

Autoimmune Disease and the Eye

Anthony DeWilde, OD FAAO

1

Disclosure

Financial disclosures: No financial disclosures

2

anthony.dewilde@va.gov

3

Goals

Manifestations

Diagnosis/Treatment

Referral

4

American Autoimmune Related Diseases Association

- Takes ~4.5 yrs to be diagnosed
- See 4 different doctors before they are diagnosed

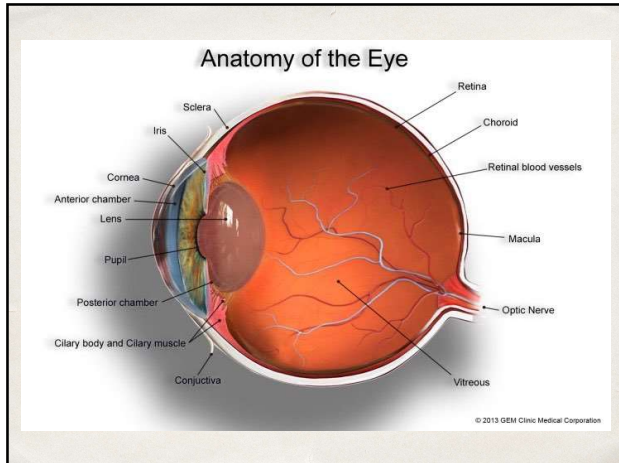
2nd highest cause of chronic illness in the US

5

Autoimmune Disease

Ankylosing Spondylitis	Myasthenia Gravis
Chron's Disease	Psoriasis
Giant Cell Arteritis	Rheumatoid Arthritis
Graves' Disease	Sarcoidosis
Lupus Erythematosus	Sjögren's Syndrome
Multiple Sclerosis	Ulcerative Colitis

6



7

External

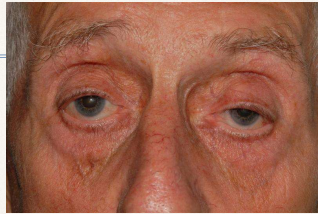
Ptosis

Exophthalmos

Diplopia

8

Ptosis



Myasthenia Gravis

Any patient with Diplopia or Ptosis

Especially women under 40, men over 60

9

Myasthenia Gravis

Greek and Latin meaning

"grave muscle weakness"

10

Myasthenia Gravis

Chronic autoimmune neuromuscular disease

Muscle weakness and fatigue

Eyelid muscles first affected in most cases

11

Myasthenia Gravis

15% have Ocular only

Can take up to 3 years to become General

60-90% start with ocular manifestation

12

Myasthenia Gravis

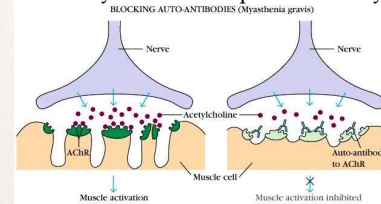
Can involve breathing and swallowing

Myasthenic Crisis

13

Myasthenia Gravis

Antibodies destroy or alter receptors for acetylcholine



14

Myasthenia Gravis

In office testing

Ice-pack test

Upgaze test

Lid squeeze

Cogan lid twitch

Orbicularis resistance

15



Figura 1 - Aspecto clínico da ptose palpebral miastênica. A) Pré-teste do gelo; B) Pós-teste.

Arq. Bras. Oftalmol. vol.73 no.2 São Paulo Mar./Apr. 2010

16

Myasthenia Gravis

Other testing

Tensilon (rarely done)

Acetylcholine receptor antibodies

Anti-MuSK antibody (muscle specific kinase)

EMG

17

Myasthenia Gravis

Labs

Anti-AchR

Anti-MUSK

Will be negative in 50% of Ocular MG

Positive in 90% of General MG

18

Myasthenia Gravis

Treatment

Cholinesterase inhibition (pyridostigmine)

Corticosteroid

Immunosuppressants

Plasmapheresis

Intravenous IVIg

19

Myasthenia Gravis

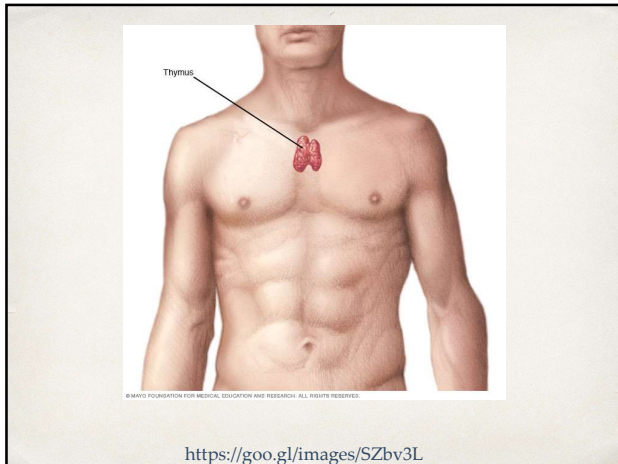
Surgery

15% of MG patients have tumor of Thymus

Every patient needs Chest X-Ray or CT

Often require Thymectomy

20



21

Myasthenia Gravis

Refer to Neurology

Test Thymus

Test for generalized Myasthenia Gravis

22

Myasthenia Gravis

RH - 55 Y/O

Healthy eyes

New CN IV Palsy

+DM, +HTN

NO neuro symptoms

23

Myasthenia Gravis

Resolved 6 weeks later

24

Myasthenia Gravis

4 months later

Ptosis

Ice pack

Pre 2 mm

Post 9 mm

25

Myasthenia Gravis

Upgaze fatigue

+ Cogan lid twitch

AchR Antibodies very elevated

26

Myasthenia Gravis

RH has difficulty with meds

Variable diplopia!!

What's best Tx for this?

Remains ocular only

27

Myasthenia Gravis

TH is 65 y/o black male

Complains of diplopia 10/2015

Dx: Medial Rectus Palsy with ptosis

28

Myasthenia Gravis

TH has DM, HTN

No other neuro complaints

Pupils normal

What tests do you order?

29

Myasthenia Gravis

Resident said RTC 6 weeks

30

Myasthenia Gravis

TH complains of diplopia 12/2015

No improvement

What tests?

31

Myasthenia Gravis

Ice pack 3mm -> 5mm

Cover test showed greater exo and hypo

Ptosis!

Ordered labs

32

Myasthenia Gravis

ACHr mod AB – 83 (normal 0-32)

ACH Binding AB – 7.1 (normal 0-0.3)

ACH receptor blocking AB – 46 (normal 0-15)

Chest x-ray and Chest CT normal

EMG performed looking for Generalized MG

33

Myasthenia Gravis

Under care of Neuro

Pyridostigmine

Eye patch

34

Exophthalmos

Graves' Disease/Thyroid Eye Disease

35

Graves' Disease

Autoimmune Disease

Skin

Thyroid

Orbit

Mental Health

36

Patient DS

20/25 OD and OS

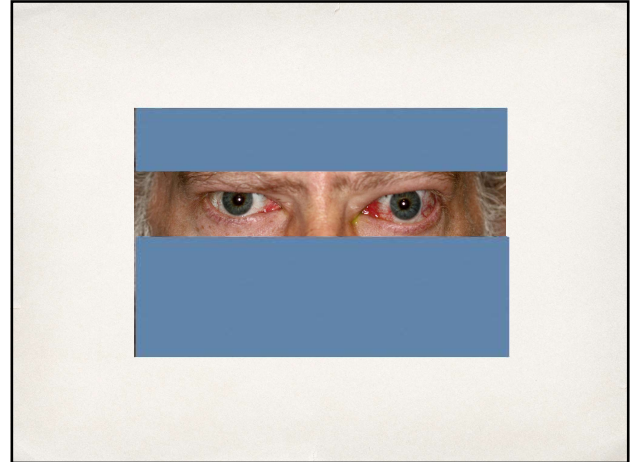
IOP 18/18

No APD

Diplopia in lateral and downgaze

Pain in lateral gaze

37



38

Exam

Exophthalmos OS

Hertel 19/23

Lagophthalmos

Conjunctival edema and injection

Eyelid edema

39

Labs

TSH = 0.003 (normal = 0.47-5.00)

T4 = 20.3 (normal = 4.5-12)

40



41



42

Referral

Endocrine

Oculoplastics

Inform PCP of findings

43

5 months later

IOP 18/24

? APD OS

Start IOP Timolol 0.5%

Start Oral Pred (40 mg)

44

6 months later

IOP as high as 38/28

Oral Pred now 80 mg

+ APD OS

IOP 19/19 on Travatan, Cosopt, Alphagan

Refer for Orbital Decompression

45

After Orbital Decompression

Develops Diplopia

But...IOP 12/14 on meds

46

Now S/P:

Orbital Decompression

Strabismus Surgery

Eyelid Retraction

Now has 20/80 cataract

47

Last Visit

20/20

Single vision

Normal IOP

48

Graves' Disease

77% are Hyperthyroid

Sweat, tremor, weight loss

3% are Hypothyroid

Cold, weight gain, hair loss

20% are Euthyroid

"Autoimmune Thyroid Disease"

49

Graves' Disease

Nomenclature

Graves' is typically Hyperthyroid!

Consider hypothyroid/euthyroid patients

50

80% of Euthyroid patients will develop Thyroid Dysfunction

51

Thyroid Eye Disease can precede Thyroid Dysfunction by 18 months

52

Graves' Disease

30-50% of Graves' patients have orbitopathy

2-5% serious complications

53

Graves' Disease

Dry eye

Injection

Eyelid retraction

Diplopia

Compressive Optic Neuropathy

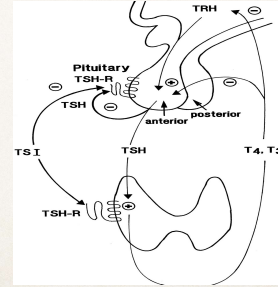
54

Graves' Disease

Increased antithyroid antigens
 TSH receptor antibodies
 Increased T3, T4
 Decreased TSH

55

Graves' Disease



56

Graves' Disease

Increase in
 Fibroblasts
 Hyaluronic Acid
 Collagen
 Adipose

57

Graves' Disease

Exophthalmos

Hertel

Asian upper limit = 18

White upper limit = 21

Black upper limit = 24

58

Graves' Disease

Free T3 and T4
 TSH
 Anti-thyroglobulin (TSI)
 Thyrotropin-Binding Inhibitory Immunoglobulin (TBII)
 Thyroid Peroxidase (TPO)
 Refer to Endocrine

59

Graves' Disease

CT allows measurement of

Orbital fat

Lacrimal gland

Extraocular muscles

MRI for serial imaging

60

Graves' Disease

Treatment

- Quiet inflammation - Steroid
- Stabilize Thyroid
- Medication
- Surgery
- Radioiodine

61

Graves' Eye Disease Symptoms

GRAVES' OPHTHALMOPATHY OR GRAVES' ORBITOPATHY (GO)

Treatment

- Ocular Comfort
- Prism
- Surgery

Graves' eye disease symptoms:

- Swelling around the eyes
- Bulging eyes
- Crity sensation in the eyes
- Pressure or pain in the eyes
- Puffy eyelids or retracted eyelids
- Reddened or inflamed eyes
- Light sensitivity
- Double vision
- Dry, gritty and irritated eyes
- Trouble moving the eyes
- Vision loss

Normal:

- In graves disease sometimes also gether

62

Graves' Orbitopathy

Surgery

- Orbital Decompression (plus radiation)
- Strabismus
- Eyelid
- Cataract

<http://thyroideyes.org/resources/Thyroid>

63

Graves' Orbitopathy

Biological Therapies

Teprotumumab (Tepezza)

- binds to IGF-1R
- Improved proptosis!

Am J Ophthalmol 2019;208:281-288

64

Proptosis Response (Reduction of ≥ 2 mm) Over Time

Time Point	Teprotumumab (N=41) (%)	Placebo (N=42) (%)
Baseline	0	0
Week 6	56.1	7.1
Week 12	75.6	14.3
Week 18	82.9	14.3
Week 24	82.9	9.5

Difference: 73.4% (95% CI 58.8, 88.0)

Am J Ophthalmol 2019;208:281-288

65

Element*	Each visit	Comparison with previous visit	Score
Roundness behind the globe over last four weeks	x		x
Pain with eye movement during last four weeks	x		x
Redness of the eyelids	x		x
Redness of the conjunctiva	x		x
Swelling of the eyelids	x		x
Chemosis (edema of the conjunctiva)	x		x
Ipsilateral chemosis (both body of medial canthus of eye)	x		x
Increase in proptosis ≥ 2 mm		x	x
Decreased eye movements $\geq 15^\circ$ any direction		x	x
Decreased visual acuity ≥ 1 line on Snellen chart		x	x

Am J Ophthalmol 2019;208:281-288

66

Graves' Disease

Affects up to 1/3 of Graves' patients

Attention

Mood

Anxiety

67

Graves' Disease

Smoking makes disease worse

Smoking makes treatment less effective



68

Diplopia

Graves' Disease (common)

Myasthenia Gravis (common)

Multiple Sclerosis (common)

Giant Cell Arteritis (uncommon)

69

Multiple Sclerosis

Is MS an autoimmune disease?

70

Multiple Sclerosis

Demyelinating disease

Can cause diplopia

Transient

71

Multiple Sclerosis

Consider testing if:

Young patient

Other neurologic symptoms

Lhermitte symptom

Uhthoff phenomenon

Optic Neuropathy

72

Episcleritis

Not as likely to be autoimmune

Consider testing if

- Recurrent
- Nodular

73

Scleritis

- Rheumatoid Arthritis*
- Lupus
- Ulcerative Colitis
- Ankylosing Spondylitis
- Reactive Arthritis
- Psoriatic Arthritis

74

Scleritis



<http://www.aaopt.org/theeyeshaveit/red-eye/scleritis.cfm>

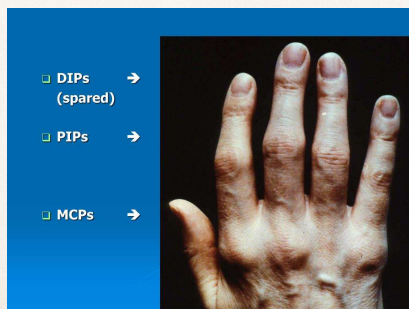
75

Rheumatoid Arthritis

- Inflammatory damage to small joints
- Mostly hands and feet
- Pain, swelling, and possible deformity
- Can cause pain in larger joints
- Hip, shoulder, knees, ankles, and elbows

76

Rheumatoid Arthritis



77

Rheumatoid Arthritis

- Diagnosed with a combination
- Blood work
- X-ray
- Clinical signs/symptoms

78

Rheumatoid Arthritis

Treated with NSAIDs for mild cases

Steroids

DMARDs (i.e. Methotrexate)

Immune modulating drugs (i.e. Enbrel)

79

Rheumatoid Arthritis

Most likely systemic cause of scleritis is RA

Only 50% of patients with scleritis have associated condition

80

Rheumatoid Arthritis

Patients with RA and scleritis have

Widespread and aggressive systemic disease

May need more aggressive therapy

81

Lupus

Autoimmune disease that affects

Joints, skin, kidneys, blood cells, brain, heart and lungs

Symptoms include

Fatigue, shortness of breath, chest pain

82

Lupus

Classic "butterfly" rash on cheeks and nose



83

Lupus

Most commonly seen in women of childbearing age

Difficult to diagnose

84

Lupus

NSAID

Corticosteroid

Plaquenil

Immune suppression

85

Cornea/Dry Eye

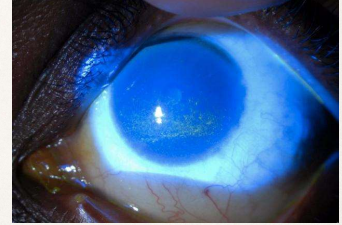
Graves' Disease

Sjögren's Syndrome

Lupus

Rheumatoid Arthritis

Image: Will's Eye



86

Sjögren's Syndrome

Autoimmune disease that mainly causes: dry eye and dry mouth

Can also have joint pain, fatigue, persistent cough

Typically in women over 40

87

Sjögren's Syndrome

Can have association with RA or Lupus

Diagnosis is made by signs/symptoms, blood test

Lip biopsy?

88

Sjögren's Syndrome

Treat specific symptoms

Dryness

Dry eye

Treat salivation (pilocarpine), may also use Plaquenil

89

Uveitis


Possible association with autoimmune disease

Less than 50% have known cause

90

Uveitis


Scatter approach



91

Uveitis

Tailored approach



92

Uveitis

Tailored approach

- Examine/Classify
- Working List
- Case History

93

Uveitis

Examine/Classify

- Anterior/Posterior/Pan
- Granulomatous/Non
- Acute/Chronic
- Unilateral/Bilateral

94

Uveitis

- Ankylosing Spondylitis
- Inflammatory Bowel
- Reactive Arthritis
- Psoriasis
- Sarcoidosis
- JIA

95

Uveitis

Case History

- Ask specific questions
- Decide if special testing needed

96

Uveitis

Acute Anterior Unilateral Nongranulomatous

Ankylosing Spondylitis

Inflammatory Bowel

Psoriasis

Reactive Arthritis

97

Uveitis

Ankylosing Spondylitis

Lower Back Pain

Worse with Rest

Wake up with pain

Better with NSAIDS



98

Uveitis

Ankylosing Spondylitis

Lower back X-Ray

Refer to Rheumatology

Treated with Immune Modulators



99

Uveitis

Inflammatory Bowel

GI symptoms

Cramps, diarrhea, bloody stools

Diet modification, Immune modulation, Surgery

Refer to GI

100

Uveitis

Psoriasis

Skin plaques - joints, scalp

Arthritis ~ 5%

Steroid creams, Immune modulation

Refer to Dermatology



101

Psoriasis



102

Uveitis

Reactive Arthritis

Acute Arthritis

Typically knee, ankle, foot

Skin lesions, urethritis, diarrhea

Pain modification

103

Uveitis

Reactive Arthritis

No test for this

Refer to Rheumatology

104

Uveitis

Chronic Anterior Bilateral Granulomatous

Sarcoidosis

105

Uveitis

Sarcoidosis

Multisystemic, Granulomatous Disease

90% have lung involvement

Skin involvement common

Order chest x-ray

Vitamin D 25-(OH)

106

Uveitis

Sarcoidosis

Night sweats

Weakness

Fatigue

107

Uveitis

Sarcoidosis

Order chest x-ray

ACE is non-specific

IL2R lab test - very specific

May need Pulmonary consult

108

Uveitis

Asymptomatic Anterior Unilateral Nongranulomatous

Juvenile Idiopathic Arthritis

109

Uveitis

Juvenile Idiopathic Arthritis

Joint pain/stiffness/swelling

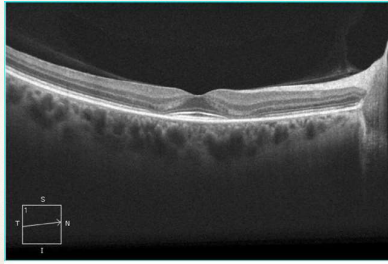
Unilateral cataract

Pediatrician/Rheumatology referral

110

Retina

Plaquenil



111

Plaquenil

Ganglion, Photoreceptor, RPE

Atrophy

Scotoma

Irreversible Damage

112

Plaquenil

HCQ

1000 g

400 mg/day

>7 years

113

Plaquenil

Quantify risk

1-7 years

1/1000

>7 years

1/100

114

Plaquenil

Quantify risk

Under 5 years = 1%

10 years = 2%

20 years = 4%

115

Plaquenil

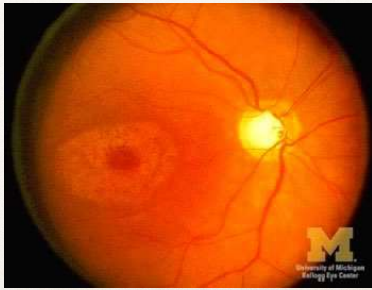
Find HCQ toxicity before visible on fundus evaluation

Prevent irreversible vision loss

Modify risk if possible*

116

Plaquenil



117

Plaquenil

2002 Recommendations

High risk if > 6.5 mg/kg/day

Color vision

10-2 or Amsler

118

Plaquenil

2011 Recommendations

High risk if 1000g cumulative dose

NO Color vision or Amsler Grid

10-2 combined with

OCT, FAF, mfERG

119

Plaquenil

2016 Recommendations

High risk if > 5 mg/kg/day REAL weight

or 6.5 mg/kg/day IDEAL weight

120

Plaquenil

2016 Recommendations

Continues testing recommendations from 2011

121

Plaquenil

Low risk drug if correct dosage

If proper dosage, should never see "bull's eye maculopathy"

122

Plaquenil

Consider modifying risk by modifying dosage

Only come in 200 mg tablets

Patient may want to take fewer than 14 tablets/week

123

Plaquenil

Study of 500 patients started on Plaquenil

50% were on too high dose for ocular safety

Ophthalmology 2017;124:604-608

124

Plaquenil

Safe weight for 400 mg/day - based on REAL weight

180 lbs

For every 13 lbs less than this subtract 1 tablet/week

125

Plaquenil

<https://www.eyedock.com/plaquenil-calcs>

126

Plaquenil

Testing

- mfERG
- FAF
- VF
- OCT

127

Plaquenil

VF

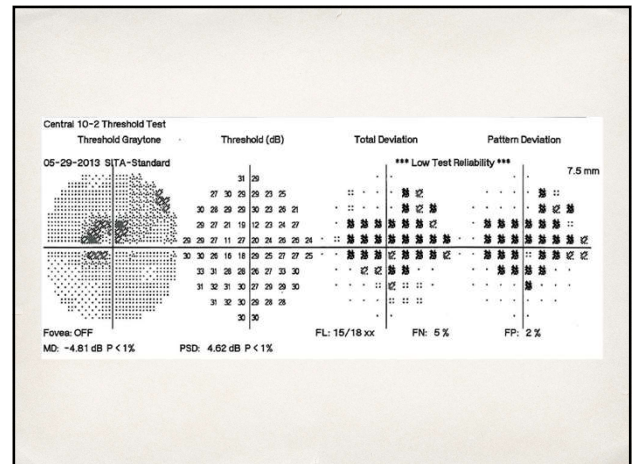
24-2, 30-2 not sufficient (but consider if Asian)

10-2 white on white (or red)

128

Plaquenil

129



130

Plaquenil

False Positives

What is Sensitivity/Specificity?

Consider risk of developing toxicity

131

Plaquenil

Risk before 7 years = 1/1000

Risk after 7 years = 1/100

If Specificity = 90%

10-100 times more FALSE positives than TRUE

132

HVF

Pro:

- Available
- Inexpensive
- Interpretation

133

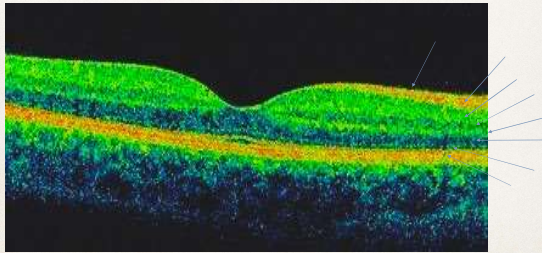
HVF

Con:

- Subjective
- Patients dislike
- False Positives

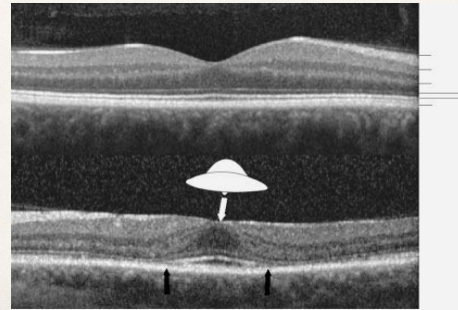
134

Plaquenil

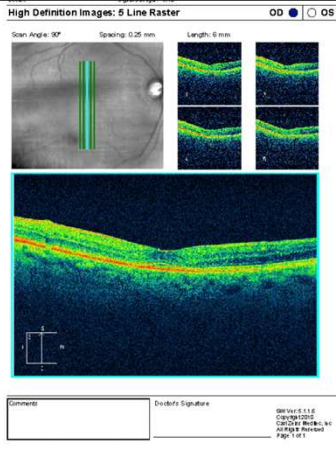


135

Flying Saucer



136



137

OCT

Pro:

- Available
- Objective
- Interpretation

138

OCT

Con:

Early detection

Cost

139

Plaquenil

(+) HVF, (+) SD-OCT

(+) HVF, (-) SD-OCT

(-) HVF, (+) SD-OCT

(-) HVF, (-) SD-OCT

140

Plaquenil

Frustrations

False positives

No gold standard

We are the authority

Benefits of Plaquenil

141

Case 1

60 Year Old White Female

Blur at distance

Photophobia

Dry eye

142

Case 1

Plaquenil x 20 years

400 mg/day

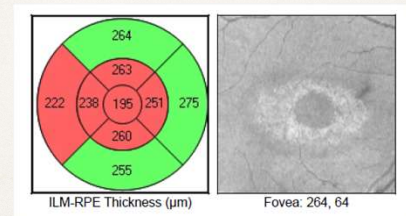
Lupus

5'4"

105 lbs - safe dosage is 200 mg

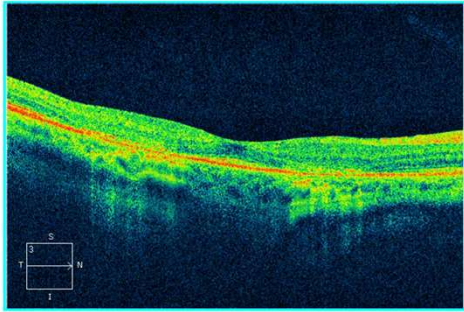
143

Case 1 - OD OCT



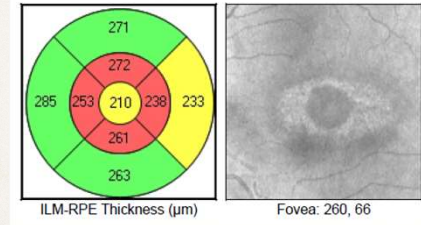
144

Case 1 - OD OCT



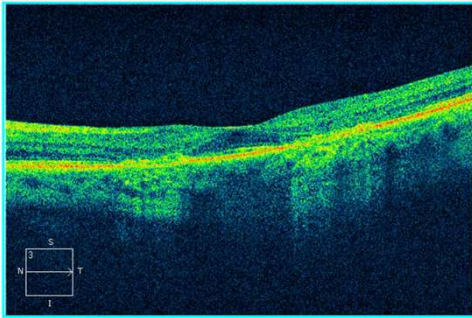
145

Case 1 - OS OCT



146

Case 1 - OS OCT



147

Case 1

Plaquenil toxicity
Should have been on lower dose
Need to discontinue medicine

148

Case 2

86 Year Old White Male
Blur at distance
Ocular History: Early AMD

149

Case 2

Medical History
Psoriatic Arthritis
HTN
CAD
Hyperlipidemia

150

Case 2

Medications

Plaquenil

Fluocinonide

Coreg

ASA 325 mg

151

Case 2

5'7" tall

130 lbs - would need 10 tablets/week

152

Case 2

Patient at VA since 1999

Every exam: RPE changes OS>OD

Called AMD

20/20- OD and OS

153

Case 2

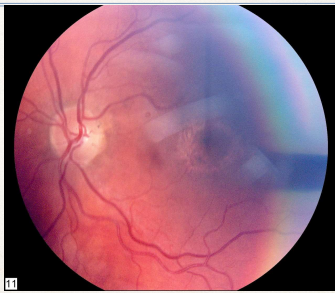
September 2010

Ring shaped atrophy OS

Fundus Photos/OCT

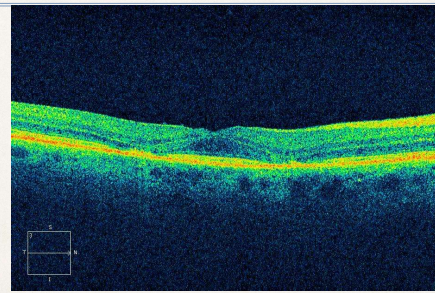
154

Fundus OS



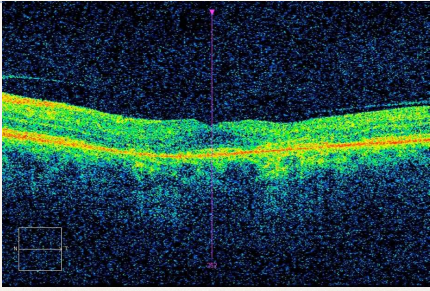
155

SD-OCT - OS



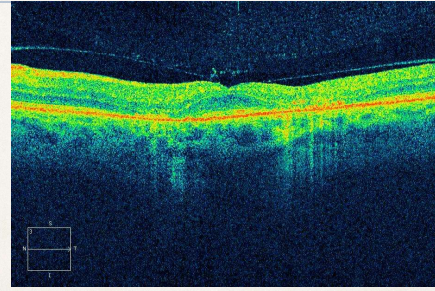
156

SD-OCT - OS



157

SD-OCT - OD



158

Management

Discontinue Plaquenil

See Rheumatologist -- Patient refused initially

159

Management

Patient eventually discontinued meds

Asymptomatic

Good outcome?

160

Case 3

71 Year Old White Male

Evaluation for Plaquenil Maculopathy

No vision complaints

161

Case 3

On Plaquenil for 7 years

200 mg BID

RA/Lupus

Normal kidney, liver

Normal BMI

162

Case 3

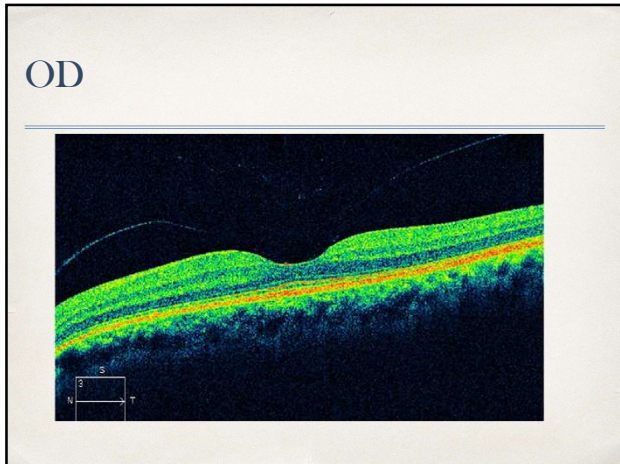
5'11" tall
 155 lbs - should be on 12 tablets/week

163

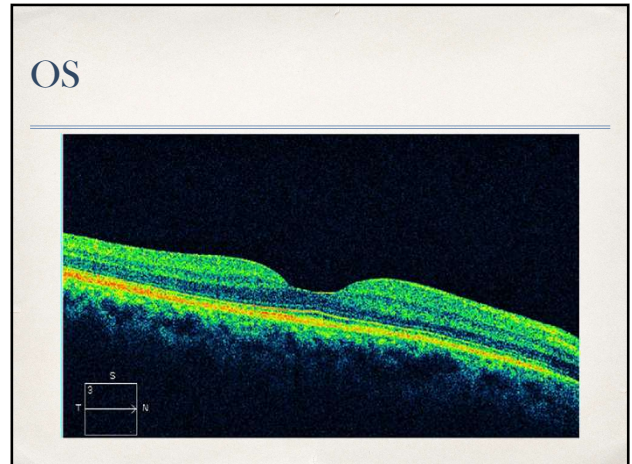
Case 3

BCVA 20/20 OD/OS
 Anterior Segment Unremarkable
 Posterior Segment - Mild ERM OD

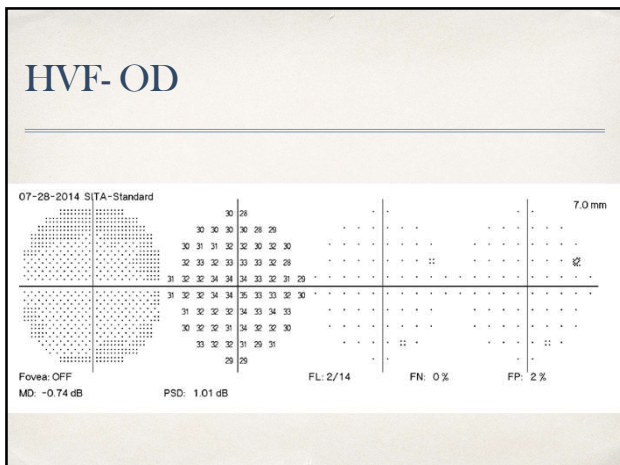
164



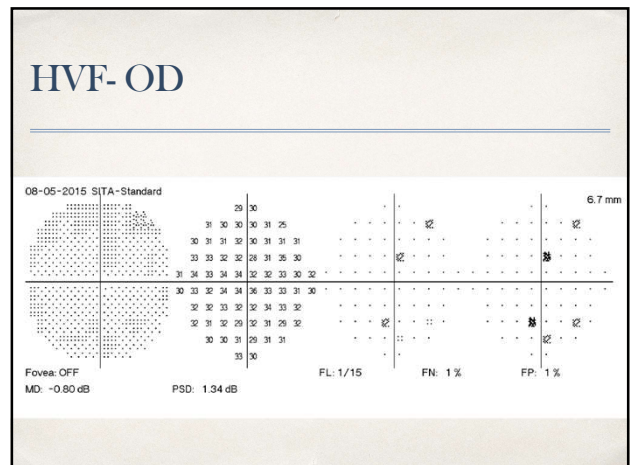
165



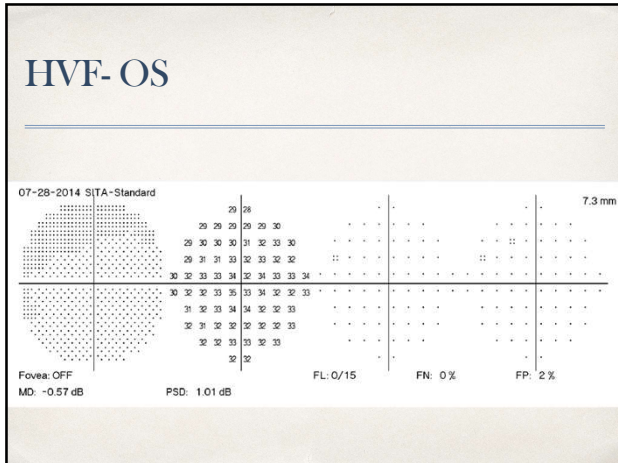
166



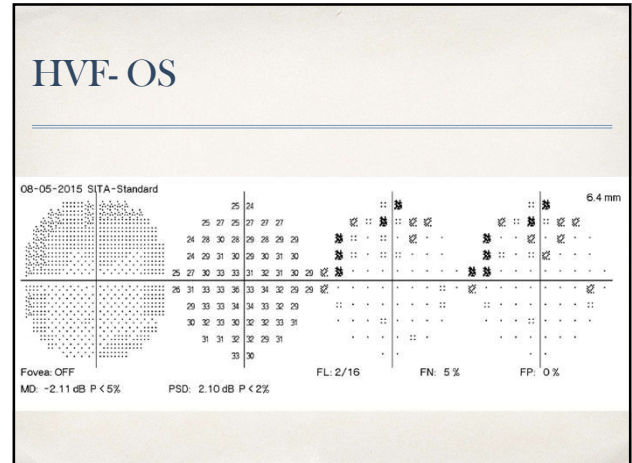
167



168



169



170

Case 3

Normal macula
Normal OCT
?HVF

171

Case 3

Do we continue medication?
Do we discontinue medication?

172

Case 3

Plan
Continue medication
RTC 6 months - retest

173

Case 4

64 Y/O White Male
10 years on Plaquenil for RA
+AMD

174

Case 4

5'11"
182 lbs

175

Case 4 - HVF OD

12-15-2014 SITA-Standard GHT: Within normal limits *** Low Test Reliability *** 7.0mm

Fovea OFF MD: -2.86 dB P < 2% VFI: 99% PSD: 2.10 dB FL: 8/18 xx FN: 3% FP: 3%

176

Case 4 - HVF OS

12-15-2014 SITA-Standard GHT: Within normal limits *** Low Test Reliability *** 6.8mm

Fovea OFF MD: -2.89 dB P < 2% VFI: 99% PSD: 1.82 dB FL: 5/19 xx FN: 2% FP: 0%

177

Case 4 - OCT OD

8:142 C: 10

178

Case 4 - OCT OD

8:133 C: 10

Case 4 - OCT OS

8:133 C: 10

179

180

Case 4

Informed Rheumatologist

They discontinued Plaquenil

Was this the right call?

Could we have done better?

181

Vascular

Arterial Disease

Vasculitis

182

Arterial Disease

CRAO

Giant Cell Arteritis

5-15%

183

Vasculitis

Wegener's

Polyarteritis Nodosa

Giant Cell Arteritis

184

Optic Nerve

Optic Nerve Edema

Optic Atrophy

185

Optic Nerve

Giant Cell Arteritis

Graves' Disease

Lupus

Multiple Sclerosis

Sarcoidosis

186

Giant Cell Arteritis

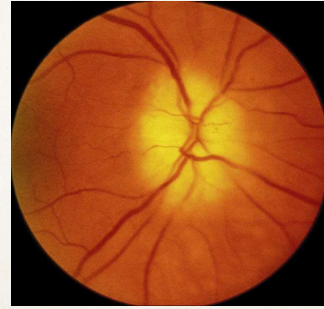
Profound Vision Loss

Bilateral in 14 days in 1/3 if Untreated

Systemic Complications

Treatable

187



188

Systemic Symptoms

Jaw Claudication (Odds Ratio 9.0)

Neck Pain (Odds Ratio 3.4)

Anorexia (Odds Ratio 2)

Hayreh SS, et al. Giant Cell Arteritis: Validity and Reliability of Various Diagnostic Criteria. Am J Ophthalmol 1997;123:285-96

189

Less Predictable

Headache

Fever

Scalp Tenderness

Malaise

Hayreh SS, et al. Giant Cell Arteritis: Validity and Reliability of Various Diagnostic Criteria. Am J Ophthalmol 1997;123:285-96

190

Headache

A-AION - 46% had Headache

NA-AION – 54% had Headache

Could Mislead

Hayreh SS, et al. Giant Cell Arteritis: Validity and Reliability of Various Diagnostic Criteria. Am J Ophthalmol 1997;123:285-96

191

Average Number of Symptoms = 3

192

Testing

Labs – ESR, CRP, CBC, Platelets
 Fluorescein Angiography
 Ultrasound, PET, MRI – Limited Benefit
 Temporal Artery Biopsy

193

Labs

ESR
 > 33 mm/h
 Sensitivity 92%
 Specificity 92%

194

Labs

CRP
 > 2.45 mg/dl
 Sensitivity 100%
 Specificity 82%

195

ESR + CRP

Sensitivity 100%
 Specificity 97%

ell Arteritis: Validity and Reliability of Various Diagnostic Criteria. Am J Op

196

Don't Forget CBC

Check for inflammation
 Check for Anemia, Polycythemia
 Platelets

197

Platelets

Odds Ratio:
 ESR > 47 mm/hr = 1.5
 CRP > 2.45 mg/dL = 5.3
 Platelets > 400,000/ μ L = 4.2
 All 3 elevated = 8

Walvick MD, Walvick MP. Giant Cell Arteritis: Laboratory Predictors of a Positive Temporal Artery Biopsy. Ophthalmology 2011;118:1201-1204

198

MR. A

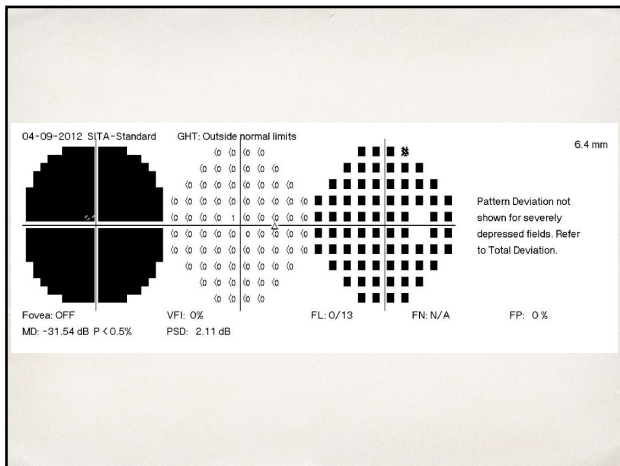
Labs
 ESR = 56
 CRP = 1.37
 Pending Temporal Artery Biopsy

205

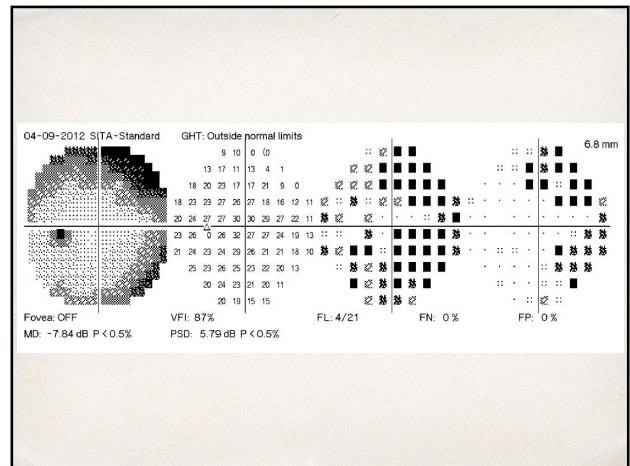
MR. A

Started on 40 mg Pred
 When he tapers, headaches return
 What about vision?
 20/70 and VF reduction

206



207

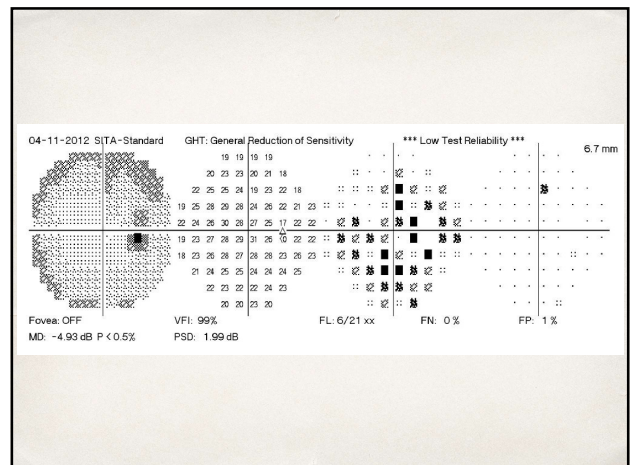


208

MR. A

When Pred resumed, vision returned to 20/25
 Visual Field improved

209



210

