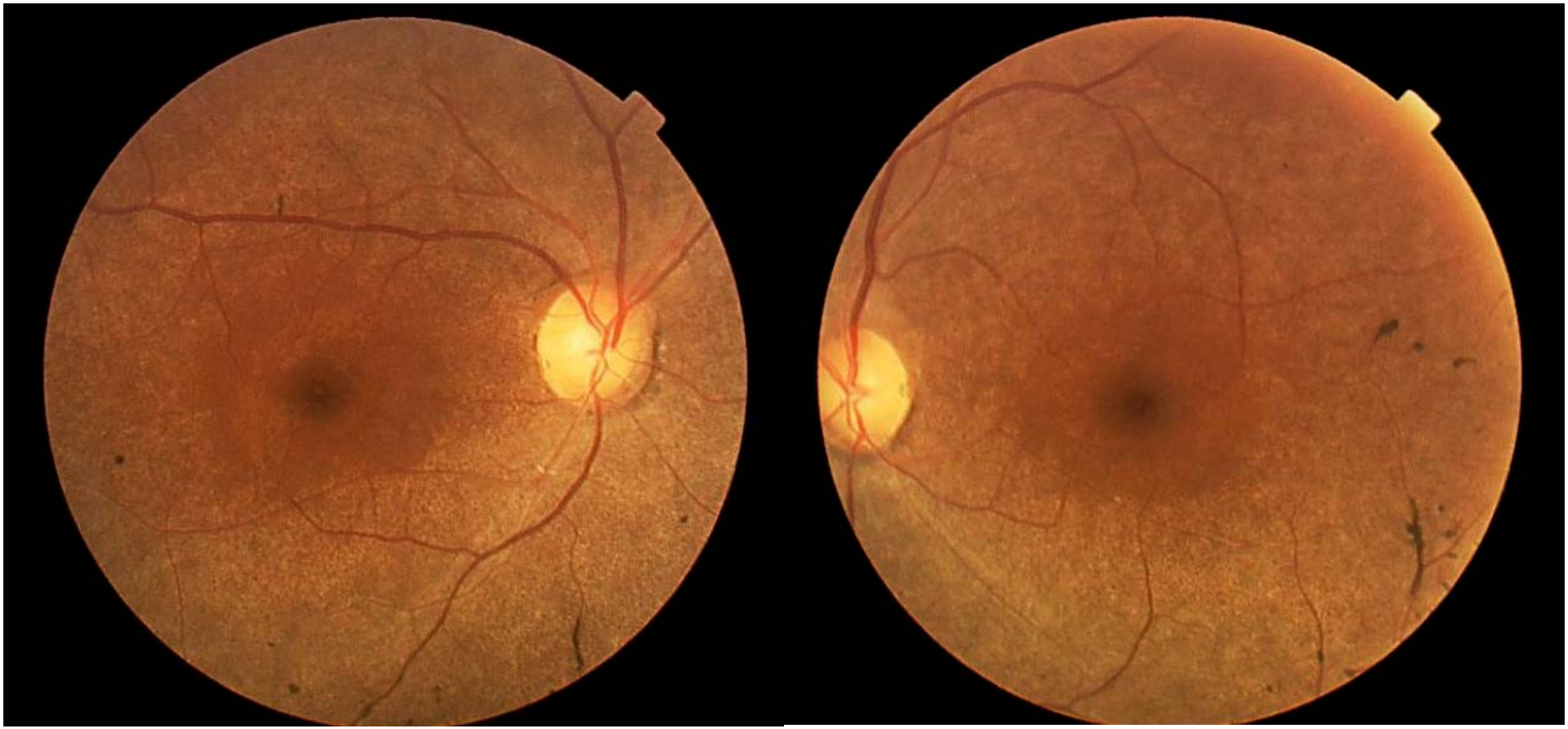
Slit Lamp Examination

LLA: few inspissated glands OU
C/S: c&w OU
K: clear OU
I/P: round OU
AC: d&q OU
L: TR NS OU

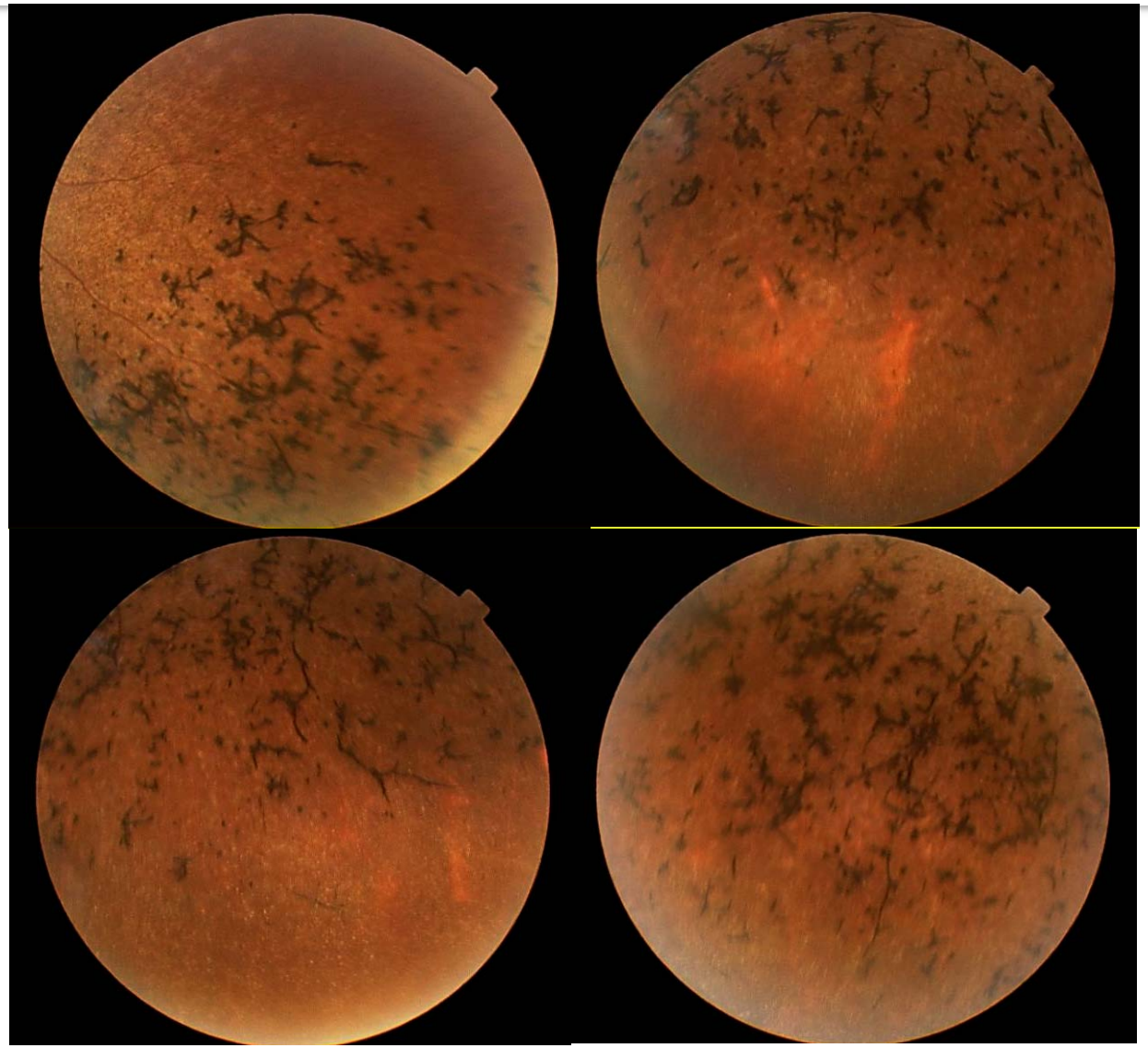
Dilated Fundus Examination

Vit: TR ant vit cell OD, clear OS
Disc: pink, sharp OU c/d: 0.25/0.3
Mac: see photos
Vessels: see photos
Periph: see photos

Color Photos



Color Photos



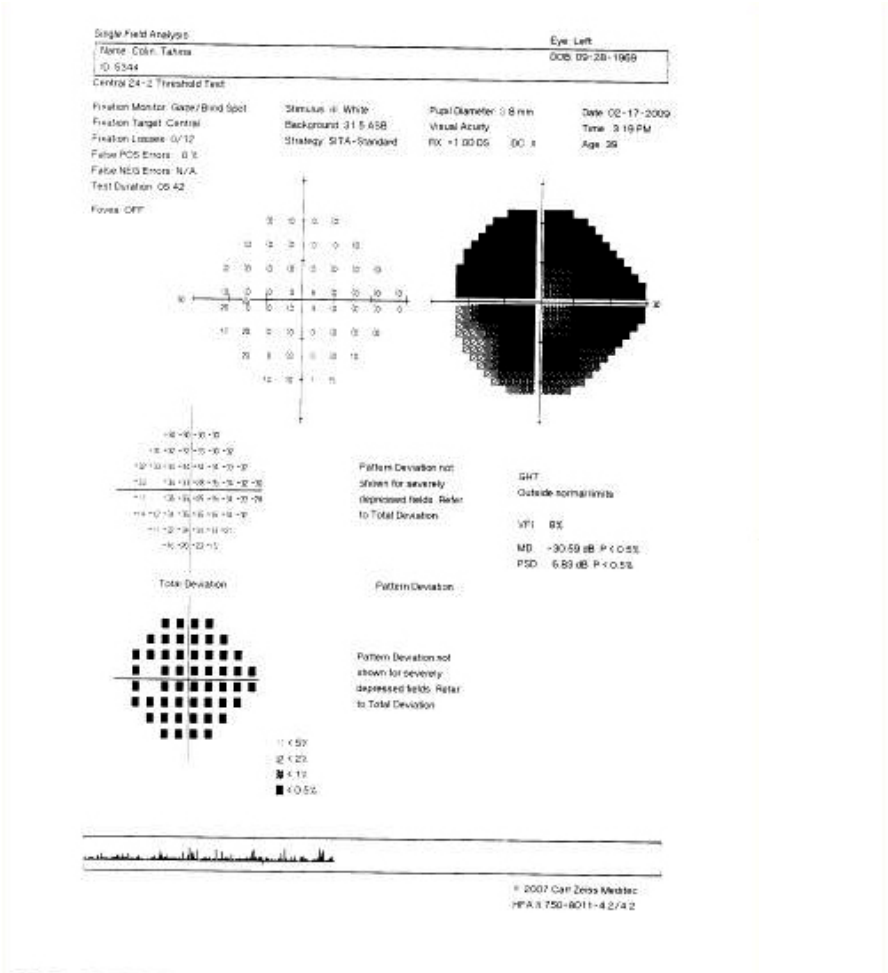
Differential Diagnosis

- Pigmentary retinopathy
  - Non-syndromic
  - Syndromic
- Traumatic retinopathy
- Syphilis
- TORCH
- CAR/MAR
- DUSN
- Retinal drug toxicity
- Prior vascular occlusion
- Diffuse posterior uveitis

What now?

- Automated Visual Field
- ERG
- Color plates
  - Full OU
- FTA-Abs/RPR
  - Negative
- Consider FA
  - No beneficial to dx RP, but may be beneficial to r/o other conditions
- ROS
  - Denies hearing loss, h/o orbital/ocular trauma, renal problems, etc

HVF 24-2


Single Field Analysis
Eye: Left
Name: Colin, Tahira
DOB: 09-28-1969
ID: 5344
Central 24-2 Threshold Test
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 0/12
False POS Errors: 0 %
False NEG Errors: N/A
Test Duration: 05:42
Foveal: OFF
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard
Pupil Diameter: 3.8 mm
Visual Acuity
Rx: +1.00 DS
DC: X
Date: 02-17-2009
Time: 3:19 PM
Age: 39
Pattern Deviation not shown for severely depressed fields. Refer to Total Deviation
GHT
Outside normal limits
VFI: 8%
MD: -30.59 dB P < 0.5%
PSD: 6.89 dB P < 0.5%
Total Deviation
Pattern Deviation
Pattern Deviation not shown for severely depressed fields. Refer to Total Deviation
< 5%
< 2%
< 1%
< 0.5%
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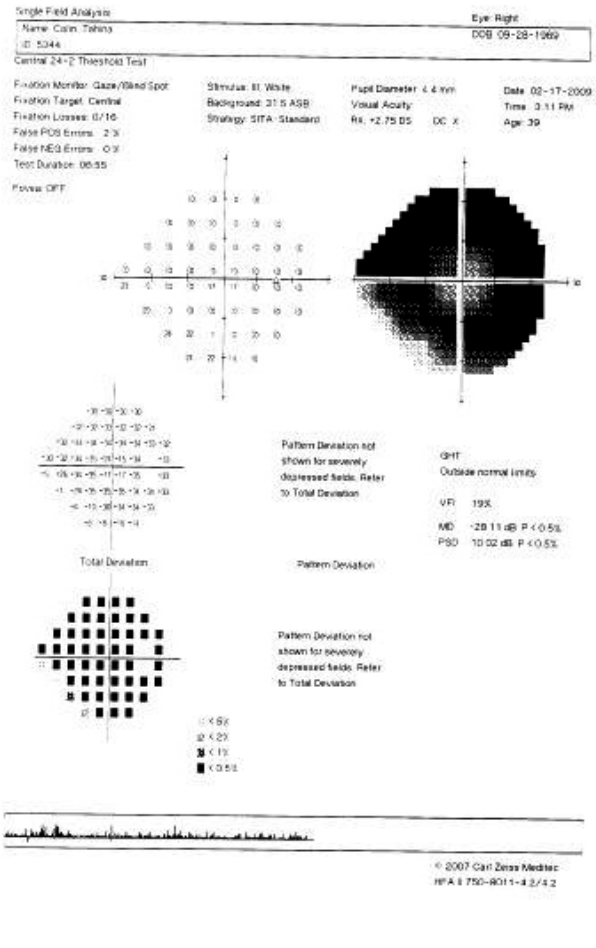
HFA II 750-8011-4.2/4.2


Single Field Analysis
Eye: Right
Name: Colin, Tahira
DOB: 09-28-1969
ID: 5344
Central 24-2 Threshold Test
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 0/16
False POS Errors: 2 %
False NEG Errors: 0 %
Test Duration: 06:55
Foveal: OFF
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard
Pupil Diameter: 4.4 mm
Visual Acuity
Rx: +2.75 DS
DC: X
Date: 02-17-2009
Time: 3:11 PM
Age: 39
Pattern Deviation not shown for severely depressed fields. Refer to Total Deviation
GHT
Outside normal limits
VFI: 19%
MD: -28.11 dB P < 0.5%
PSD: 10.02 dB P < 0.5%
Total Deviation
Pattern Deviation
Pattern Deviation not shown for severely depressed fields. Refer to Total Deviation
< 5%
< 2%
< 1%
< 0.5%
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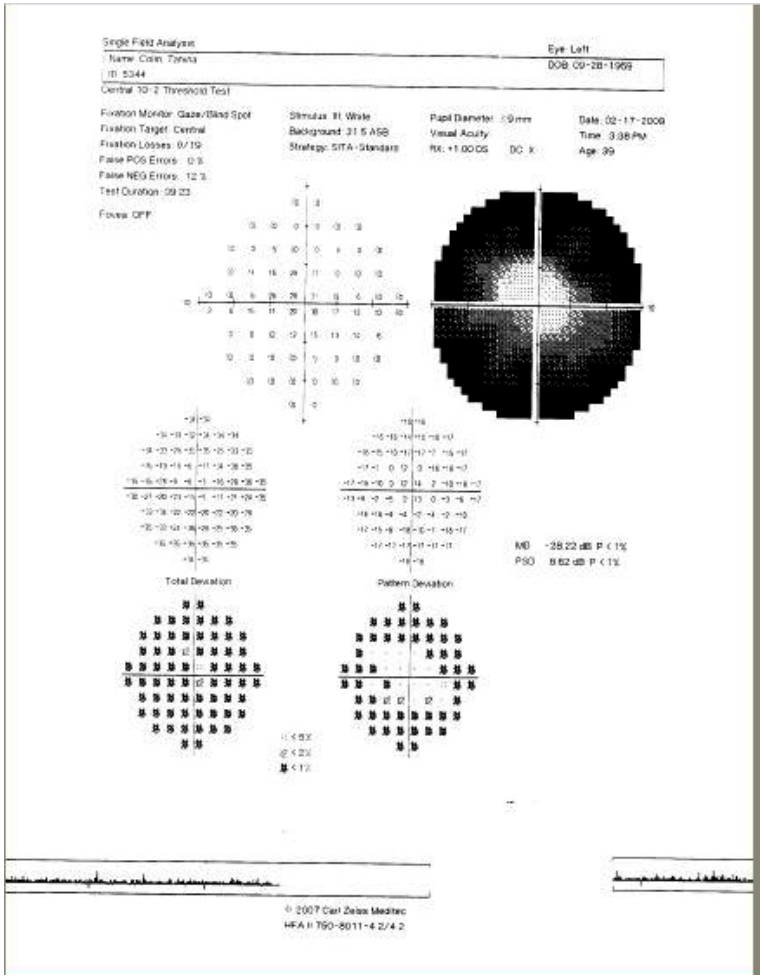
HVF 10-2


Single Field Analysis
Eye: Left
Name: Colin Tahara
ID: 5344
DOB: 09-28-1969
Central 10-2 Threshold Test
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 0/19
False POS Errors: 0 %
False NEG Errors: 12 %
Test Duration: 09:23
Fovea: OFF
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard
Pupil Diameter: 3.9 mm
Visual Acuity
Rx: +1.00 DS
DC: X
Date: 02-17-2009
Time: 3:38 PM
Age: 39
MD -28.22 dB P < 1%
PSD 8.62 dB P < 1%
Total Deviation
Pattern Deviation
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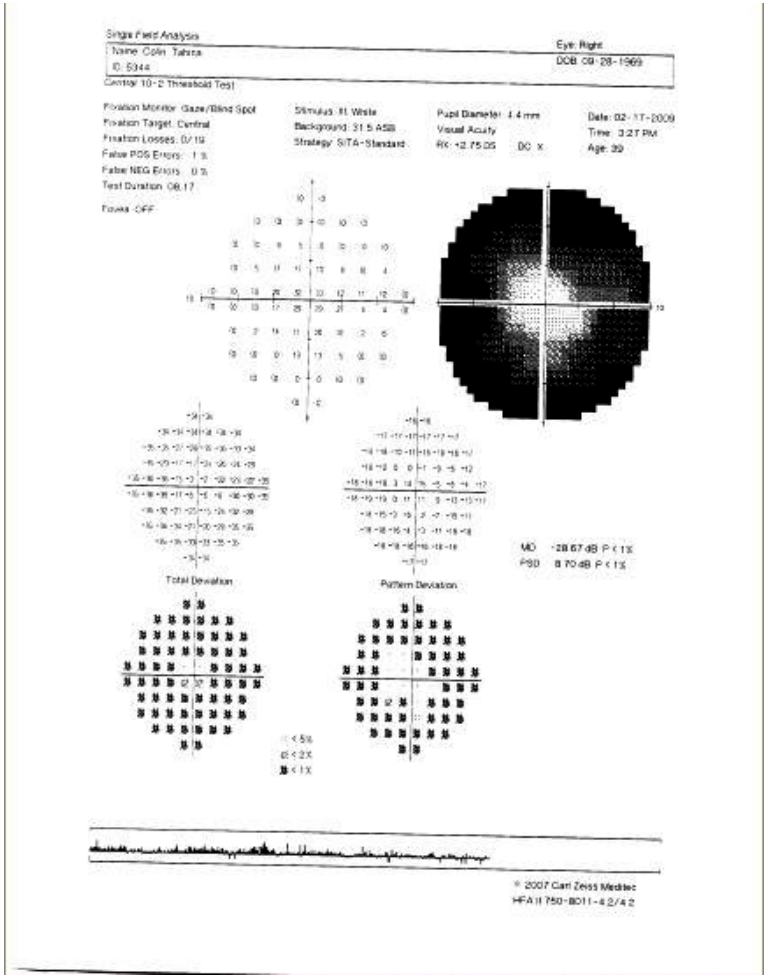
Single Field Analysis
Eye: Right
Name: Colin Tahara
ID: 5344
DOB: 09-28-1969
Central 10-2 Threshold Test
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 0/19
False POS Errors: 1 %
False NEG Errors: 0 %
Test Duration: 08:17
Fovea: OFF
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard
Pupil Diameter: 4.4 mm
Visual Acuity
Rx: +2.75 DS
DC: X
Date: 02-17-2009
Time: 3:27 PM
Age: 39
MD -28.67 dB P < 1%
PSD 8.70 dB P < 1%
Total Deviation
Pattern Deviation
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HFA II 750-8011-4.2/4.2

Retinitis Pigmentosa

- Misnomer, since the pathogenesis is not inflammatory in nature
- Also known as: pigmentary retinopathy, rod-cone dystrophy, tapetoretinal degeneration
- Worldwide prevalence 1 in 4000-5000
  - Highest frequency of occurrence reported in Navajo Indians at 1 in 1878
- About 70% of pts have a family history of RP
- Slow and progressive disease

Retinitis Pigmentosa

- Non-syndromic form comprises the majority of cases of RP
  - ~65% of RP cases are non-syndromic in the US
- Syndromic
  - Usher syndrome, Bardet-Biedl syndrome, Refsum disease, etc

Clinical Presentation

- Typically presents in young adulthood
  - Can present anytime from infancy to the mid-30's to 50's
- Nyctalopia
  - Often one of the earliest symptoms
  - Pts may c/o being "disoriented" in dim light, or c/o slow adaptation to dark conditions
- Visual field loss
  - Often not noticed by the pt
  - Pts may c/o being "clumsy", bumping into things

Clinical Presentation

- Visual acuity
  - Variably affected
  - Often affected by CME or cataract (classically PSC)
- Photopsias
  - Small, shimmering, blinking lights

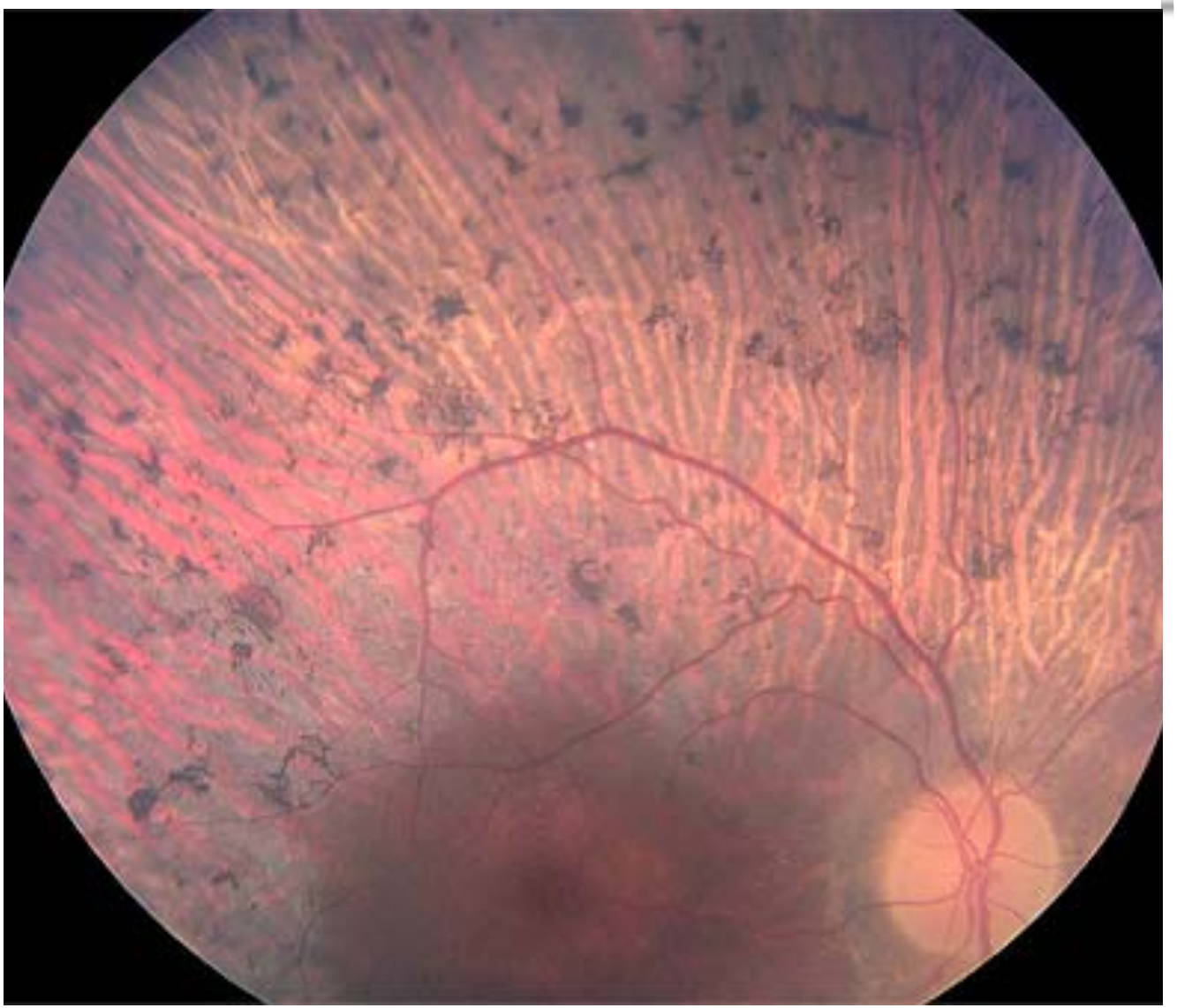
Physical Findings

Triad of findings:

Waxy, pallor of optic nerve
Believed to be due to a combination of gliosis and atrophy

Attenuation of retinal vessels

Bone-spicule pattern of intraretinal pigmentation



Medical Knowledge/Practice Based learning and improvement

Physical Findings

- Cystoid macular edema can develop
- Abnormalities in the vitreoretinal interface
  - Cellophane maculopathy
- Cataract formation affect ~50% of RP pts
  - Classically posterior subcapsular cataract
- Dust-like pigmented substance in vitreous
  - Composed of pigment granules rather than inflammatory cells, as is suggested in the name "retinitis"

Physical Findings

- Myopia
  - In one study from 1978, 75% of 268 eyes with RP were found to have myopia, compared with 12% in the general population
- Classic visual field defect is a ring scotoma, with eventual central island of vision
  - Progressive, gradual constriction of the field over time

Physical Findings

- Visual acuity is generally maintained, but there is significant loss of contrast sensitivity
  - Gives pts a perception of decreased vision while visual acuity actually remains very good
- Color vision general remains intact until the macula becomes significantly involved
  - Generally a blue cone deficiency

Diagnosis

- Visual field
- Electroretinography (ERG)
  - Measure of the total retinal response
  - RP patients demonstrate depressed ‘a’ and ‘b’ waves
  - Correlates with the size of the remaining visual field
- Multifocal ERG
  - Useful in monitoring patients with more advanced

ERG

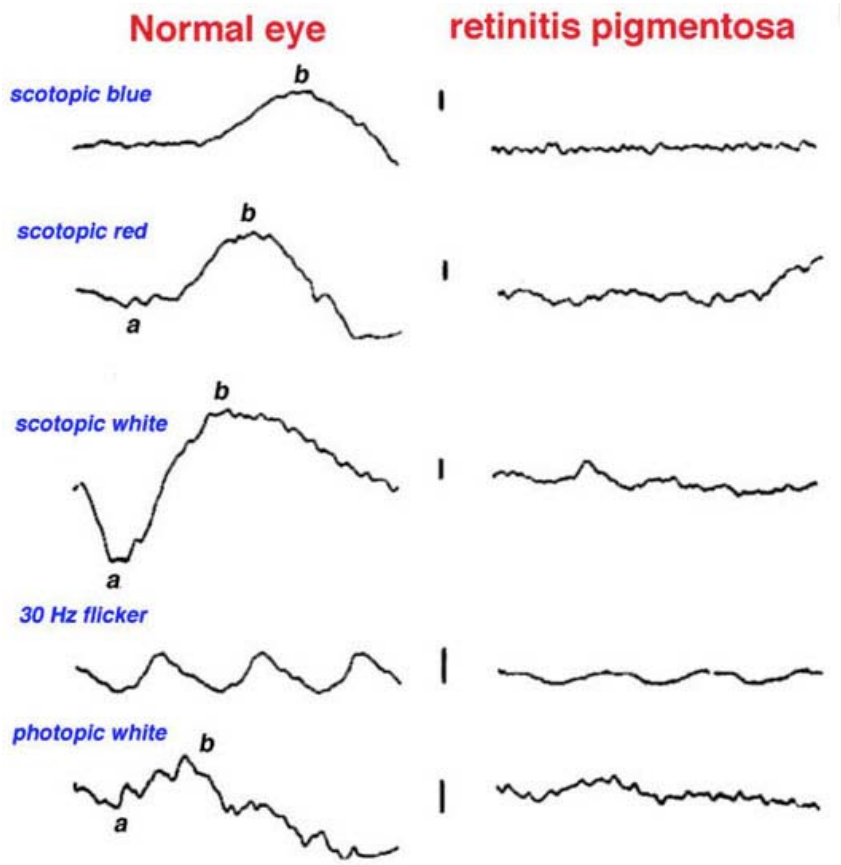


Fig. 13. ERG recordings in a normal patient and one with retinitis pigmentosa.

Medical Knowledge/Practice Based learning and improvement

Genetics

- Over 84 different genetic types of RP have been discovered

Inheritance pattern in the United States

Inheritance Pattern	Prevalence
Autosomal dominant	30%
Autosomal recessive	20%
X-linked	15%
Recessive early-onset	5%
Sporadic	30%

Medical Knowledge/Practice Based learning and improvement

Gene Mutations

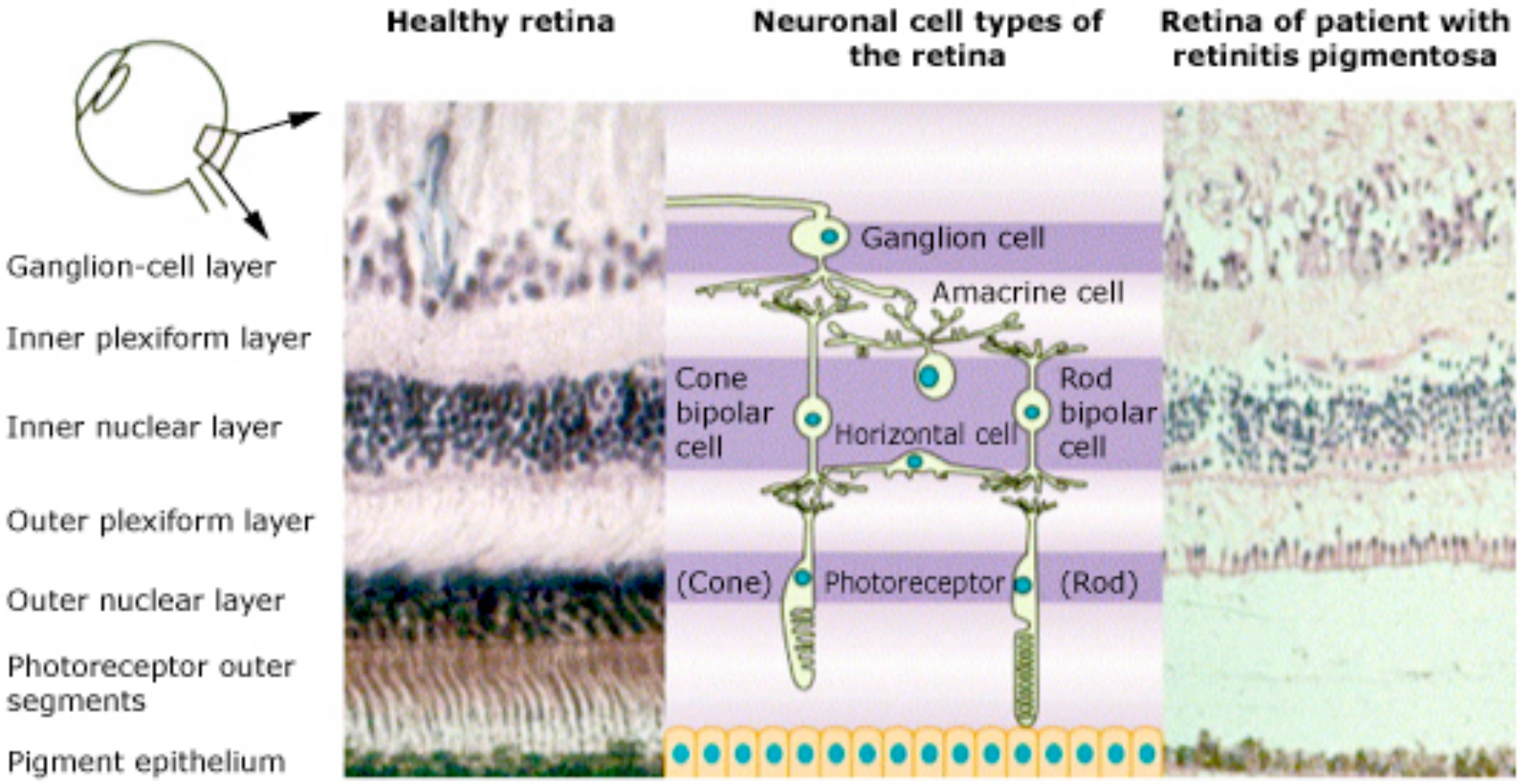
The following accounts for ~30% of all RP:

- Autosomal dominant
  - RHO – comprises ~25% of AD RP
- Autosomal Recessive
  - USH2A (Usherin) – 20% of AR RP
    - Both non-syndromic and syndromic (Usher Syndrome)
- X-linked
  - RPGR (GTPase regulator) – 70-80% of X-linked RP

Pathophysiology

- Genetic defects cause apoptosis
  - Predominantly, apoptosis of the rod photoreceptors
  - May also affect the RPE and cone photoreceptor, which leads to loss of rod photoreceptors
- Rod photoreceptors are most concentrated in the mid-periphery, hence the classic appearance of RP in this location

Pathophysiology



Medical Knowledge/Practice Based learning and improvement

ERG

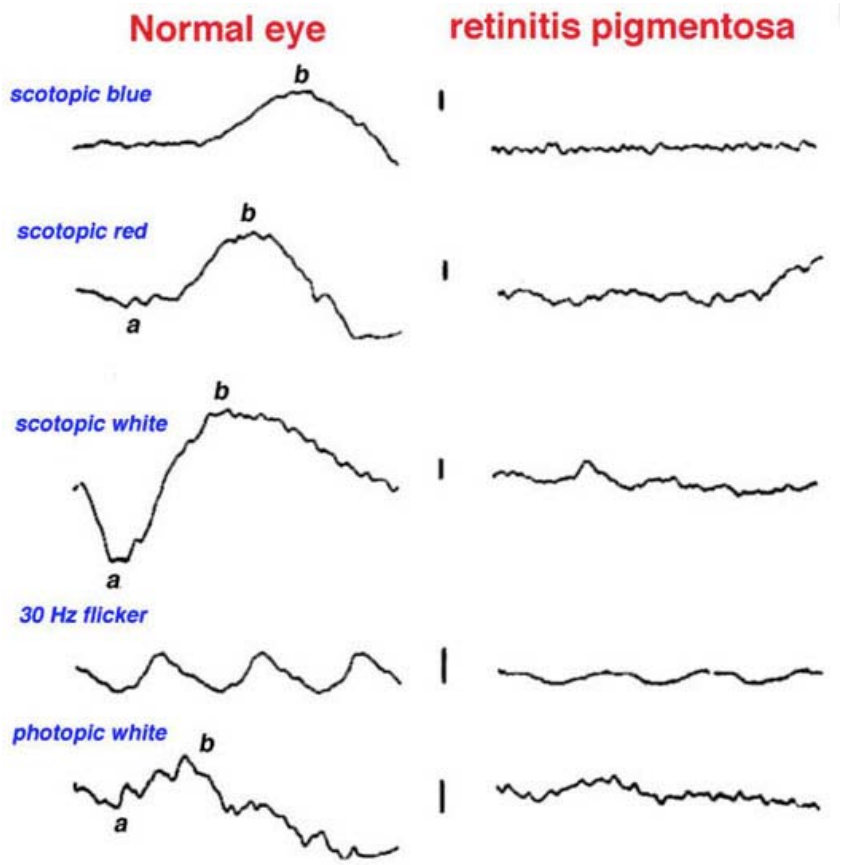
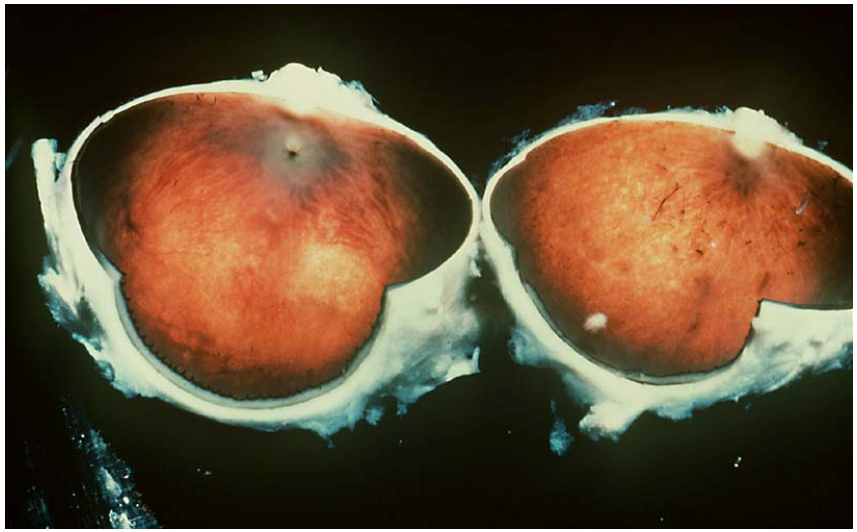
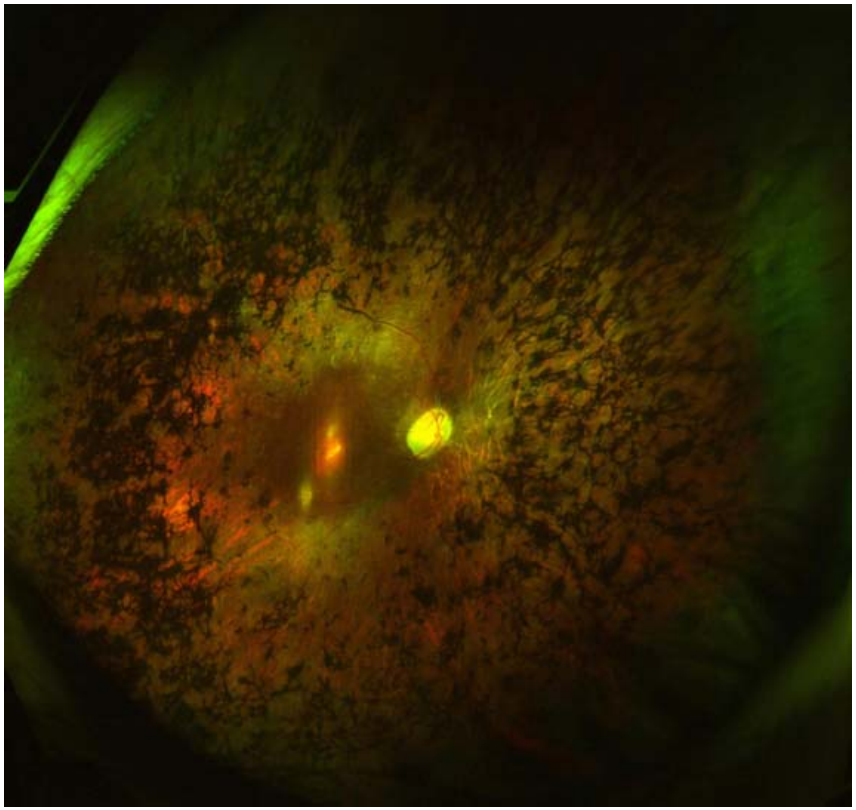


Fig. 13. ERG recordings in a normal patient and one with retinitis pigmentosa.

Medical Knowledge/Practice Based learning and improvement

Pathology





Medical Knowledge/Practice Based learning and improvement

Treatment

- No cure
- Nutritional supplementation or avoidance
  - Vitamin A supplementation controversial
  - Avoid vitamin E
  - Omega-3 fatty acid
    - Major structural lipid of photoreceptor outer segment membranes – possibly involved in rhodopsin regeneration
    - Systemic review of 6 studies demonstrated trends suggestive of improved outcomes with omega-3 fatty acid supplements

Experimental Therapy

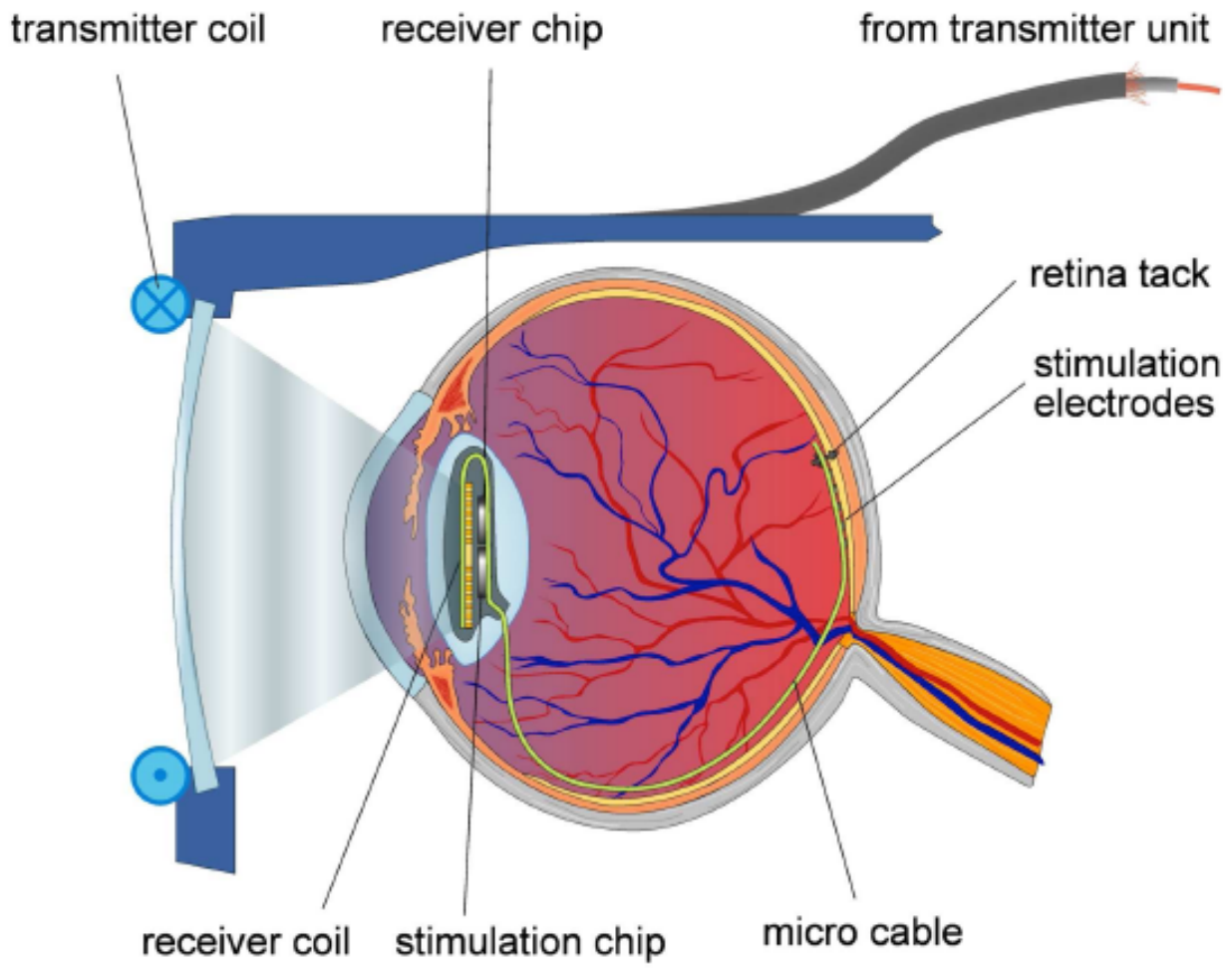
- Retinal prosthetic
- Retinal implantation of retina and retinal pigment epithelium
- Gene therapy

Retinal Prosthesis

- Implantable microelectrode arrays are implanted onto the epiretinal surface
- Data and energy are transmitted via an inductive link from the outside of the eye to the implant
- In the EPI-RET-3 project that included 6 legally blind pts with RP, visual sensations reported as dots, arcs, or lines of different colors and intensities
- Based on current studies, it is believed that ambulatory vision and limited character recognition is a reasonable goal.

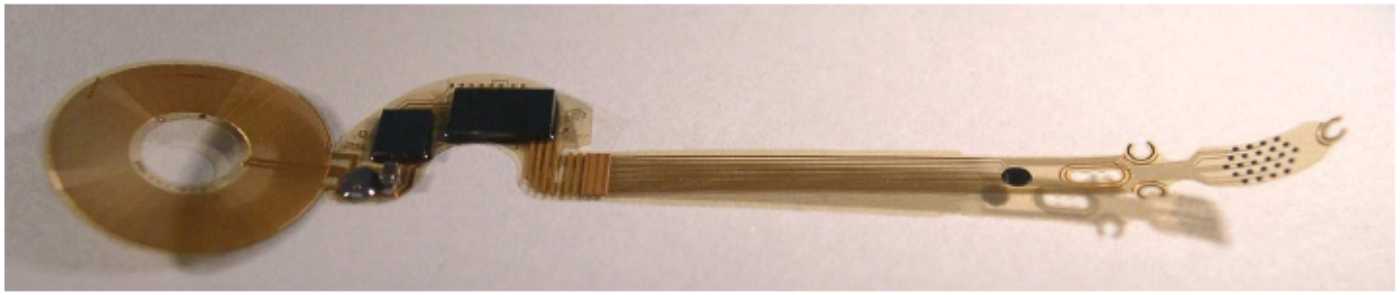
Medical Knowledge/Practice Based learning and improvement

Technical Concept



Retinal Prosthesis

Implant – Fabrication



Fully assembled retinal implant

Encapsulated implant with folded microcoil

Retinal Implantation of Retina/RPE

- The retinal implantation of fetal RPE is based on the theory that this tissue might rescue abnormal photoreceptors in RP
  - Several animal models have been investigated, with the common difficulty of integrating the tissue into the host retina – difficulty encountered in the development of synaptic connections b/w host and implant
- In one study by Radtke et al, 7 of 10 pts (6 with RP, 4 with ARMD) showed improved visual acuity after implantation of neural progenitor cell layers with RPE
- Studies are under way exploring the possibility of utilizing embryonic stem cells

Gene Therapy

- Gene therapy strategies:
  - Corrective expression of the mutated gene, directly reversing the effect of the deficiency resulting from the mutation
  - Non-specific gene therapy, with therapeutic expression of factors that improve the underlying problem indirectly
- Several vectors have been investigated, with the recombinant adenovirus-associated vector (rAAV), found to be one of the optimal and most commonly used vectors
- The vector-gene is administered by subretinal injection

Prognosis

From a multicenter population study, pts with RP who were at least 45 years old were found to have:

- 52% with 20/40 or better vision in one eye
- 25% with 20/200 or worse vision
- 0.5% with no light perception

Our Patient

- Pt plans to return to next visit with more information concerning her father's vision problems.
- Pt was referred for low vision evaluation.
- Plan for referral for ERG.
- Pt encouraged to follow-up for genetic counseling.

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Thank You!

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Dr. Marcus Edelstein