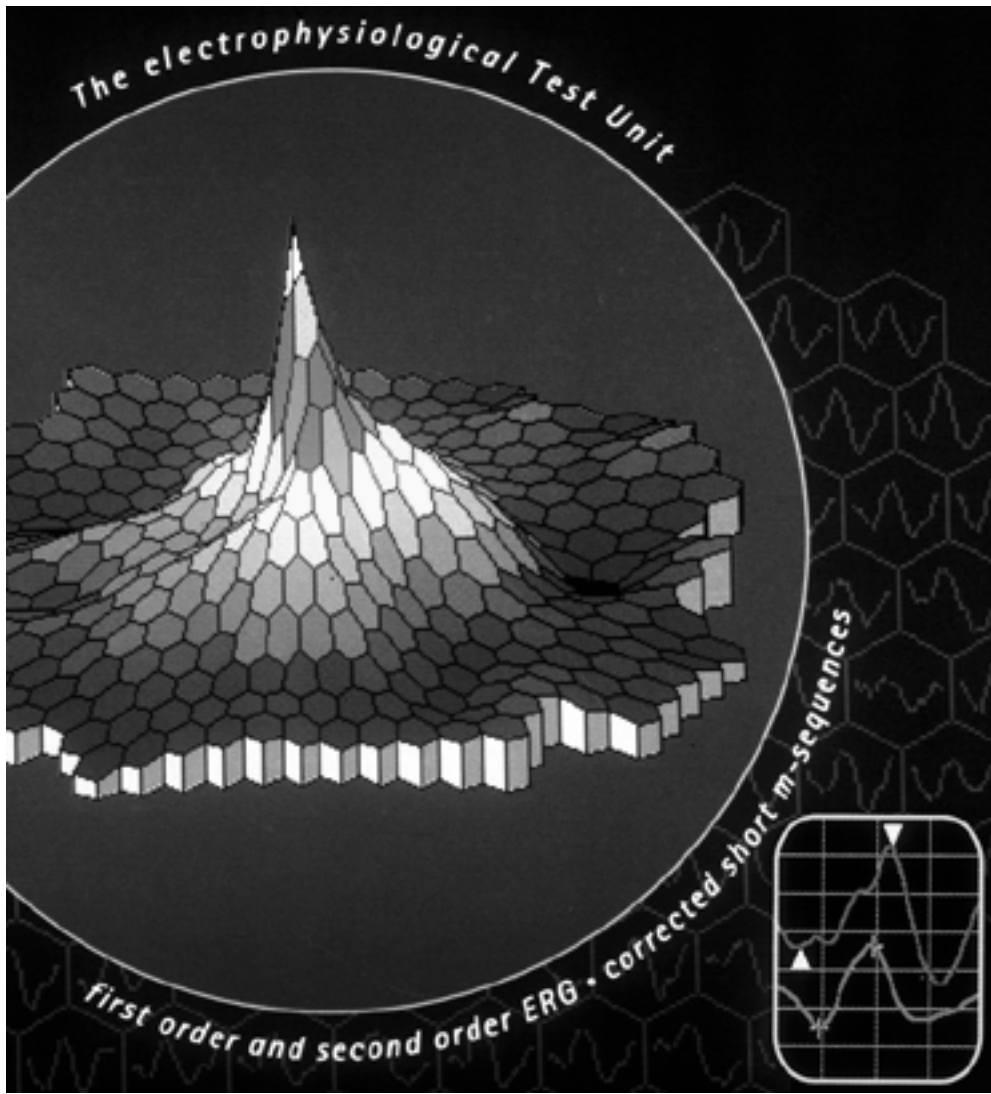


# **ELECTRODIAGNOSIS AND HEREDITARY RETINAL DISEASE**

Revised 2002



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## I. DIAGNOSTIC TESTING

### I.

Diagnostic testing, in conjunction with clinical findings is essential in the differentiation of retinal and choroidal dystrophies.

The following describes some of the current concepts regarding the interpretation of these tests.

#### TESTS:

- |   |                                      |   |                                |
|---|--------------------------------------|---|--------------------------------|
| 1 | Color Vision                         |   |                                |
| 2 | Dark Adaptation                      | ⇒ | Subjective (Psychophysical)    |
| 3 | Electroretinography (ERG)            |   |                                |
| 4 | Electrooculography (EOG)             | ⇒ | Objective (Electrophysiologic) |
| 5 | Visually Evoked Potential (VER, VEP) |   |                                |

### 1. Color Vision Tests

#### Pseudoisochromatic plates (Ishihara, AO-HRR)

- Ishihara plates distinguish red/green colorblinds (protans and deutans) from normals.
- AO-HRR uses universal geometric symbols, plates for Y/B as well as R/G defects.
- The Farnsworth D-15 (15 markers) separate severe defects from mild defects and normal.
- Farnsworth 100-Hue test, with 85 markers, identifies defects as protan, deutan, or tritan.
- Anomaloscopes are devices for distinguishing between anomalous trichromats and dichromats, and between protan and deutan type.

Test	Mode of Operation	Defects Detected	Sensitivity	Base of Administration
<b>Ishihara</b>	Color confusion	R-G only	Extremely sensitive	Difficult for pre-school children and low I.Q.
<b>A.O. H-R-R</b>	Saturation	R-G, B-Y	Will miss very mild R-G; good classification	Excellent for all ages
<b>Farnsworth D-15 Panel</b>	Color confusion	R-G, B-Y	Will only detect severe anomal. Trichrome and dichrom.; good classification	Easy to administer
<b>Farnsworth-Munsell 100 Hue</b>	Hue discrimination	R-G, B-Y and normal "color insensitive"	Extremely sensitive; classify by error scoring	Tedious to administer
<b>Nagel Anomaloscope</b>	Luminosity Match	R-G only	Very sensitive; classify by anomaly (R-G) quotient	Good

<b>Sloan Achromatopsia Test</b>	Hue-Brightness Match	Achromatopsia only	Grossly sensitive; incomplete achromat	Easy to administer
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*\*Carr & Siegel Electrodiagnostic Testing of the Visual System*

## **2. Dark Adaptation**

Nyctalopia, the inability to see at night, is extremely common in retinal and choroidal dystrophies and is indicative of rod dysfunction.

Rods and cones recover sensitivity at different rates in the dark after a bright light

Cones recover more rapidly, however, rods are more sensitive and reach their maximum sensitivity at about 25 to 35 minutes (Final threshold).

In the fovea, there is a rod-free area about 300 $\mu$  (0.3 mm.) (40 minutes in diameter). Only a monophasic cone curve is obtained upon testing this area.

### Retinal Thresholds

At the final rod threshold, points are measured at interval of 5 degrees across both nasal and temporal retinal areas in the horizontal meridian.

## **3. Electroretinogram (ERG)**

### ERG Components

- ERP (Early Receptor Potential) :Originates from cone photopigments.
- A-wave: initial negative component originates in the photoreceptors.
- B-wave: complex positive deflection following the a-wave derived from Muller cells ( mid-retinal area) reflects activity of bipolar region
- C-wave: positive deflection following the b-wave thought to originate in the basal portion of the pigment epithelium.
- Oscillatory Potentials (O.P.): Positive wavelets on the ascending limb of the b-wave thought to originate from the interplexiform or amacrine cell

### Basic Principles of Clinical Electroretinography

The full-field Ganzfeld Electroretinogram (ERG) is a mass retinal response to a flash of light across the entire retina.

Focal retinal responses can be elicited by checkerboard pattern or sinusoidal grating called PERG. The pattern ERG waveforms currently are thought to originate from ganglion cell activity.

Multifocal ERG- response elicited from multiple, small areas across retina.

## **4. Electrooculogram (EOG)**

The EOG is a mass response of the eye to changes in light over time. The test is dominated by the rod system.

Evaluation of the Record

Any LR:DT (Arden) ratio less than 170% is abnormal.

Pathology of the EOG

In Vitelliform Macular Dystrophy (Best's disease) EOG is abnormal. This can be explained by the widespread deposit of lipofuscin found in the RPE.

### **EOG in Specific Diseases**

In general, the EOG is an adjunct to the ERG .

Vitelliform Macular Dystrophy (Best's): ERG normal ,EOG abnormal.

Diffuse Cone Abnormalities EOG normal in congenital, total, color blindness.

### **Visually Evoked Cortical Potential (VEP,VER)**

Summated electrical responses recorded over occipital cortex as a result of retinal (macular) stimulation.

#### **Pattern VEP**

Cortical neurons respond more critically to a patterned checkerboard stimulus than to an unpatterned stimulus .

The primary use of the VEP is to determine macular function or detect optic nerve disease.

#### **Flash VEP and Foveal Function**

Flash VEPs cannot provide reliable data about foveal function. Once the ERG rules out retinal disease, and one finds the VEP abnormal, the location of the disease can be placed either concentrated at the macular or further along the visual pathway.

## **II. Genetics**

### **Autosomal Dominant Inheritance**

- Trait usually appears in every generation. Exception: Best's Disease
- Trait is transmitted by an affected person to 50% of offspring (on average)
- Unaffected persons may transmit trait to their children
- Equal sex incidence

### **Autosomal Recessive Inheritance**

- Trait appears only in siblings, not in their parents offspring, or other relatives
- Parents of affected child may be related
- Equal sex incidence
- One fourth of siblings of propositus, on average affected

### **Sex-Linked Recessive Inheritance**

- Affected males transmit trait to all daughters ( not sons )
- Affected females transmit trait to half their children of either sex

## **III. Rod and Rod-Cone Dystrophies:**

A. Retinitis Pigmentosa (Pigmentary Dystrophy)

B. Atypical Retinitis Pigmentosa

1 Without pigment (sine pigmento)

2 Unilateral

- 3 Sector
- 4 Central , or Inverse
- C. Syndromes Associated with Retinitis Pigmentosa
- D. Leber's Congenital Amaurosis

### Rod and Rod-Cone Dystrophies

A group of hereditary disorders characterized by an early degeneration of the rods, with cones affected later in the disease. Characterized by nyctalopia (night blindness), decreased peripheral visual fields, abnormal dark adaptometry and ERG.

### **A. Retinitis Pigmentosa (RP)**

- Incidence: 5 per 1,000 .
- Heredity: - Sporadic (Isolated) pattern
  - Autosomal Dominant: most benign
  - The most common mode of transmission is autosomal recessive, followed by the dominant and sex-linked forms.

In most studies, the sex-linked and recessive forms are usually the most disabling and rapidly progressing. (VA 20/200 or less by age 30).

### Clinical Findings:

- Attenuated retinal vasculature
- Bone spicule clumping in mid-periphery
- Pallor of the optic disc: (waxy appearance) associated disc hamartomas and drusen (probably not hyaline bodies but gliomas).
- Other associated findings:
  - Macular : cystoid macular edema (60-90%)
  - Posterior subcapsular cataracts
  - Vitreous opacities
  - Visual field constriction: ring scotoma (10-40 degrees). Central 5 degrees remains until late
  - Myopia
  - Chronic open-angle glaucoma
  - Other: keratoconus, strabismus, microphthalmos

Clinical course: Symptoms early teens, by 30, 90% patients diagnosed. Nyctalopia followed by decreased peripheral vision.

### Diagnostic Tests:

Color Vision: Abnormalities parallel cone degeneration, advanced stage blue-yellow defects most common.

Fluorescein Angiography: Diffuse hyperfluorescence(atrophy RPE and cc), bone spicule pigment deposits ,vasculature attenuated, CME .

Dark Adaptation:. Early: curve biphasic with normal cone response, but decreased rod response.( elevated threshold)..Late monophasic, no rod-cone break, flat.

ERG: abnormal to non-recordable (Berson difference in Dominant form).

EOG: abnormal

Visual Fields: ring scotoma between 10-40degrees).Late, central field 5 to 10 degrees (gun barrel.)

Histological Finding: degeneration of the photoreceptors, pigment migration, vessel attenuation, and atrophy of the inner retinal layers and disc..

Etiology of Retinitis Pigmentosa

*See RetNet( internet details all genetic defects in tabular form)*

## **B. Atypical Pigmentary Dystrophy**

### **1. Retinitis Pigmentosa Sine Pigmento (without pigment)**

Pigmentary changes variable; range from the typical "bone-spicule" to subtle "stippled" appearance of the fundus. Advanced cases of retinitis pigmentosa with no pigment are uncommon. Fluorescein show changes in the non-pigmented forms, which can represent early stages. Fundus changes with abnormal diagnostic tests confirm diagnosis.

### **2. Unilateral Pigmentary Dystrophy**

An extinguished ERG in the involved eye with a normal ERG in the other. Most cases , sporadic, definite hereditary pattern.Differential diagnosis must include trauma, inflammation, vascular occlusive.

Nyctalopia not prominent because of the unilateral nature of the disease .

Deafness may also occur.

### **3. Sector Retinitis Pigmentosa**

Pigmentary dystrophy limited to specific sectors of the retina, hereditary pattern either dominant/recessive.

1. 50% both inferior temporal quadrants
2. Pigmentary changes and attenuated vessels limited to these areas (remainder of retina normal)
3. Symmetrical
4. Visual fields: bitemporal field defects can be seen if both nasal quadrants involved.
5. ERG: Usually subnormal/never extinguished. Can have normal/abnormal EOG.

Clinical Findings:

1. Excellent central vision/and minimal nyctalopia
2. Asymptomatic until the 5<sup>th</sup> or 6<sup>th</sup> decade
3. Progression extremely slow
4. Deafness few cases

### **4. Central "inverse"**

Uncommon pigmentary changes macular. Progresses to profound central visual loss.

Clinical Findings:

1. Decreased visual acuity, color abnormalities, and central scotomas.
2. Visual fields: central scotoma.
3. Dark Adaptation normal
4. ERG is abnormal, photopic more involved
5. Color vision: abnormal

**C. Retinitis Pigmentosa Associated Syndromes**

Laurence-Moon and Bardet-Biedl.

	Laurence-Moon	Bardet-Biedl
Pigmentary Retinopathy	choroidemia-like	Cone-rod-like
Mental Retardation	+	+
Hypogenitalism	+	+
Short stature	+	+
Polydactyly	-	+
Obesity	-	+
Spastic Paraplegia	+	-

**Usher's Syndrome (AR)**

- RP with deafness
- Variable vestibular, speech and retardation
- ERG non- recordable

**Refsum's Syndrome**

- \* Cerebral ataxia      \* Anosmia
  - \* Polyneuritis        \* Auditory defect
  - \* Retina degenerates(no bone spicules)
  - \* Increased CSF protein without pleocytosis
- Treatment : Low phytenic acid diet.

**Bassen-Kornsweig**

- Abetalipoproteinemia with Vitamin A malabsorption and steatorrhea causes RP
  - Acanthocytosis (on peripheral blood)
  - Ataxic neuropathy
  - Growth retardation
- Treatment with:I.M. Vit A (returns to normal dark adapt, ERG response increase).

**Spielmeier Vogt-Batten-Mayou**

- R.P.-like with bull's eye macula
- Seizures, progressive dementia, ataxia
- Vacuolation of peripheral lymphocytes
- Metachromasia of skin fibroblasts in cell culture (carriers also).

**Progressive External Ophthalmoplegia**

- 50% with positive family history
- Facial weakness, ptosis, ophthalmoplegia with diplopia
- Dysphagia
- Small stature
- Cardiac conduction defects (can have heart block)

- Retinal findings:
  1. salt and pepper RPE changes
  2. progresses to a R.P.-like disease.

#### Leber's Congenital Amaurosis (Congenital RP)

- Autosomal Recessive
- Blind infant, nystagmus
  - Fundus can be normal, progress to clumps of pigment (Range)
  - Hyperopic, Oculo-Digital sign
- Associated: Macular coloboma, Keratoconus.
- ERG: extinguished.

### **IV. Vitreo-Tapeto Retinal Dystrophies**

#### 1. Goldmann-Favre

Autosomal Recessive

Clinical findings:

Vitreous veils

Peripheral and foveal retinoschisis

Peripheral pigmentary changes similar to RP are present

Optic nerve pallor and attenuated vessels

Complicated cataracts

Course: Onset first/second decade

1. Nyctalopia
2. Decreased vision
3. progressive to severe loss of visual acuity.

Tests: B/Y color; Dark Adaptation, ERG, EOG, and VF are abnormal

#### 2. Wagner's Vitreoretinal Dystrophy

Autosomal Dominant

Clinical Findings:

Optically empty vitreous with strands.

Myopia

Pigmentary retinopathy

Retinal breaks and holes (no RD)

Cataracts

Clinical Course:

- No nyctalopia
- Color vision, DA, VF, EOG: Normal
- ERG: subnormal (b-wave) milder than Goldmann-Favre minimal decrease in scotopic ERG)

#### A. Stickler's Syndrome

Autosomal Dominant

Joint involvement:

Hyperextensibility

Midfacial Hypoplasia

Ocular findings:

Optically empty vitreous with bands  
Retinoschisis

B. Snowflake Vitreoretinal Dystrophy

Autosomal Dominant

- Sheathings of the retinal vessels peripherally with heavy clumps of pigmentation. Eventual rhegmatogenous retinal detachment
- Cataracts/myopia

Course: Similar to Wagner's

**V. Hereditary Macular Diseases**

1. Autosomal Recessive, Dominant, & X-linked
  1. Bilateral
  2. Symmetrical
  3. Positive Family History (examine family members whenever possible)
2. Tests:
  - A. Objective (Electrophysiologic)
    1. ERG
    2. EOG
    3. VER (VEP)
  - B. Subjective (Psychophysical)
    1. Dark Adaptometry (Retinal Profiles)
    2. Visual Fields
    3. Color vision
  - C. Fluorescein Angiography
3. Clinical Uses of Electrophysiologic Tests (Objective)
  - A. Children under 8 years
  - B. R/O generalized tapetoretinal degeneration (Retinitis Pigmentosa)
  - C. R/O stationary vs. progressive disease
  - D. Determine anatomic site of physiologic abnormality
  - E. Aid in genetic counseling (carrier state, i.e. Best's Disease)
  - F. Pre-surgical evaluation (in opaque media)

**HEREDITARY MACULAR DISEASES**

	Heredity	ERG	EOG	DA
Best's (Vitelliform) Dystrophy	A.D.	Normal	Abnormal	Normal
Patterned Pigment Dystrophies				
1. Butterfly Dystrophy	A.D.	Normal	Abnormal	Normal
2. Reticular Dystrophy of RPE (Sjogren's Disease)	A.D./A.R.	Normal	Abnormal	Normal/Abnormal
3. Macroreticular	A.D./A.R.	Normal	Abnormal	--
Stargardt's (Fundus Flavimaculatus)	Autosomal Recessive	Normal	Normal	Normal
Dominant Progressive Foveal Dystrophy (Stargardt's)	A.D.	Normal	Normal	Normal

Progressive Cone Dystrophy	Autosomal Dominant	Abnormal Photopic	Normal	Abnormal
Sorsby's Dystrophy	A.D.	Normal	Normal	Normal
Congenital Retinoschisis	X-linked	Decreased b-wave	Normal	Normal
Dominant Hereditary Drusen	A.D.	Normal	Normal	Normal
Benign Concentric Annular Macular Dystrophy	Autosomal Dominant	--	--	--
Dominant Slowly Progressive Macular Dystrophy (Singerman-Patz)	Autosomal Dominant	Normal	Normal	--
Dominant Cystoid Macular Edema	Autosomal Dominant	Normal	Abnormal	--
Fenestrated Sheen Macular Dystrophy	Autosomal Dominant	Abnormal Photopic	Abnormal	--
Central Areolar Dystrophy	Autosomal Dominant	Normal	Normal	Normal
Goldmann-Favre	A.R.	Abnormal	Abnormal	Abnormal

### Congenital Stationary Nightblindness

	Heredity	ERG	EOG	DA
<u>Abnormal Fundus</u>				
• Fundus Albipunctatus	A.R.	Abnormal	Abnormal	Abnormal
• Oguchi	A.R.	Abnormal	Normal	Abnormal
<u>Normal Fundus</u>	A.R., A.D., X-linked	Abnormal		

#### A. Best's Vitelliform Degeneration

Autosomal dominant

Age of Onset: 1<sup>st</sup> decade

Clinical findings:

Early: Yellow egg yolk in macula

Later: "Scrambled-egg" scarred lesion in macula (20/200)

ERG: Normal

EOG: Abnormal; also identifies "carriers" of the disease even with normal fundus.

Histology: accumulation of lipofuscin throughout the RPE (no dark choroid)

#### B. Butterfly Dystrophy

Autosomal dominant

ERG: normal

EOG: abnormal

Fundus: pattern in macula "butterfly-shaped"

C. Stargardt's Disease

Autosomal Recessive

First decade of life.

Stargardt's disease is identical to Fundus Flavimaculatus consists of numerous yellow "flecks" around the macular area and scattered throughout the posterior retina a high incidence of macular degeneration.

Clinical Findings:

a. Development of a "bull's-eye" lesion and a "beaten bronze" appearance.

Clinical Course: In early stages, vision 20/25 to 20/60 eventually progresses to 20/200.

Color Vision: red-green defect initially

Fluorescein Angiography: a bull's-eye lesion is present. Silent/dark choroid due to lipofuscin in RPE.

Dark Adaptation: normal

ERG: Normal or slightly abnormal

EOG: Usually normal until the later stages.

Histological Findings: Lipofuscin found widespread in the RPE.

D. Dominant Progressive Foveal Dystrophy:

Similar to Stargardt's disease except dominant mode of inheritance.

Peripheral flecks may or may not be present.

The disc and retinal vessels are normal.

Clinical Course: Progression slower, eventually reduced to 20/200.

E. Progressive Cone Dystrophies

Diffuse cone disease with normal or minimally abnormal rod responses.

Abnormalities in color vision, decreased central vision, and an abnormal photopic ERG.

Heredity: Most sporadic

Clinical Findings

- "Bulls-eye" lesion, diffuse pigmentary changes in the macula
- Optic pallor and atrophy
- Retinal vessel attenuation
- Peripheral retinal changes vary (flecks similar to FF to RP like picture)
- Acquired nystagmus present in 20%

Clinical Course: vision between 20/60 and 20/100. Photophobia

Tests:

Color vision: Abnormal early, preceding visual loss

Dark adaptation: rod phase only

Color Vision Abnormalities Severe

Abnormal Farnsworth-Munsell 100, the Sloan achromatopsia test, and Nagel anomaloscope.

Fluorescein: Multiple "window" defects

ERG: Abnormal photopic flicker fusion can progress to a decreased scotopic b-wave with high intensity flashes (thought to be a cone function).

EOG: Normal or abnormal  
 Visual Fields: Central Scotoma.

### Stationary Cone Disorders

Stationary defects in color vision. Vision reduced in rod monochromatism, normal or near normal in anomalous trichromatism, Dichromatism, and cone monochromatism. Congenital, lack of progression distinguishes from other cone dystrophies.

### Color Defects with Decreased Vision

- a. Rod monochromatism (complete): congenital achromatopsia.  
 Autosomal Recessive  
Clinical Findings:
  - Normal retinal examination
  - Photophobia
  - Pendular nystagmusClinical Course: Decreased vision, photophobia, and nystagmus. Stable.  
 Color Vision: Abnormal  
 Fluorescein: Normal  
 Dark Adaptation: Cone limb is abnormal/absent. Rod foveal threshold is normal  
 ERG: photopic abnormal , normal or mildly abnormal scotopic.  
 EOG: Normal  
 Visual fields: Central Scotoma..  
 Histology:.. Extrafoveal cones are decreased in number. Rods are normal.
- b. Rod Monochromatism (incomplete): Differs only in degree from rod monochromatism. The vision is better (20/40 – 20/100), nystagmus and photophobia are less severe or absent, and some color vision may be present. ERG changes are less.
- c. Blue-Cone Monochromatism  
 Heredity: Sex-linked  
 Clinical Findings: findings of rod monochromatism but less severe.  
 Adaptation:  
 Some cones sensitive to blue remain:
  - Poor vision
  - Nystagmus
  - Myopia
 ERG: Absent flicker Peak Central Sensitivity: 440 nm  
 Fundus: Normal

### F. Hereditary Familial Drusen

Yellow white retinal deposits at the level of RPE and Bruch's membrane. Occur in the posterior pole. Described as Hutchinson-Tay Choroiditis, Doyme's Honeycomb Choroiditis and Malattia Leventineses  
 Autosomal dominant

Small white dots in macular area become larger, more numerous, confluent calcified by fifth decade.

Vision between 20/30 and 20/80 unless SRNV → 20/200

Fluorescein: Early, show typical window defects when SRNV leakage occurs

Color, Dark Adaptation, ERG, EOG, VF – normal

Histology : Drusen; acid mucopolysaccharide (sialic acid)

Treatment: Laser for SRNV.

#### G. Juvenile Retinoschisis (Congenital)

Hereditary: Sex-linked

Onset: fourth decade (males)

Splitting of inner retina, Vitreous heme secondary to broken retinal vessels.

ERG: absent b-wave

EOG: normal

Dark Adaptation: normal

#### H. Sorsby's Pseudo-Inflammatory Macular Dystrophy

Hereditary: dominant

Onset: fourth decade

progresses to very poor vision (20/100 or less)

macular exudates, hemorrhage and scar.

ERG; normal

EOG: normal

Dark Adaptation: normal

Visual Fields: central scotoma

### **VI. Choroidal Dystrophies**

#### Choroidal Atrophy of Choriocapillaris

##### A. Regional

1. Central areolar
2. Diffuse generalized choriocapillaris atrophy
3. Peripapillary

##### B. Generalized

1. Gyrate Atrophy
2. Choroideremia

##### A 1. Central Areolar Choroidal Dystrophy

Hereditary: Dominant

Clinical findings: Lesions bilateral, symmetrical; gradually enlarge over years (VA to 20/200)

Onset: third decade

Fundus: Early loss of foveal reflex followed by atrophy of pigment epithelium and choriocapillaris leaving the larger choroidal vessels visible. Optic disc pallor and vessel attenuation are rare. Sharply outlined zone of pigment epithelium and choriocapillaris atrophy in and around the fovea.

Symptoms and Clinical Course: Decreased vision and color.

Diagnostic Tests:

Color vision: Reduced in proportion to visual acuity

Fluorescein Angiography: Central RPE and choriocapillaris atrophy

Visual Fields: Central Scotomas

ERG, EOG, Dark Adaptation: Normal

A. 2. Diffuse Generalized Choriocapillaris Atrophy:

Hereditary: Autosomal Dominant

Clinical Findings:

Onset: third decade.

Fundus: Usually begins in central or peripapillary area. Peripheral lesions may also appear independently of central ones and progress towards center.

Eventually, entire fundus shows choriocapillaris atrophy. Retinal vessels attenuation and optic pallor are common (not as early as RP)

Symptoms and Clinical course: The initial decrease in visual acuity/color vision common early symptoms progress slowly. Nyctalopia field constriction becomes quite severe as the disease progresses. Patients are incapacitated by the fifth decade although some do retain useful vision for many years.

Tests:

Color vision: Reduced in proportion to visual acuity

Fluorescein Angiography: Choriocapillaris atrophy

Visual Fields: Peripheral constriction

Dark Adaptation: Abnormal

ERG: Abnormal

EOG: Abnormal

B 1. Gyrate Atrophy

Inheritance: Autosomal recessive

Age of onset: second or third decade

Symptoms

Nyctalopia

Constricted visual field

Signs:

Scalloped, well-circumscribed borders of loss of choriocapillaris and RPE

Myopia

Visual field very restricted, but patient may retain good central vision.

ERG: Abnormal (may be absent)

Diagnosis:

Hyperornithinemia (elevated serum ornithine)

Mild/severe form exists, reduction in ornithine has been obtained with vitamin B6 (pyridoxine)\* therapy.

Restriction of arginine may be beneficial.

Carrier: Carriers have decreased ornithine ketoacid transaminase (OKAT) (in cultures of skin fibroblasts)

B. 2. Choroideremia:

Inheritance: Sex-linked

Carrier sign: salt and pepper changes of fundus in mother of affected

Functional studies normal in mother

Age: first decade

Symptoms: Nyctalopia, decreased peripheral field

Signs:

1. Early: Granulation in macula; midperiphery: degeneration to posterior pole. Retinal pigment epithelium and Choriocapillaris.
2. Late: Only normal RPE and choriocapillaris in macula

ERG: Abnormal

Dark Adaptation: Abnormal

EOG: Abnormal

Note: Female carrier signs are found in: \* (Carrier signs not seen in juvenile retinoschisis), (*typical Board question*)

- Albinism
- Choroideremia
- RP

### **VIII. Congenital Stationary Night Blindness**

#### **A. Fundus Albipunctatus (Congenital Stationary Nightblindness)**

Heredity: Autosomal Recessive

Signs and Symptoms: congenital stationary nightblindness, good vision, multiple, small yellow white lesions, (varying shapes) usually spare fovea, optic nerves and retinal vasculature normal.

ERG: Abnormal

EOG: Abnormal

Dark Adaptation: Abnormal

Visual Field: Normal

VEP: Normal

After 3 hours dark adaptation regeneration of rhodopsin finally allows for normal ERG, EOG, and Dark Adaptation.

Course: Maintain good vision throughout life, no macular degeneration. New milder form recently discussed which indicates variable expressivity in this disease. Lesions more confluent extend out to periphery and functional testing more benign.

\* (See bibliography Margolis, S., Siegel IM, Ripps H; Variable Expressivity in Fundus Albipunctatus, Ophthalmology 94,1416, 1987)

#### **B. Oguchi's Disease**

Heredity: Autosomal Recessive

Onset: congenital

Symptoms: Nightblindness (nyctalopia)

Signs: Unusual brilliant, golden-yellow, metallic sheen in posterior pole and mid-periphery. Color deep to vessels "Mizuo-Nakamura phenomenon": Abnormal color of fundus disappears after 2-3 hours dark adaptation.

Return of abnormal sheen on light exposure.

\*ERG: Abnormal (absent b-wave)

\*EOG: Normal

\*Dark Adaptation: Normal

Fluorescein Angiography: Normal

Color Vision: Normal

Visual Fields Normal

Fundus Reflectometry: Normal

VEP: Normal

Histopathology: Abnormal layer of fuscine granules between RPE and Rods & Cones.

(Yamanaka AJO 68:19, 1969) Abnormal position of cone nuclei, double row of cones? (Kuwabara et al: Acta Soc. Ophthal. Jap. 67:1323, 1963)

### **IX. Bibliography**

Allikmets, R. et al A photoreceptor cell specific ATP-binding transporter gene (ABCR) is Mutated in recessive Stargardt Macular Dystrophy Nature Genet. 1997:15,236-46

Arden GB, Carter RM, Hogg C, Siegel IM, Margolis S: "A Gold Foil Electrode: Extending the Horizons for Clinical Electroretinography." Investigative Ophthalmology, 18, 421-25, 1979

Berson E, et al: Ocular Findings in Patients with Autosomal Dominant RP and a Rhodopsin Gene Defect (Pro-23-His), Archives of Ophthalmology, 109; 92-101, 1991 (Jan).

Carr R, Siegel IM: Electrodiagnostic Testing of the Visual System: A Clinical Guide, F.A. Davis Co., Phila. 1990

Carr RE, Margolis S, Siegel IM: "Fluorescein Angiography and Vitamin A and Oxalate Levels in Fundus Albipunctatus." American Journal of Ophthalmology, 82: 549-58, 1976

Dryga T, Berson E, Ruo V, Oprian D: "Heterozygous Mutation in Rhodopsin Gene as a Cause of Congenital Stationary Night Blindness." Nature Genetics, 4: 280-3, 1993 (Jul)

Fishman GA, Sokol S: "Electrophysiologic Testing in Disorders of the Retina, Optic Nerve, and Visual Pathways." American Academy of Ophthalmology, San Francisco, 1990

Humphries P, Kenna P, Farrar L: "Molecular Genetics of RP." Science 256: 804-13, 1992, (May)

Kraushar M, Margolis S, Morse P, Nugent M: "Pseudohypopyon in Best's Vitelliform Macular Dystrophy." American Journal of Ophthalmology, 94, 30-37, 1982

Margolis S: "Electrotests Aid in Diagnosis of Retinal and Optic Nerve Disease." 4, Ophthalmology Times, 1981, Oct

Margolis S, Siegel I, Ripps H: "Variable Expressivity in Fundus Albipunctatus," Ophthalmology, 94: 1416-22, 1987

Miyake Y: "Layer-by-Layer Analysis of Macular diseases with Objectively Measured Visual functions." Journal of Ophthalmology, 34: 225, 1990

Musarella M: "Mapping of X-Linked Recessive RP Gene." Ophthalmic Pediatrics & Genetics, 2 (2): 77-88, 1990

Muserella, M. Gene Mapping of Ocular disease Survey of Ophthal. 1992:36, 4, 285-311

\*RetNet: Summary of Genes Causing Retinal Diseases 1-2  
<http://www.sph.uth.tmc.edu/Retnet/sum-dis.htm> last updated January 1, 2000

\*RetNet: Cloned and/or Mapped Genes Causing Retinal Diseases 1-24  
<http://www.sph.uth.tmc.edu/Retnet/sum-dis.htm> last updated January 1, 2000

\*RetNet: What's New in Genes Causing Retinal Diseases 1-4  
<http://www.sph.uth.tmc.edu/Retnet/sum-dis.htm> last updated January 1, 2000

Smith D, Oestreicher J, Musarella MA: "Clinical Spectrum of Leber's Congenital Amaurosis in the Second to Fourth Decades of Life." Ophthalmology, 97: 1156-1161, 1990.

To K, Nadel A, Perlstein S, Margolis S: "Bilateral Optic Disc Neovascularization in Association with RP." Canadian Journal of Ophthalmology, 26: 152-155, 1991

*\*You may want to copy RetNet from the internet. It lists all the chromosomal and genetic defects in different diseases.*