Autoimmunity and the Eye

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Disclosure

Professor of Optometry
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Serve on the speaker bureau, advisory, or contributed board for:
Vision Service Plan (VSP), American Diabetes Association (ADA), Allergan (AbbVie Company), Genentech (Roche), Regeneron

All financial relationships have been mitigated.

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Course Objectives

At the conclusion of this course, attendees will be able to:

- Recognize the variable clinical presentations of common autoimmune conditions.
- Appreciate integration of innovative imaging modalities into clinical practice to aid early diagnosis.
- Know the latest in management and treatment options.
- Understand the critical role of co-management.

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ELSEVIER

Current Opinion in Immunology
Volume 80, February 2023, 102266

Review

The increasing prevalence of autoimmunity and autoimmune diseases: an urgent call to action for improved understanding, diagnosis, treatment, and prevention

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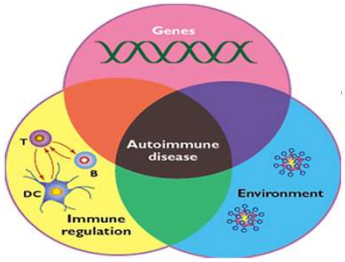
Autoimmune Diseases Facts

- An estimated 50 million Americans are living with an autoimmune disease.
- Women make up 80% of those affected by autoimmune diseases.
- There are over 100 identified autoimmune diseases.
- The prevalence of autoimmune diseases is rising
  - Studies highlighting a ~50% rise in antinuclear antibodies



Autoimmune facts. Autoimmune Association. https://autoimmune.org/autoimmune-awareness-month/ Accessed March 2026

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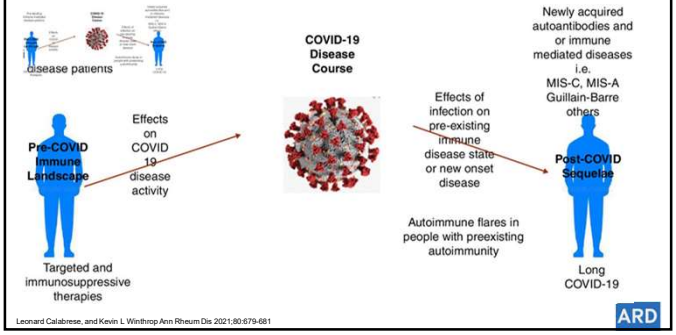
COVID-19 and Autoimmune Diseases



Leonard Calabrese, and Kevin L Winthrop Ann Rheum Dis 2021;80:679-681

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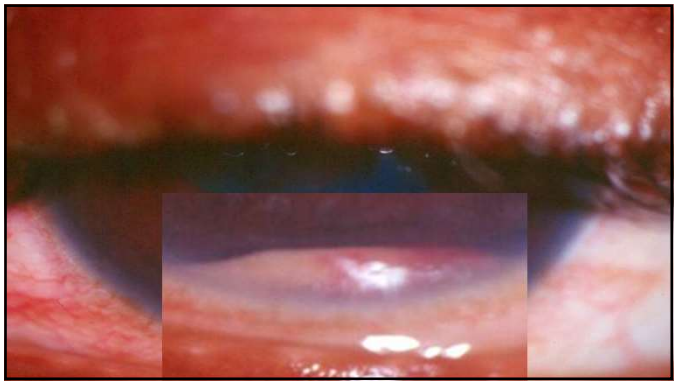

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Rheumatoid Arthritis (RA)

- Inflammation of the synovial membrane of the joints and/or other internal organs
- Prevalence: 1-2%
- Occurrence:
  - Any age
  - 3:1 Females
  - Unknown etiology
    - Interplay between genetic (HLA-DRB1), predisposition, and environmental triggers

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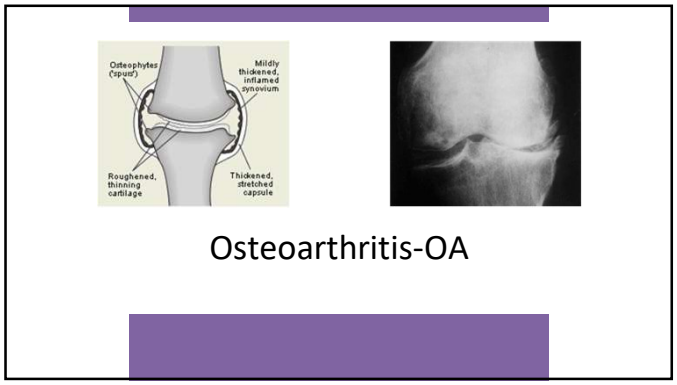

Osteoarthritis-OA

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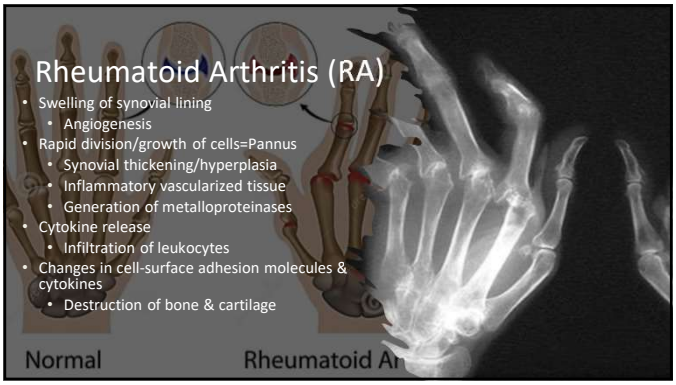

Rheumatoid Arthritis (RA)

- Swelling of synovial lining
  - Angiogenesis
- Rapid division/growth of cells=Pannus
  - Synovial thickening/hyperplasia
  - Inflammatory vascularized tissue
  - Generation of metalloproteinases
- Cytokine release
  - Infiltration of leukocytes
- Changes in cell-surface adhesion molecules & cytokines
  - Destruction of bone & cartilage

Normal Rheumatoid Ar

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Ocular complications are associated with:
Severe disease
Increased mortality

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Multinodular scleritis in a patient with rheumatoid arthritis. *Clin Rheumatol* **40**, 4359–4360 (2021)

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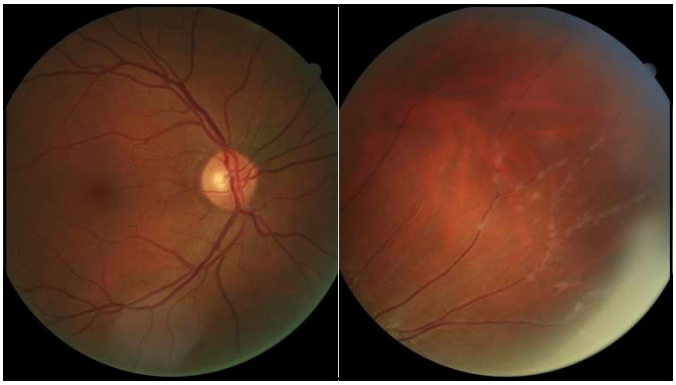

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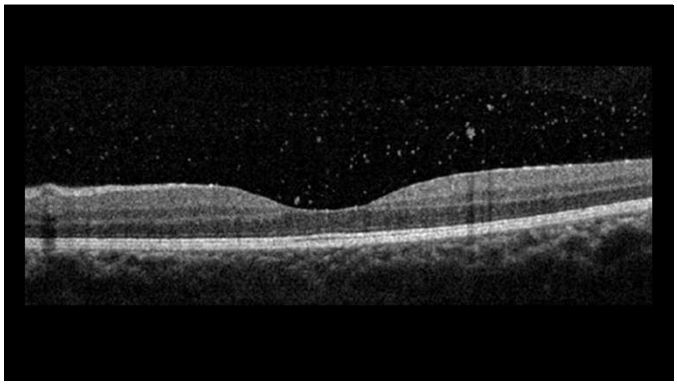

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Laboratory Findings

- ↑ Erythrocyte Sedimentation Rate (ESR)
- ↑ C-reactive protein (CRP)
- (+) Rheumatoid factor (RF)
- (+)Antinuclear antibodies (ANA)
  - •10% - 37% in healthy individuals over the age of 65
  - •False positives- drugs and infections
- (+) Anticyclic citrullinated peptide (anti-CCP)
- Synovial fluid: turbid with many leukocytes
- Radiographic imaging

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American College of Rheumatology: Criteria for the Diagnosis of Rheumatoid Arthritis

Joint Involvement	Points
1 large joint (shoulder, elbow, hip, knee and ankle)	0
2–10 large joints	1
1–3 small joints (MCP, PIP, MTP, carpal;with or without large joint involvement)	2
4–10 small joints (with or without large joint involvement)	3
10 joints (at least 1 small joint)	5
Serology	
Negative RF and anti-CCP	0
Low positive RF and/or anti-CCP	2
High positive RF and/or anti-CCP	3
Acute-phase reactants	
Normal CRP and/or ESR	0
Abnormal CRP and/or ESR	1
Duration of Symptoms	
< 6 weeks	0

A diagnosis of definite RA is supported by at least one swollen joint not otherwise explained and score of 6/10 from the above criteria.

Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum* 2010;62:2569

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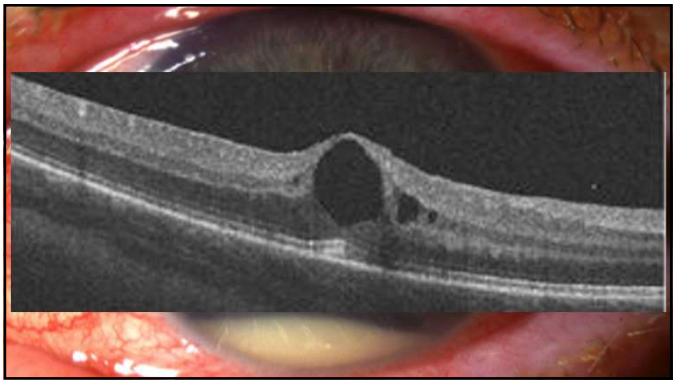

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Juvenile Idiopathic Arthritis (JIA)
~~Juvenile Rheumatoid Arthritis (JRA)~~

- Most common type of arthritis affecting children
  - Children under 16 (usual onset between 2-4 years of age)
  - Symptoms and signs ≥ ***6 weeks***
    - Swollen, red, painful joints
      - Typically, worse in the morning or after a nap
      - Earliest signs of JIA may be limping in the morning
    - Fever
    - Some children may have growth problems
- Oligoarticular JIA (four or fewer joints), **Polyarticular JIA (five or more joints)**, Systemic JIA (fever and rash in addition to joint pain)

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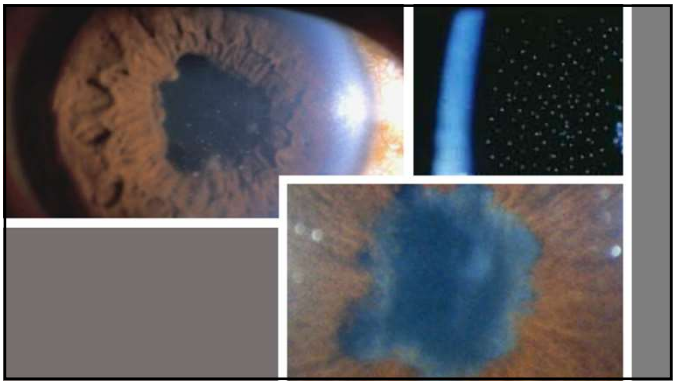

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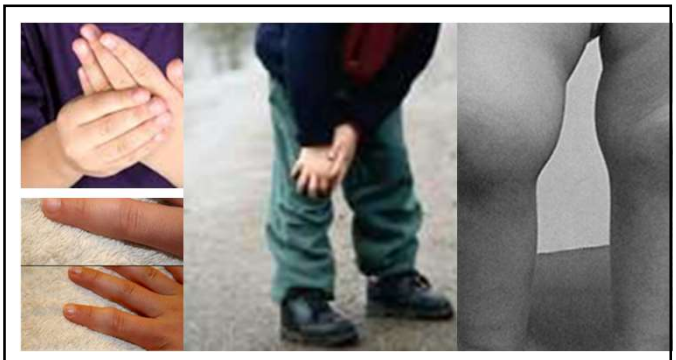

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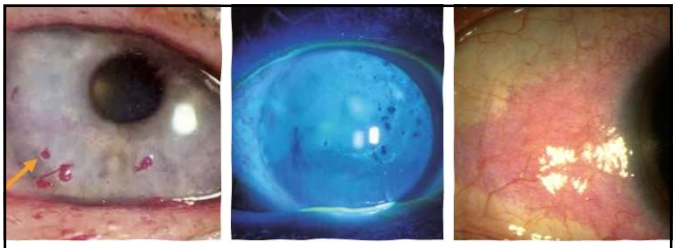

A Multifactorial Condition that affects approximately 38 million individuals in the U.S.
***less than 10% of diagnosed patients are being treated.

2023 Dry Eye Products Markets Report, Market Scope, 2023

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Sjogren's Syndrome

- Systemic chronic inflammatory disorder characterized by lymphocytic infiltrates in exocrine organs
  - Lacrimal, salivary, and sweat glands
- Occurrence:
  - 4/5/6th decade
  - 9:1 Females
  - Autoimmune- HLA- B8/ DR3
  - Antibodies to the Ro antigen

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Sjögren's Syndrome

Primary
- Sjogren's syndrome that occurs alone

Secondary
- Rheumatoid Arthritis
- Systematic Lupus Erythematosus
- Scleroderma
- About 50% of patients have secondary Sjogren's

Sicca Syndrome
- Xerophthalmia (dry eyes)
- Xerostomia (dry mouth)
- Xeroderma (dry skin)
- Parotid gland enlargement

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Sjögren's syndrome

- The Sjö® Test 
  - Traditional markers (SSA, SSB, ANA, RF) along with three proprietary markers: Salivary protein-1 (SP1), Carbonic anhydrase-6 (CA6), and Parotid secretory protein (PSP).
- Blood test:
  - Antinuclear Antibody (ANA) and Rheumatoid Factor (RF)
  - SSA (or Ro) and SSB (or La) autoantibodies
    - present in about 70% and 40% of patients, respectively

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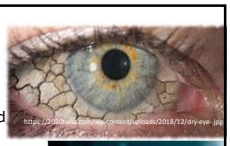
Mainstays of Therapy

- Cyclosporine A
- Artificial Tears
- Punctal Plugs- absorbable, permanent, NLD Hyaluronic Acid
- Petroleum based and Water Based Ointments
- Autologous Serum Tears
- Devices (contact lenses, googles) & Surgery (Tarsorrhaphy)



New Modalities

- Varenicline (Tyrvaya)- Nasal Spray, increases Tear Production
- Perfluorohexyloctane (Miebo)- Drop, creates an anti-evaporative layer
- Vyve (0.1% in Perfluorobutylpentane)
- Reproxalap (fast-acting, non-steroid)
- TRYPTYR (TRPM8 agonist for tear production)
- Intense Pulsed Light (IPL) and Radiofrequency (RF)

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TREATMENT OVERVIEW

- Non-pharmacologic therapy
- Pharmacologic therapy
  - Non-disease modifying drugs
  - NSAIDs
  - Corticosteroids
    - Prednisone < 10mg PO daily
- Disease-modifying antirheumatic drugs (DMARDs)
- Non-biologics
- Biologics

DRUG	DOSE	MONITORING
Methotrexate	PO/IM: 7.5-15mg weekly	• Baseline LFTs, CBC, SCr/BUN, hepatitis panel • CBC, AST/ALT, albumin q1-2 months
Leflunomide	PO: 100mg daily x 3 days, then 10-20 daily OR 10-20 mg daily w/o LD	• Baseline LFTs, CBC • CBC, AST/ALT monthly, then q6-8 weeks
Hydroxychloroquine	PO: 200-300mg BID x 1-2 months, then can ↓ to 200mg daily or BID	• Baseline eye exam • Ophthalmoscopy q9-12 months
Sulfasalazine	PO: 500mg BID, then ↑ to 1000mg BID	• Baseline CBC • CBC weekly x 1 month, then q1-2 months
Minocycline	PO: 100-200mg daily	• LFTs, BUN/SCr with long-term treatment

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Biologics

- Infliximab (Remicade)
- Etanercept (Enbrel)
- Adalimumab (Humira)
- Golimumab (Simpani)
- Certolizumab (Cimzia)
- Ixekizumab (Taltx)
- Anakinra (Kin
- Abatacept (Orencia)
- Rituximab (Rituxan)
- Toclizumab (Acetemra)
- Tofacitinib (Xeljanz)

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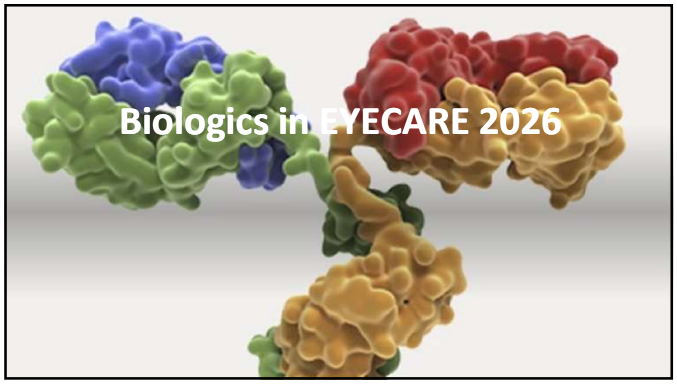

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Biologics in EYECARE 2026

- **--mab** (monoclonal antibodies), **--cept** (fusion of receptor and protein), **--fusp** (fusion protein), **--kin** (interleukin antagonist) and --interferon
- Adverse side effects called immune-related adverse events (irAEs)
  - Dry Eyes
  - Uveitis
  - Vasculitis
    - Subretinal fluid/ Choroidal detachment
  - Neuropathy
    - CN palsies
    - optic neuritis

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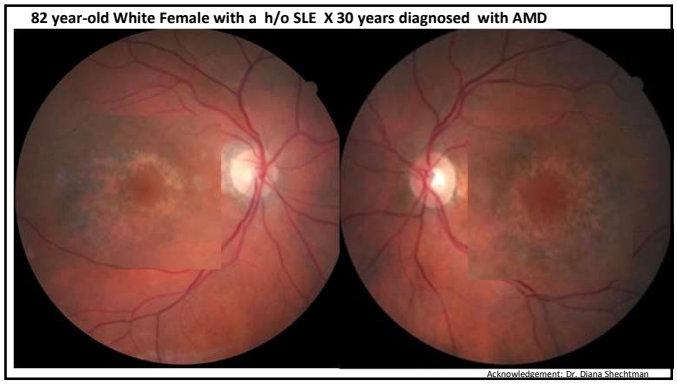

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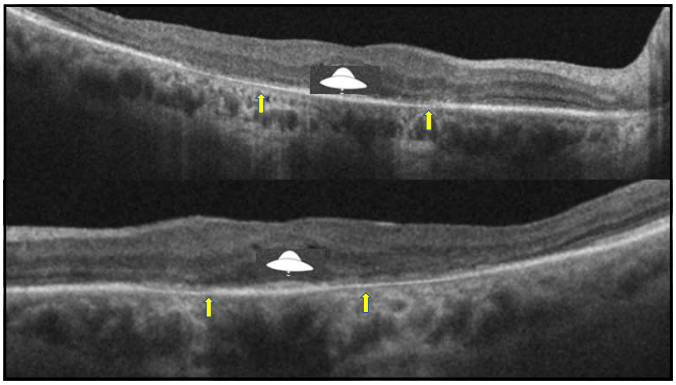

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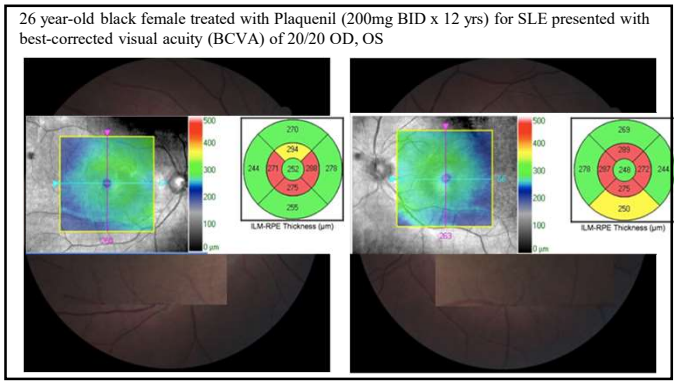

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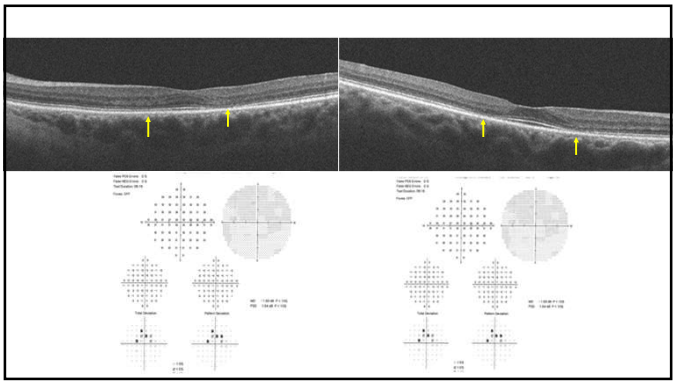

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Systemic Lupus Erythematous (SLE)

- An inflammatory, multisystem, autoimmune disease of unknown etiology with protean clinical and laboratory manifestations and a variable course and prognosis
- Occurrence:
  - Women in their reproductive years
  - **10:1 Females**
  - Variation in race/ethnicity:
    - More common in Black (3–6x)
    - Hispanic and Native Americans (2–3x)
    - Asian (2x) populations

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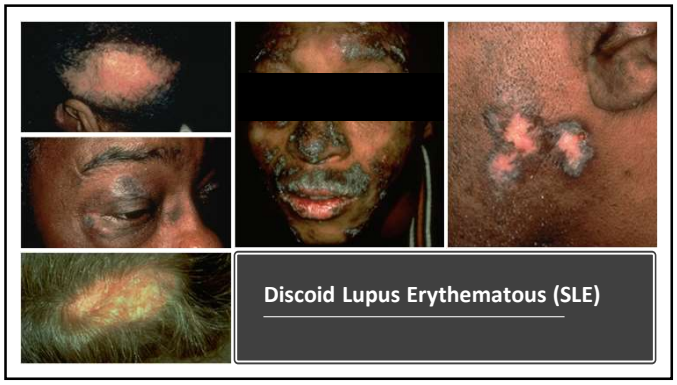

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Revised Criteria for the Classification of Systemic Lupus Erythematosus

- Malar rash: red flat or raised over the cheeks, sparing the nasolabial folds.
- Discoid rash: red raised patches with keratotic scales, atrophy and scarring may occur in older lesions.
- Photosensitivity: skin rash as a result of exposure to sunlight.
- Oral ulcers: painless ulcers in the mouth or nasopharyngeal areas.
- Arthritis: nonerosive arthritis (pain, swelling or effusion) in = >2 peripheral joints.
- Serositis: pleuritis (pleuritic pain or rub or pleural effusion) **or** pericarditis (ECG or rub or evidence of effusion).
- **Renal**: proteinuria (> 500 mg daily) persistent **or** cellular casts (RBC, granular, tubular or mixed).
- CNS: seizures **or** psychosis in absence of alternative explanation (e.g. drugs or metabolic disorders such as electrolyte abnormality or uremia).
- Hematologic: hemolytic anemia (with reticulocytosis) **or** leucopenia (< 4000/mm) on 2 or more occasions; **or** lymphopenia (< 1500/mm) on 2 or more occasions **or** thrombocytopenia (<100,000) in absence of medications know to decrease platelets.
- Immunologic: antiphospholipid antibodies present based on either an abnormal serum level of IgG or IgM anticardiolipin antibodies or a positive test result for lupus anticoagulant **or** Anti-DNA antibody **or** Anti-Sm antibody **or** false positive VDRL (or RPR).
- Antinuclear antibodies: elevated level of ANA at any time, in absence of drugs known to cause "drug-induced lupus".

More than 4 criteria need to be present during an interval of observation

•2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus. *American college of rheumatology* [accessed August 3, 2025]

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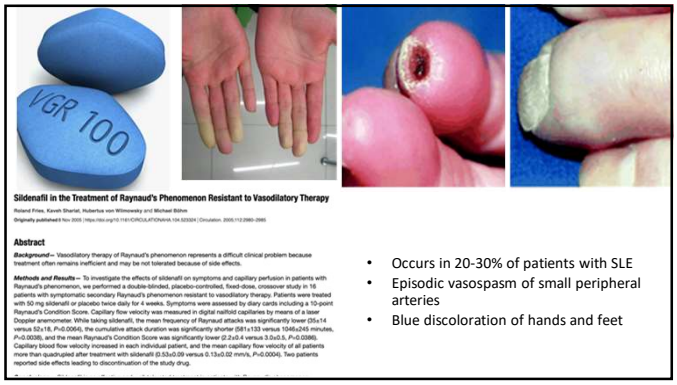

- Occurs in 20-30% of patients with SLE
- Episodic vasospasm of small peripheral arteries
- Blue discoloration of hands and feet

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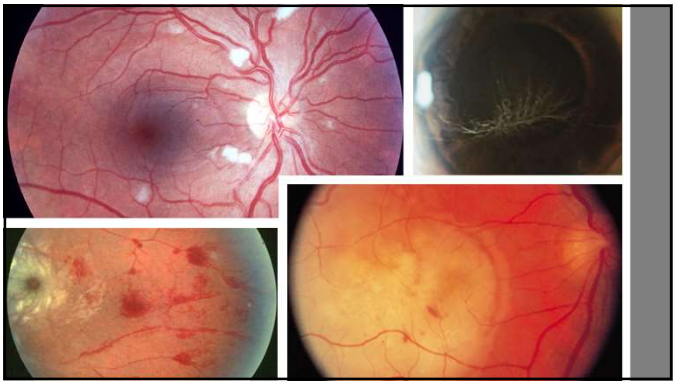

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Hydroxychloroquine (HCQ) and Chloroquine (CO) Screening Guidelines

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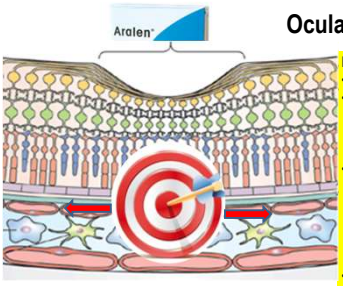

Ocular Toxicity of HCQ/ CQ

Bind to RPE Melanin

- Inhibit lysosomal function of the RPE
- Decrease phagocytosis of the photoreceptors
  - Increased accumulation of lipofuscin
- Pigment-containing RPE cells migrate into the outer nuclear and outer plexiform layers
  - Sparing of foveal center and the resulting "bull's eye" maculopathy
- Irreversible photoreceptor loss and RPE damage

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Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016 Revision)

Daily dose	>5.0 mg/kg (real weight) for Hydroxychloroquine >2.3 mg/kg (real weight) for Chloroquine
Drug use time	More than 5 years
Renal disease	Abnormal glomerular filtration rate
Concomitant drugs used	Tamoxifen use
Macular disease	Can affect the evaluation and susceptibility to chloroquine and hydroxychloroquine

Adapted from: Marmor MF, Kellner U, Lai TY, Melles RB, Mieler WF: American Academy of Ophthalmology. Ophthalmology. 2016 Jun; 123(6):1386-94.

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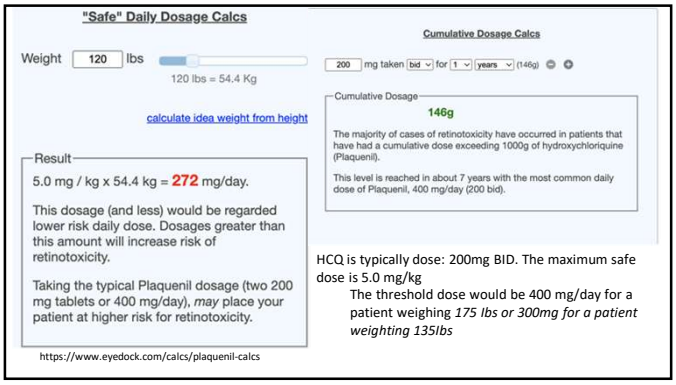

https://www.eyedock.com/calcs/plaquenil-calcs

HCQ is typically dose: 200mg BID. The maximum safe dose is 5.0 mg/kg

The threshold dose would be 400 mg/day for a patient weighing *175 lbs or 300mg for a patient weighting 135lbs*

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Lesser Risk Factors

Age	• Elderly patients might seem to be at higher risk • A recent demographic study found no significant association between age and risk of toxicity
Liver disease	• No clear association between liver disease and toxicity has been demonstrated
Genetic factors	• There have been suggestions that some patients have a genetic predisposition to HCQ toxicity • More research necessary

Ask about common side effects of CQ/HCQ therapy

- Pruritus, headaches, dizziness and gastrointestinal upset to detect those that are non-compliant and those that are receiving a dose that is too high.
- Less frequent side effects include discoloration of the oral cavity, nails, skin and hair and rash

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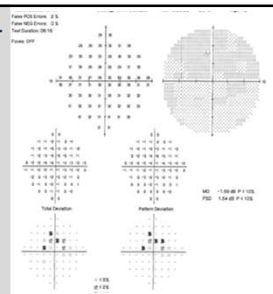
Table 3. Clinical Examination Techniques

Recommended Screening Tests
- Primary tests: ideally do both
  - Automated visual fields (appropriate to race)
  - SD OCT
- Other objective tests (as needed or available):
  - mfERG
  - FAF
- Newer tests of possible value in future
  - Microperimetry
  - Adaptive optics retinal imaging

Not Recommended for Screening
- Fundus examination
- Time-domain OCT
- Fluorescein angiography
- Full-field ERG
- Amsler grid
- Color testing
- EOG

EOG = electro-oculogram; ERG = electroretinogram; FAF = fundus autofluorescence; mfERG = multifocal electroretinogram; SD OCT = spectral-domain optical coherence tomography.



White 10-2: White Stimulus/ 24-2 or 30-2 VF for Asian Patients

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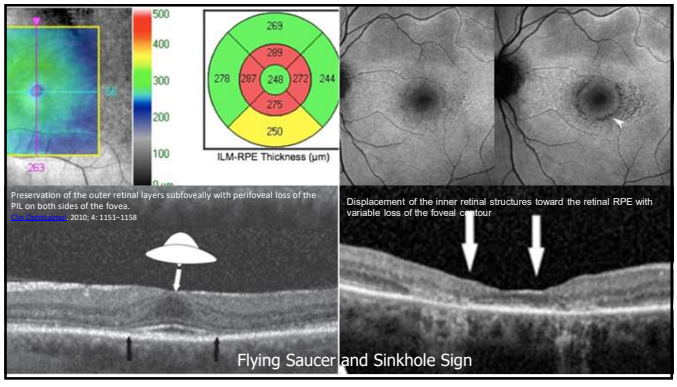

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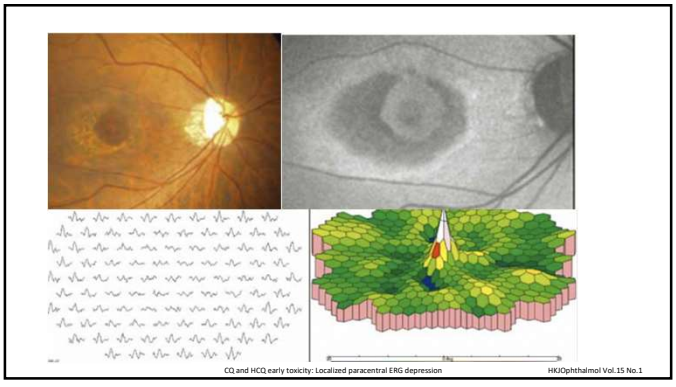

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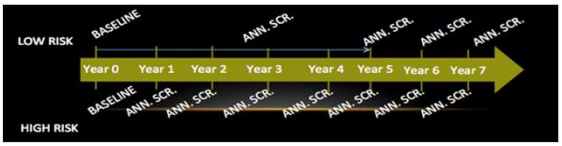
Management

- Co-manage with PCP/Rheumatologist to STOP medication immediately maculopathy
  - Goal is to minimize progression of visual loss
  - If not possible (medication is critical to manage underlying disease)
    - Close monitoring (every 3-6 months) to assess progression
      Document that patient accepts risk of permanent vision loss



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Long Term Risk Stratification

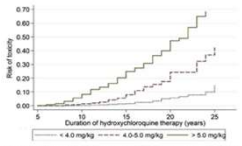

Figure 4. Kaplan–Meier curves showing the cumulative risk of retinopathy over time, with different levels of hydroxychloroquine (HCQ) use. When use is between 4.0 and 5.0 mg/kg, the risk is very low within the first 5 to 10 years, but it increases markedly thereafter. Reprinted with permission from Melles RB, Marmor MF. The risk of toxic retinopathy in patients on long-term hydroxychloroquine therapy. JAMA Ophthalmol 2014;132:1453–60.[7]

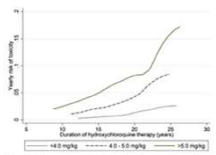

Figure 5. Incremental annual risk of toxicity for a patient at different levels of hydroxychloroquine (HCQ) use who is found to be free of retinopathy at a given point in time. The annual risk is low within the first 10 years of use, but increases with longer durations of therapy. Reprinted with permission from Melles RB, Marmor MF. The risk of toxic retinopathy in patients on long-term hydroxychloroquine therapy. JAMA Ophthalmol 2014;1321453–60.[7]

Adapted from: Marmor, MF, Kellner, U, Lai, T, Ronald B. Melles, R, Mieler, WF. Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016 Revision). Available at: https://www.aao.org/education/clinical-statement/revised-recommendations-on-screening-chloroquine-h

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Patients should still get yearly CEE
Case reports of patients with HCQ toxicity as early as 1.9 months on treatment

Yam JC, Kwok AK: Ocular toxicity of hydroxychloroquine. *Hong Kong Med J* 2006, 12(4):294-304

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SEQUENTIAL CHANGES IN HYDROXYCHLOROQUINE RETINOPATHY UP TO 20 YEARS AFTER STOPPING THE DRUG

Implications for Mild Versus Severe Toxicity

BRANDON H. PHAM, BS,* MICHAEL F. MARMOR, MD†

Results

- Early and moderate cases stabilized in FAF appearance, foveal thickness, ellipsoid zone line length, and visual acuity for up to 9 years after stopping HCQ.
- By contrast, severe cases demonstrated a continual loss of these parameters for up to 20 years off the drug.
- Presence of RPE damage at initial examination predicted progressive retinopathy over many years.

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Thyroid Eye Disease (TED)

- An autoimmune disease caused by the activation of orbital fibroblasts by autoantibodies directed against thyroid receptors
- 3 million Americans affected
- Associated with Hyperthyroidism- 90% of the cases
- 10% Euthyroid, Hypothyroidism, Hashimoto's thyroiditis
- Thyroid-associated ophthalmopathy (TAO)/ Graves orbitopathy (GO)

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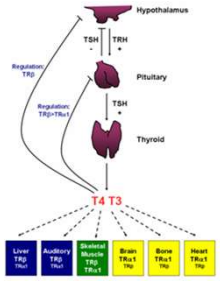
Hypothalamic-Pituitary-Thyroid Axis

- The hypothalamus produces thyrotropin-releasing hormone (TRH).
- The pituitary gland produces thyroid-stimulating hormone (TSH).
  - Normal: TSH range of 0.4–4.0/4.5 mU/L
  - Hypothyroidism (underactive): high TSH (>4.0–5.0 mU/L) and low T4
  - Hyperthyroidism (overactive): low TSH (<0.4 mU/L) and high T3/T4
  - Euthyroid: Abnormal TSH with normal T4



55

Hashimoto Thyroiditis

- Autoimmune disease that destroys thyroid cells by cellular-mediated and AB-mediated immune processes.
- The most common cause of hypothyroidism*
- Elevated TSH
- Low T4
- Thyroid-associated eye disease occurs in 6% of patients with Hashimoto's Thyroiditis

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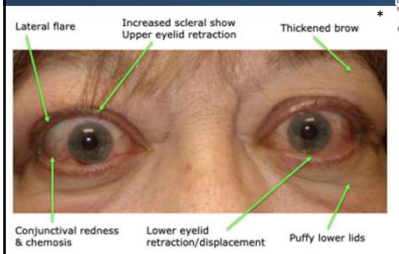
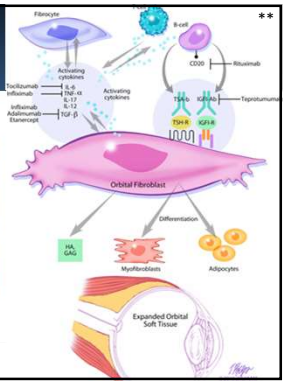
Thyroid Eye Disease (TED) Pathophysiology





*https://londonoculoplastics.co.uk/thyroid-eye-disease/
**Hodgson, N, Rajai, F. Current Understanding of the Progression and Management of Thyroid Associated Orbitopathy: A Systematic Review. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC7054489/

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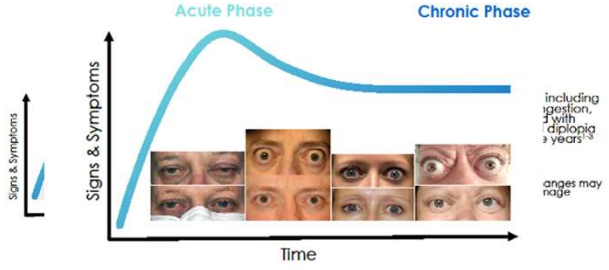

including
igestion,
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diplopia
3 years[1-3]

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Source: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-thyroid-eye-disease
Courtesy of AMGEN TED Disease State + Teprotumumab HCP Deck

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Thyroid Eye Disease (TED) Signs

Class	Abbreviation	Description	Detailed Description
O	N	No signs or symptoms	No complaints, No findings in physical examination (PE)
1	O	Only signs, no symptoms	No complaints, PE: Eyelid retraction Stare
2	S	Soft tissue involvement	Swelling of eyelids Chemosis Photophobia Grittiness
3	P	Proptosis	Exophthalmus
4	E	Extraocular muscle involvement	Restricted eyeball mobility (often diplopia)
5	C	Corneal involvement	Keratitis, Corneal Ulcer
6	S	Sight loss	Decreased visual acuity, impaired color of vision

Tab. 15.3 Eyelid signs in Graves disease

Eyelid sign	Explanation
▪ Dalrymple sign	Upper eyelid is retracted with visible sclera superior limbus and widened palpebral fissure with developir exposure keratitis (overactive muscle of Müller)
▪ Von Graefe sign	Upper eyelid retracts when the eye depresses (overa muscle of Müller)
▪ Gifford sign	Upper eyelid is difficult to evert (due to eyelid edem
▪ Stellwag sign	Rare blinking
▪ Kocher sign	Fixed gaze
▪ Eyelid flutters when closed	

Current Knowledge on Graves' Orbitopathy. J. Clin. Med. 2021

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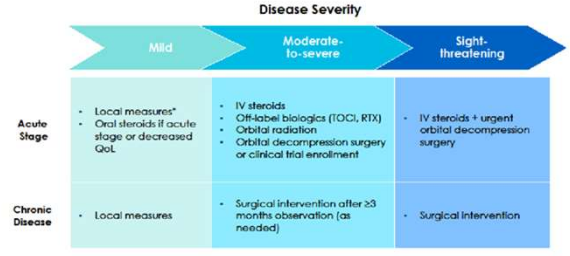
Historically, Treatment Options for TED Selected Based on Disease Activity and Severity[1,2]



IV, intravenous; N/A, not applicable; QoL, quality of life; TOCI, tocilizumab, RTX, rituximab.
*With or without selenium supplementation.

Courtesy of AMGEN TED Disease State + Teprotumumab HCP Deck

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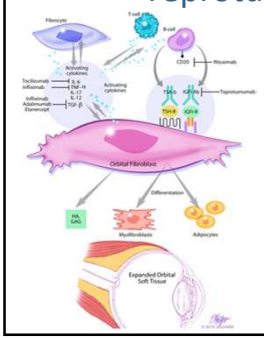
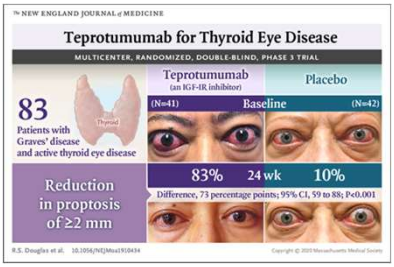
Teprotumumab (Tepezza)





N Engl J Med 2020; 382:341-352N Engl J Med 2020; 382:341-352

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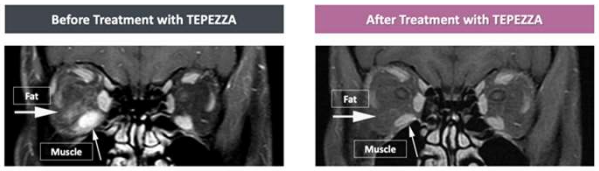
TEPEZZA Decreased Proptosis and Reduced Orbital Swelling



- At Week 24, patient had a 5mm reduction in proptosis, no inflammatory signs and symptoms of TED, and a decrease in the Gorman diplopia score from 3 to 0
- Orbital fat volume was reduced; inferior rectus muscle size decreased by 49 percent, and medial rectus muscle volume decreased by 41 percent

HORIZON MRI: Magnetic resonance imaging

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Teprotumumab (Tepezza)

Phase 4: Safety

During Double-masked Treatment Period, N (%)	Placebo (N=20)*	TEPEZZA (N=81)
Any adverse events	16 (80.0)	33 (80.5)
Serious adverse events*	1 (5.0)	1 (2.4)
Adverse events leading to study drug discontinuation†	1 (5.0)	1 (2.4)
Adverse events leading to death	0	0
Adverse events of special interest	7 (36.0)	15 (36.6)
Infusion reaction	3 (15.0)	2 (4.9)
Hyperglycemia	2 (10.0)	6 (14.6)
Hearing impairment	2 (10.0)	9 (22.0)
New Onset/exacerbation IBD	0	0
Other Adverse Events		
Muscle spasms	2 (10.0)	17 (41.5)
Nausea	1 (5.0)	2 (4.9)
Alopecia	0	2 (4.9)
Diarrhea	4 (20.0)	8 (19.5)
Fatigue	2 (10.0)	9 (22.0)
Dysgeusia	1 (5.0)	4 (9.8)
Headache	2 (10.0)	7 (17.1)
Dry skin	0	5 (12.2)
Nail bed disorder	0	2 (4.9)
Eye pain	1 (5.0)	5 (12.2)
Eye pruritus	0	3 (7.3)
HbA1c increased	0	3 (7.3)
Hypertension	0	3 (7.3)

*Includes patient who received one dose of teprotumumab-trbw in error
†EDP: left conductive hearing loss in pt with congenital hearing abnormality; PSOI: DKA in patient with undiagnosed diabetes mellitus who received teprotumumab for one infusion (first infusion) in error, despite being randomized (assigned) to placebo group ‡EDP: conductive hearing loss (above) occurred in the double-masked period, pt completed the masked period and discontinued in the open-label period. PSOI: infusion reaction (dull cardiac-related chest pain, pressure-like, non-radiating, slight difficulty breathing)

Douglas RS, et al. J Clin Endocrinol Metab. 2021;106(2):516-26.

Courtesy of AMGEN TED Disease State + Teprotumumab HCP Deck

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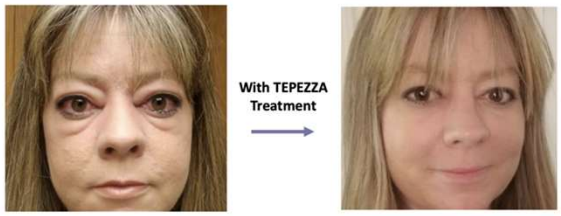
TEPEZZA Patient Treated with Full Course of Therapy



"Before and After" selfies of one of my patients who completed full course of TEPEZZA therapy

HORIZON Patient shown had completed two infusions of TEPEZZA at the time the photos were taken. The patient has since completed the full course of TEPEZZA treatment. Participant in the TEPEZZA Expanded Access Program. Photos used with permission from patient of Dr. Douglas.

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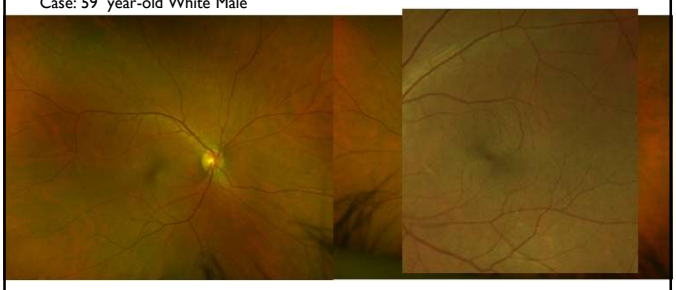
Case: 59 year-old White Male



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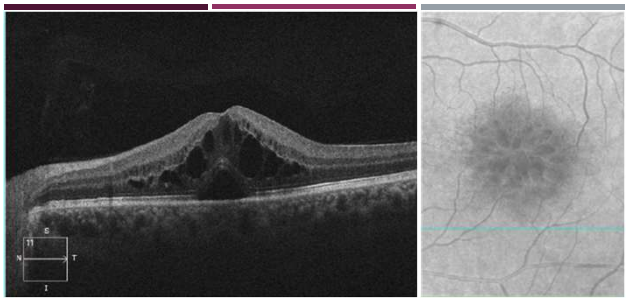

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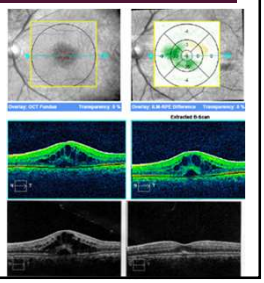
UVEITIC MACULAR EDEMA (UME)

- Diagnosed with Uveitic Macular Edema (UME) OS
- Laboratory testing revealed Lofgren's Syndrome (Acute Sarcoidosis)
- Treatment: NSAID's, Corticosteroids, Immunomodulators (hydroxychloroquine), biologics, intravitreal injection (anti-VEGF/ steroids), intraocular implants



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Sarcoidosis

- A multisystem granulomatous inflammatory disease
  - Noncaseating Granulomas (NCG)- are comprised of epithelioid cells and giant cells
  - Delayed hypersensitivity and heightened Th1 (T helper 1) immune response in affected organs
- 16X more common in Black females
  - The disease is usually more serious
- Predominantly in the lungs and lymph nodes
- Arthritis/ Bone and joint involvement

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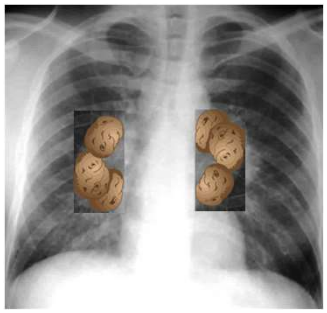
Clinical features

- Bilateral hilar lymphadenopathy AKA "Potato nodes"
- Pulmonary infiltration
- Arthritis/Bone and joint involvement
- Neurological involvement
- Cardiac involvement



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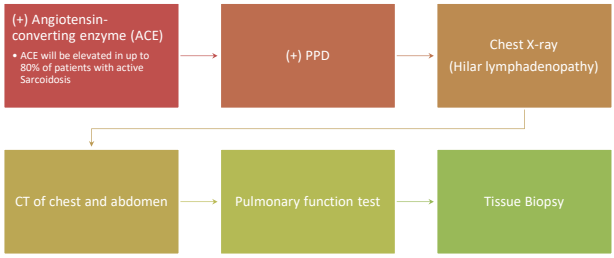
Laboratory Findings



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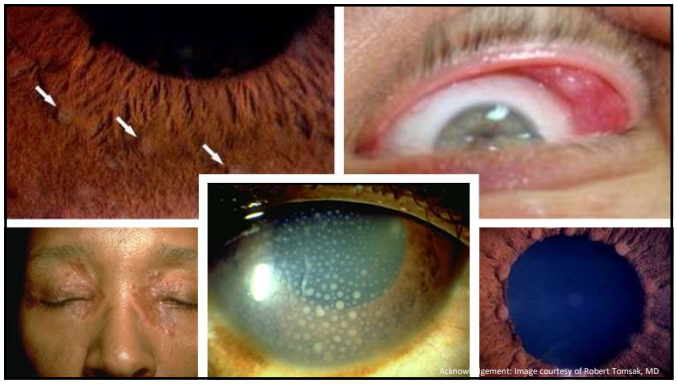

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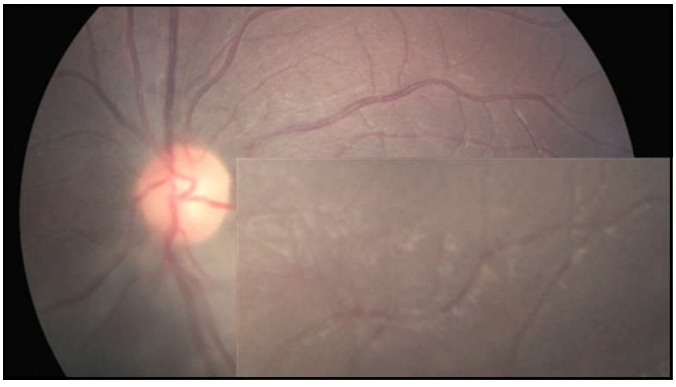

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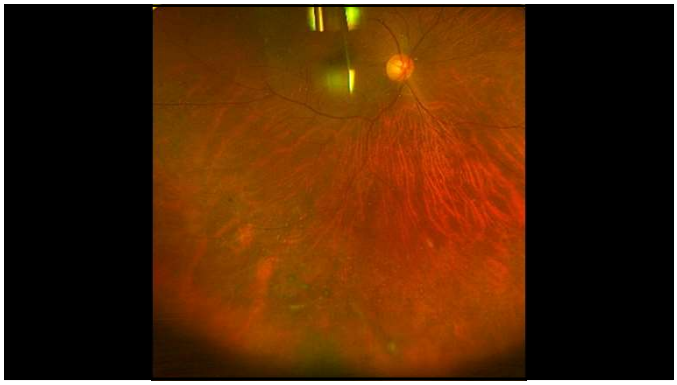

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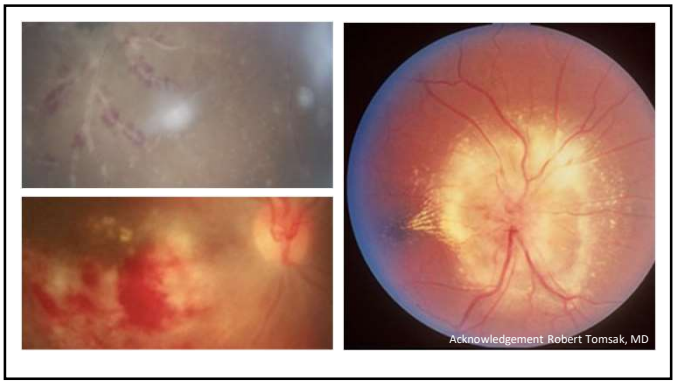

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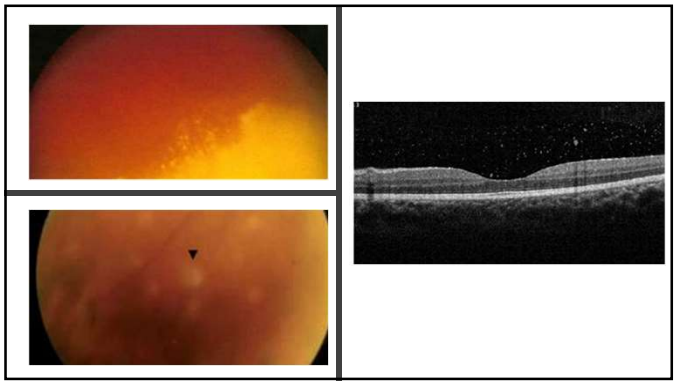

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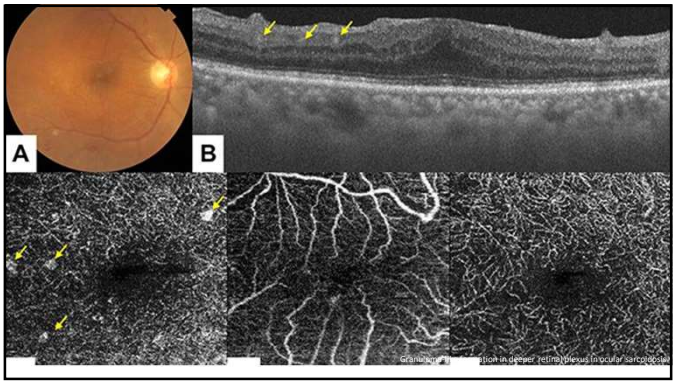

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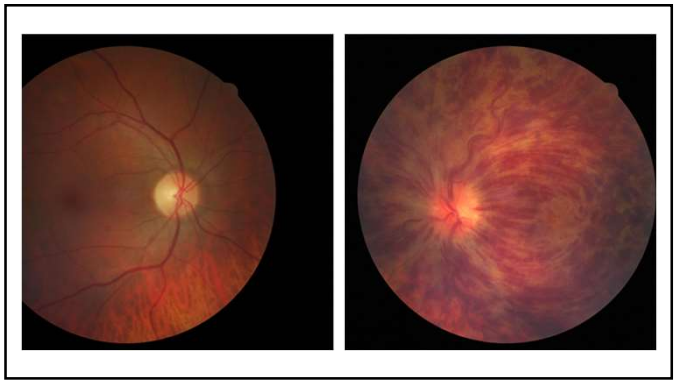

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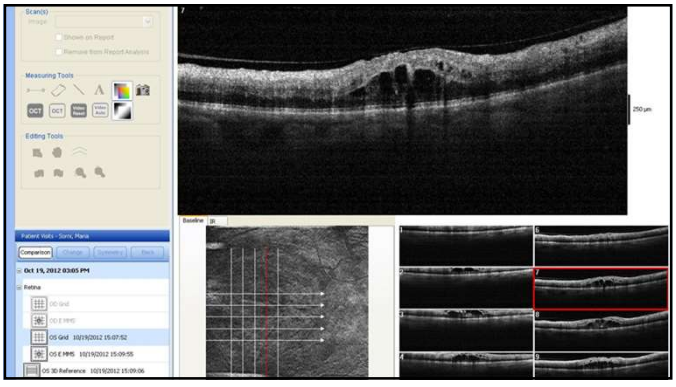

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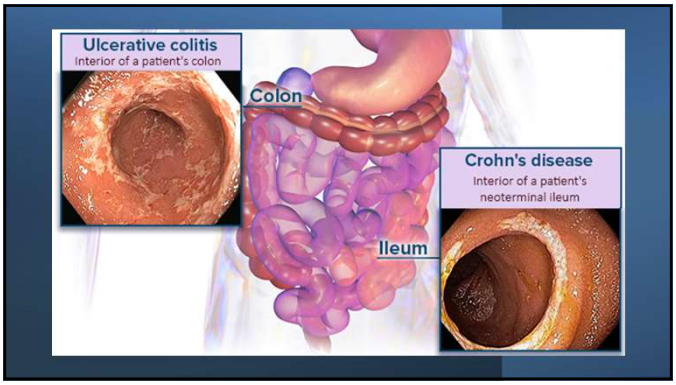
Inflammatory Bowel Disease (IBD)

- Two types:
  - **Crohn's disease**
    - Can occur anywhere in your digestive tract
  - **Ulcerative colitis (UC)**
    - Usually affects only the innermost lining
    - Patients may develop skeletal abnormalities similar to ankylosing spondylitis
    - Clinical hallmark of UC is bloody diarrhea
    - There is an increased risk of colon cancer in ulcerative colitis
      - 5% of patient will develop colorectal cancer (CRC)

World J Gastroenterol. 2008 Jul 7;14(25):3937–3947.

79



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IBD/Spondyloarthropathies (*Spondylarthritis)*

- Group of interrelated chronic inflammatory diseases that affect the vertebral column
- Clinical features:
  - Arthritis
  - Involvement of **sacroiliac joints**
  - Genetic predisposition for **HLA-B27**
  - Uveitis
  - Increase familial incidence

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Spondyloarthropathies (*Spondylarthritis)*

- Ankylosing spondylitis
  - Rare inflammatory disease
  - More common in young men
  - Onset 15-35 years of age
  - More common in Native Americans
  - **95% positive for HLA-B27**

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Spondyloarthropathies (*Spondylarthritis)*

- Reactive arthritis (Reiter's syndrome)
  - Classic triad: conjunctivitis, arthritis, urethritis/cervicitis

"Can't See, Can't Pee, Can't Climb a Tree."

- Ocular complications occur in 30% of patients
- 80-90% positive for HLA-B27
- Laboratory W/U include:
  - Chlamydia culture
  - HIV testing

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Spondyloarthropathies (*Spondylarthritis)*

- Psoriatic arthritis (PsA)
  - Chronic, immune-mediated skin disease
    - Skin disease precedes the arthritis in nearly 80% of patients
  - Conjunctivitis and uveitis
  - Pitting and/or discoloration of fingernails and/or toenails

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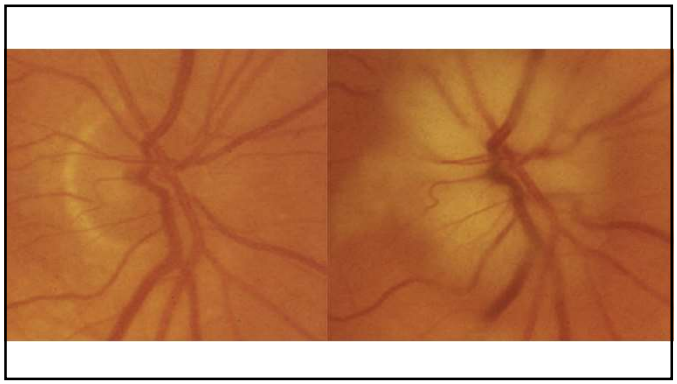

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Multiple Sclerosis

- Immune-mediated inflammatory disease that attacks myelinated axons in the CNS
- Women are 2x more likely to develop MS
- Ages of 20 and 50 years
  - Average age of onset ~34 years.
- Risk Factors:
  - Genetics
  - Infections
    - Viral
  - Environmental
    - Common in individuals of northern European descent

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Classification

- Relapsing-remitting MS (RRMS)
  - Approximately 85% of cases
- Primary progressive MS (PPMS)
  - 10-20%
- Secondary progressive MS (SPMS)
- Progressive-relapsing MS (PRMS)

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Ocular Findings

- Optic neuritis
- Optic Neuritis Treatment Trial (ONTT)
- Facial pain/ vertigo/ hearing loss
  - 30-50% of patients at some point in their illness
- Trigeminal neuralgia- Bilateral facial weakness or trigeminal neuralgia
- Facial myokymia (irregular twitching of the facial muscles)
- Chiasmal and retro chiasmal abnormalities
- Ocular motility disturbances

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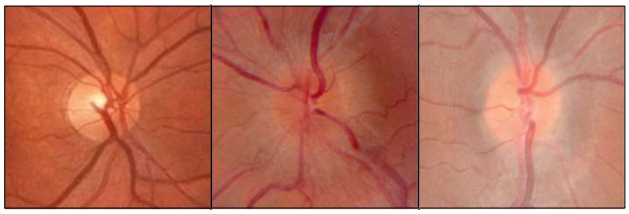
Optic Neuritis (ON)



Papillitis (35%) < retrobulbar optic neuritis (65%)
Peripapillary hemorrhage RARE (6%)

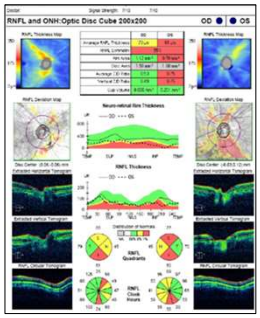
Optic neuritis, its differential diagnosis and management. Open Ophthalmol J. 2012;6:65-72

91

Optic Neuritis (ON)

SD- OCT

- Early
  - Helps detect subtle disc edema
- Later
  - Thinning of the RNFL within 3-6 months (74%)
  - Run a GCA as well
  - Unaffected fellow eyes also demonstrate reductions in RNFL compared to normal controls
- Bio marker for neuronal damage?



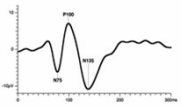
Trip SA, Schlottmann PG, Jones SJ, et al. Retinal nerve fiber layer axonal loss and visual dysfunction in optic neuritis. Annals of Neurology 2005; 58: 383–

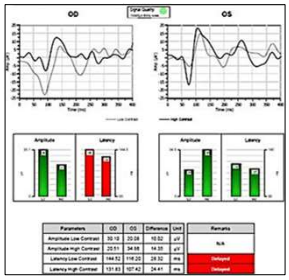
92

Optic Neuritis (ON)

VEP

- Identify subclinical lesions
- Prolonged latency (p100) with relative preservation of amplitude
- Pulfrich phenomenon
  - psychophysical percept wherein lateral motion of an object in the field of view is interpreted by the visual cortex





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Optic Neuritis (ON)

Prognosis/Clinical Course

- Recovery begins within 1 month
- 72% expected to have 20/20 vision 15 years later
- Similar prognosis at 1 year regardless of treatment
- Poorer prognosis in those with CDMS, initial poor acuity, and profound reduction in contrast sensitivity
  - Eyes that are still 20/50 at one month will usually have some degree of residual visual impairment

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Optic Neuritis (ON)

Treatment

Optic neuritis treatment trial (ONTT)

- Multicenter RCT- 448 patients
- Three treatment groups
  - Placebo
  - IV steroids then PO steroid tape
    - IV Methylprednisolone 1 g/day for 3 days, then Prednisone 1 mg/kg/day p.o. for 11 days, then
    - Taper Prednisone over 4 days (20 mg on day 1, 10 mg on days 2-4)
- Oral steroids alone
- Results
  - Similar long-term visual prognosis (at 1 year) regardless of treatment
  - IV steroids increased the rate at which vision recovered and reduced the risk of developing MS in the first 2 years
  - PO Pred increased the rate of recurrence (44% vs 29% at 10 years)

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Atypical Optic Neuritis (ON)

Table 5.3 Suggested Diagnostic Considerations, Laboratory Evaluation, and Distinguishing Features in Atypical Cases of Optic Neuritis

Entity	Laboratory Test	Comment
Optic nerve compression Neuromyelitis optica (NMO)	MRI Aquaporin-4 (AQP4), NMO antibody	Progressive loss of vision beyond 10 days Bilateral, severe vision loss; atypical course with poor recovery
Carcinomatous meningitis	CSF cytology	Systemic tumor almost always present
Syphilis	MHATP	Papillitis with hemorrhage Optic perineuritis Uveitis
Lyme	Serum Lyme titer	Endemic area Erythema chronicum migrans Optic perineuritis
Sarcoid	ACE	Optic nerve granuloma
	CXR	Uveitis Periphlebitis
Anterior ischemic optic neuropathy	ESR	Age >50 years
	CRP	Segmental disc swelling Disc hemorrhage
Lupus	ANA	Arthritis Antiphospholipid antibody syndrome
Nutritional	B_{12} level	Progressive optic atrophy
	Copper level	Pernicious anemia Ileum dysfunction Gastric surgery
Leber's hereditary optic neuropathy	Mitochondrial analysis	Males more than females Pseudodisc edema Telangiectasias
Retinal disease	OCT ERG	Macular changes

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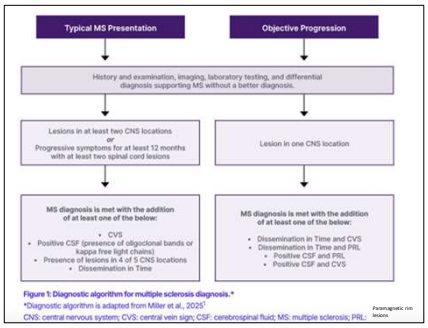
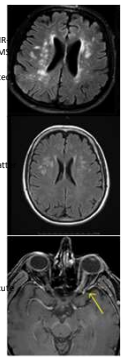
The 2024 Revised McDonald Criteria for





MRI with contrast and FLAIR abnormal in 85-95% of CDMS patients

FLAIR- (fluid level attenuated inversion recovery

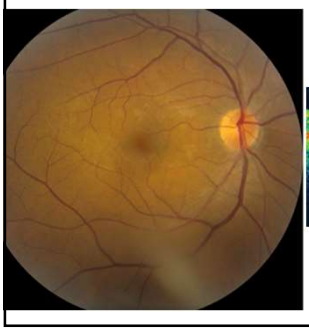
Periventricular white matter lesions - active lesions

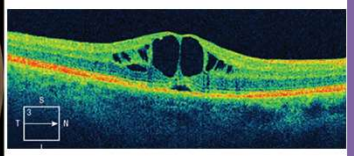
ON enhancement in acute optic neuritis

Neurol AMJ. 2025;2(1):26-29. https://doi.org/10.33590/neurolamj/ZSFM1010

97

65 yo WF present with a history of Fingolimod (Gilenya) for MS





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Fingolimod-associated macular edema (FAME)

- Fingolimod (Gilenya)- Oral sphingosine-1-phosphate immunomodulator
  - 0.5-mg once-daily therapy for patients with highly active relapsing–remitting multiple sclerosis (RRMS)
  - Macula Edema (FAME) occurs due to a breakdown of the blood-retinal barrier and vascular permeability
    - Interaction between fingolimod and $S1PR_1$ (sphingosine-1-phosphate (S1P) receptors) present on endothelial cells in retinal vessel
  - Higher dosage are at risk:
    - (1%) in the 1.25 mg group
    - (0.8%) in 0.5 mg group

J Neurol Neurosurg Psychiatry 2015; 87(5): 468–475

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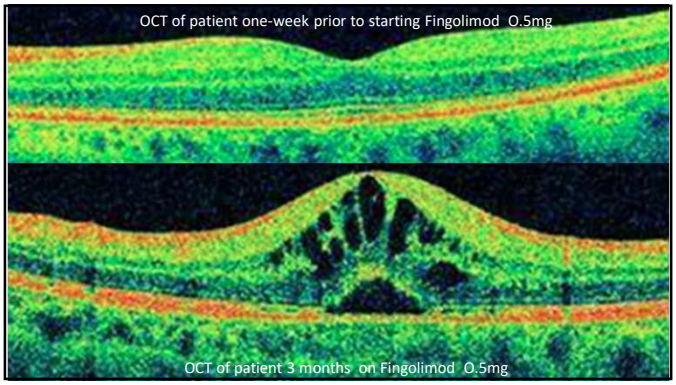

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Management

- Baseline screening patients prior to starting fingolimod
- Screening after 3–4 months with OCT
- FAME may be dose dependent
- Common in patients with diabetes, hypertension, and other vascular disease
- FAME resolve when medication discontinued
  - 84% of patients had macular edema resolution after fingolimod cessation
- Persistent FAME
  - Topical steroidal or non-steroidal, intravitreal AVT or steroids (Ozurdex), or oral corticosteroids.

Ophthalmology 2013; 120(7): 1432–1439

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Multiple Sclerosis Treatment

•Aim is to slow disease course and alleviate symptoms (no cure)
- IV high-dose corticosteroids
  - For acute exacerbations
- Immunomodulatory Agents
  - Interferon β-1a (Avonex)
  - Interferon β-1b (Betaseron)
  - Reduce exacerbations by ~$1/3^{rd}$
- Monoclonal antibodies
- Vitamin D supplementation if deficient

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Conclusion

- Autoimmune diseases are on rise.
- Early detection of the ocular complications of autoimmune diseases is essentially in preventing vision threatening complications and potentially save lives.
- Optometry plays an important role in the early detection, treatment and management of autoimmune disease.

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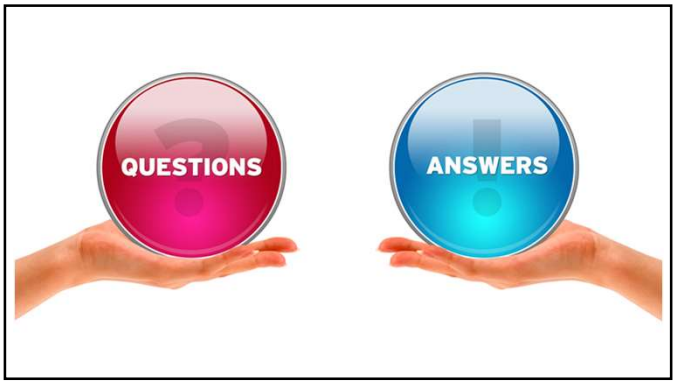

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Thank you

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