Thyroid Disease and Thyroid Eye Disease

1. Thyroid
   - Largest endocrine gland in the body
   - Butterfly shaped
   - Two lobes located on either side of the trachea in the lower portion of the neck
   - Lies just below skin and muscle layer surface
   - The thyroid is controlled by the hypothalamus and pituitary
   - The primary function of the thyroid is production of the hormones thyroxine (T4), triiodothyronine (T3), and calcitonin

2. Thyroid
   - Exocrine glands contain ducts. Ducts are tubes leading from a gland to its target organ
   - Exocrine glands have ducts for releasing the digestive enzymes
   - Salivary glands, sweat glands and glands within the gastrointestinal tract
   - Pancreas is both endocrine and exocrine
   - Exocrine (ductless gland) secreting digestive enzymes into the small intestine.
   - Endocrine (ductless gland) in that the cells of Langerhans secrete insulin and glucagon to regulate the blood sugar level.

3. Thyroid
   - Largest endocrine gland in the body
   - Butterfly shaped
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   - The primary function of the thyroid is production of the hormones thyroxine (T4), triiodothyronine (T3), and calcitonin

4. Thyroid
   - Two types of glands
   - Endocrine
   - Exocrine
   - Endocrine system is a control system of ductless endocrine glands that secrete hormones (chemical messenger) that circulate within the body via the bloodstream or lymph system to affect distant organs

5. Thyroid
   - Thyrroid is an endocrine gland
   - Two types of glands
   - Endocrine
   - Exocrine
   - Endocrine system is a control system of ductless endocrine glands that secrete hormones (chemical messenger) that circulate within the body via the bloodstream or lymph system to affect distant organs

6. Thyroid
   - Disclosures- Greg Caldwell, OD, FAAO
     - The content of this activity was prepared independently by me - Dr. Caldwell
     - Lectured for: Alcon, Allergan, Aerie, BioTissue, Kala, Maculogix, Optovue, RVL, Hema
     - Advisory Boards: Allergan, Sun, Alcon, Maculogix, Dompe, Viki, Eyenovia
     - Member: PA Medical Director, Credential Committee
     - Healthcare Registries – Chairman of Advisory Council for Diabetes
     - I have no direct financial or proprietary interest in any companies, products or services mentioned in this presentation – carotenoid scanner owner, Maculogix, Optovue OCT
     - The content and format of this course is presented without commercial bias and does not claim superiority of any commercial product or service
     - Optometric Education Consultants - Scottsdale, Minneapolis, Florida (Ponte Verde Beach), Menlo Park, MI, Nashville, and Quebec City - Owner
What is the most common cause of thyroid dysfunction?

A. Cancer  
B. Surgically induced  
C. Medication toxicity or side effect  
D. Pregnancy  
E. Autoimmune disease

In autoimmune disease the body typically produces ______ that attacks itself, this can be systemic or organ specific.

Antibodies, immunoglobulins

Primary=Thyroid gland  
Secondary= Pituitary failure  
Tertiary= Hypothalamic

Most autoimmune thyroid dysfunctions have a combination of thyroid antibodies, however depending on which AB is more abundant results in the outcome of the disease.
Hypothyroid

- TBAbs attacks the thyroid
- T3 and T4 decrease
- TSH increases

Thyroid Dysfunction

Hyperthyroidism (Thyreotoxicosis)

- Primary-autoimmune
  - Graves
    - Graves-Basedow or von Basedow’s
  - Secondary/Tertiary
    - Basedow’s basedow
- Toxic multinodular goiter
- Toxic adenoma
- Excess iodine
- Thyroiditis (inflammatory induced)
- Excess hormone production ectopic tissue
- Thyroid carcinoma

Hyperthyroidism (toxic antithyreoid antibodies)

- Primary-autoimmune
- Chronic, subacute thyroiditis
- Hashimoto’s Thyroiditis
- Autoimmune serologic disease
- Primary hyperfunction
- Basedow’s basedow
- Postpartum thyroiditis

Second/Tertiary
- Lithium medication
- Pregnancy
- Surgically induced
- Disorders of the pituitary gland or hypothalamus

Hypothyroidism (most common organ-specific autoimmune disorder)

- Primary-autoimmune
  - Chronic, subacute thyroiditis
  - Hashimoto’s Thyroiditis
  - Autoimmune serologic disease
  - Primary hyperfunction
  - Basedow’s basedow
- Secondary/Tertiary
  - Lithium medication
  - Pregnancy
  - Surgically induced
  - Disorders of the pituitary gland or hypothalamus

Grave’s (Hyperthyroidism)

- A multisystem disorder consisting of a triad
  - Hyperthyroidism with diffuse hyperplasia of the thyroid gland
  - Infiltrative dermopathy
  - Infiltrative ophthalmopathy
- Prevalence:
  - 20-40 year old female (F:M = 7:1)
- Genetic link
- Etiology:
  - Autoimmune disease: hypersensitivity reaction with thyroid stimulation by the circulation of abnormal thyroid-stimulating immunoglobulins (TSI)

Hashimoto’s Thyroiditis (Hypothyroidism)

- The most common cause of hypothyroidism in the United States
- It is named after the first doctor who described this condition, Dr. Hakaru Hashimoto, in 1912
- Autoimmune disease
- Goiter formation
- 5-10 times more common in women than in men
- The underlying cause of the autoimmune process still is unknown
  - Anti-TPO ab and Anti-TB recep present

Autoimmune atrophic thyroiditis (Hypothyroidism)

- Atrrophic thyroiditis is similar to Hashimoto’s thyroiditis
- A goiter is not present

Postpartum Thyroiditis (Hypothyroidism)

- These women develop antibodies to their own thyroid during pregnancy, causing an inflammation of the thyroid after delivery

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Systemic Manifestations of Hyperthyroid (Primary or Secondary)

- **Symptoms**
  - Nervousness
  - Heat intolerance
  - Sweating
  - Fatigue
  - Palpitation
  - Insomnia
  - Early waking
  - Alopecia
  - Vitiligo
  - Brittle nails

- **Signs**
  - Sweating
  - Muscle weakness
  - Emotionally labile
  - Tremor
  - Tachycardia
  - Hypertension
  - Bradycardia
  - Diabetes
  - ↑ Triglycerides & Ca
  - ↓ CHO
  - Microcyticanemia
  - Puffy hands and face
  - Deep voice
  - Bradycardia
  - Slow reflexes
  - Obesity
  - Hypothermia
  - Myxedema

Systemic Manifestations of Hypothyroid (Primary or Secondary)

- **Symptoms**
  - Cold intolerance
  - Weakness
  - Reduced energy
  - Lethargy
  - Muscle cramps
  - Constipation
  - Reduced appetite
  - Joint stiffness

- **Signs**
  - Cool, scaling skin
  - Puffy hands and face
  - Deep voice
  - Myotonia
  - Delirium
  - Bradycardia
  - Slow reflexes
  - Obesity
  - Hypothermia
  - Myxedema

Thyroid Eye Disease (TED)

- **Other names used**
  - Gravez’s disease
  - Gravez’s orbitopathy
  - Exophthalmos in Graves Disease
  - Thyroid Associated Orbitopathy (TAO)
  - Thyroid Orbitopathy
  - Ophthalmic Graves Disease
  - Inflammatory Eye Disease
  - Endocrine Orbitopathy

Why is this so confusing?

- **Thyroid Eye Disease**
  - Is often seen in conjunction with Grave’s Disease (hyperthyroid)
  - Is seen in people with no other evidence of thyroid dysfunction
  - Is seen in patients who have Hashimoto’s Disease (hypothyroid)

- **Most thyroid patients, however, will not develop thyroid eye disease**

Why is this so confusing?

- While eye disease may be brought on by thyroid dysfunction
  - Adequate treatment of the thyroid gland does not guarantee that the eye disease will improve
  - No particular thyroid treatment can guarantee that the eye will not continue to deteriorate
  - Once inflamed, the eye disease may remain active from several months to as long as three years
  - There may be a gradual or, in some cases, a complete improvement
Thyroid Eye Disease

Commonly known as Graves’ ophthalmopathy

About 80% of all patients with TED have the autoimmune hyperthyroid disorder known as Graves’ disease

Another 10% of all cases are seen in patients with autoimmune hypothyroidism, either Hashimoto’s thyroiditis, atrophic thyroiditis or Hashitoxicosis

Another 10% of all cases are seen in people with normal thyroid function

When thyroid function is normal, the eye condition is referred to as euthyroid Graves’ disease

Euthyroid is a term meaning that thyroid function tests are normal. Most people with euthyroid Graves’ disease develop a thyroid disorder within eighteen months of the emergence of the eye disorder

But some people with euthyroid Graves’ disease never develop thyroid dysfunction

What causes the Thyroid Eye Disease signs and symptoms?

The high and low levels of T3 and T4

The antibodies that are attacking the thyroid gland

Thyroid Eye Disease has 2 phases

A phase secondary to abnormal thyroid hormone levels

Increased or decreased FT3 and FT4 levels

Once these levels are normalized, ocular symptoms will resolve

Congestive Autoimmune form of Thyroid Eye Disease

Active phase stimulating or blocking TRAb are causing ocular activity

Resolution phase: symptoms regress and eye return to normal

Euthyroid Graves’ disease

If thyroid function is normal. How does one develop thyroid eye disease?

Hyperthyroidism eye symptoms

Excess hormone acting on the nerves that supply the eye

Dryness

Eyelid retraction

Deficient hormone causing venous congestion, impaired circulation and fluid stagnation

Periorbital edema

This form of TED resolves within a few weeks after thyroid hormone levels (FT4 and FT3) are corrected and brought back into the normal range

The pituitary hormone TSH can stay low or suppressed for many months during the course of treatment for hyperthyroidism and doesn’t mean that the patient is still hyperthyroid

TRAb levels are high, patients are smokers, nutrient deficiencies are present, or the patient continues to be exposed to environmental triggers such as smoke dairy products, the active phase can last as long as 5 years

Avoid any lid, muscle or orbital surgery

Plateau phase and Resolution “Passive” phase

An individual may be left with structural changes, such as eye protrusion, eyelid retraction, and in some cases, double vision

There are corrective procedures that can be performed to address these problems

Relying on the TSH level can be misleading and in treating TED
Similar receptors are found in the skin, fat and muscle of the orbit.

You’re in the Know

Normal Values:
- Thyroglobulin 20 IU/ml
- Peroxidase <35 IU/ml
- TSI 1.75 IU/ml

It does work!

General Ocular Symptoms

- Prominent eyes, stare
- Pain
- Laceration
- Eyelid swelling
- Foreign-body sensation
- Double vision
- Photophobia
- Decreased vision in one or both eyes

NOSPECS: Grading System

1969 by S.C. Werner

- Class 2-6 document severity
  - Class 2: No signs or symptoms
  - Class 3: Only signs, upper lid retraction
  - Class 4: Soft Tissue involvement with symptoms
  - Class 5: Proptosis
  - Class 6: EOM involvement
  - Class 7: Corneal involvement
  - Class 8: Light Loss

Within classes 2 to 6 the investigator has to differentiate the severity grades A, B, C

NOSPECS classifies severity but not the activity or stage (active/inflammatory or passive/congestive)

NOSPECS: Grading System

- 0: No symptoms or signs
- 1: Only signs (upper lid retraction without lid lag or proptosis)
- 2: Soft tissue involvement with symptoms (transient laceration, gritty sensation, retrobulbar discomfort)
  - Grade A: Absent
  - Grade B: Minimal: 5 mm or less
  - Grade C: Moderate: 6 mm or more
- 3: Proptosis associated with classes 2-6 only
  - Grade A: Absent
  - Grade B: Minimal: 5-9 mm
  - Grade C: Moderate: 10-19 mm
- 4: EOM involvement (usually with diplopia)
  - Grade A: Absent
  - Grade B: Minimal: 1 mm or less
  - Grade C: Moderate: 2 mm or more
- 5: Corneal involvement (due to proptosis, incomplete closure, lagophthalmos)
  - Grade A: Absent
  - Grade B: Minimal: 1 mm or less
  - Grade C: Moderate: 2 mm or more
- 6: Sight loss (due to optic nerve involvement)
  - Grade A: Absent
  - Grade B: Minimal: 20/200 or less
  - Grade C: Moderate: 20/200 or less
LEMO Classification

- 1991 Boergen and Pickardt
- Complements NOSPECS
- 4 finding categories
  - Lid
  - Exophthalmos
  - Muscular
  - Optic nerve
- Grade between 0 and 4 depending on severity
- LEMO, classifies severity but not the activity or stage (active/inflammatory or passive/congestive)

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LEMO Classification

Lid (L)
- 0: missing
- 1: lid edema only
- 2: real retraction (impaired lid closure)
- 3: retraction and upper lid edema
- 4: retraction and global lid edema

Exophthalmos (E)
- 0: missing
- 1: eye closing not impaired
- 2: conjunctival injection in the morning
- 3: persistent conjunctival injection
- 4: corneal complications

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LEMO Classification

Muscular (M)
- 0: missing
- 1: detectable in imaging only
- 2: Pseudoparesis
- 3: Pseudoparalysis

Optic Nerve (O)
- 0: missing
- 1: regarding color vision only or detected via VEP
- 2: peripheral scotoma
- 3: central scotoma

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Grading Scales

- New grading scales are trying to be developed to not only grade the severity but also help to determine if inflammatory or passive stage

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Lid Involvement

- Lid Retraction
- Lid Lag
- Lagophthalmus

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Lid Retraction

- Scleral show in primary gaze
- Occurs in ~40% of Grave’s patients
- Enlarged inferior rectus muscle
- Excess stimulation of Müller’s muscle
- Increased orbital volume

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Eyelid Lag: von Graefe’s Sign

- Immobility or lagging of upper eyelid on downward gaze
- Fibrosis of the inferior rectus muscle may induce lower lid retraction

Lagophthalmos

- Inability to form a complete lid closure with a normal blink due to exophthalmos/proptosis
- Often leads to corneal exposure

Soft Tissue Involvement

- Conjunctiva
- Chemosis
- Periorbital edema

Conjunctiva

- Conjunctival and epithelial injection
  - Especially near the horizontal recti insertions
- Chemosis
  - Edema of the corneal and conjunctival
  - Superior orbital fascia
  - Extraocular muscles
  - 60% association between TED and systemic thyroid disease
  - Rheumatoid arthritis
  - Sjögren’s syndrome

“If it is Red think TED”
Dr. Andy Morgenstern 12-7-2013, OMS-Contemporary Resort

Periorbital Edema

- Inflammation of the subcutaneous connective tissue
- May be first sign of thyroid eye disease
- Greatest in the morning
Infiltrative Orbitopathy (Exophthalmos/Proptosis)

- Thyroid Eye Disease is most common cause of unilateral and bilateral exophthalmos
- The term exophthalmos is reserved for prominence of the eye secondary to thyroid disease
- May need MRI to determine or obvious exophthalmos may be present
- It is permanent in 70% of cases
- Caused by increased volume of the extra ocular muscles
  - Lymphocytic infiltration
  - Proliferation of fibroblasts
  - Edema within the interstitial tissue of the muscle

Exophthalmometry

- Is race dependent (race and gender impact orbital volume)
- Kretel or luedde results
- Adults
  - Average reading 17 mm
  - 95% of population have readings between 13-21mm
- General concerns
  - A difference of 2 mm or more between the eyes
  - A measurement of more than 24 mm

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Restrictive Myopathy

- Secondary to edema and fibrosis of EOM’s
- Inferior Rectus (IR) muscle is most commonly involved
- Occurs in 30-50% of patients
- Diplopia may be transient but in 50% it’s permanent
IOP in Thyroid Eye Disease

- A rise in IOP has been reported with TED
- I would have higher suspicion when you see
  - Periorbital edema
  - Exophthalmos, proptosis
  - Restrictive myopathy
- Some literature reports IOP in up gaze to be part of the diagnoses of thyroid dysfunction

Restrictive Myopathy

Obvious restrictive myopathy but also note the periorbital edema, and conjunctival hyperemia

Corneal Exposure

- Exposure keratopathy secondary to exophthalmos and lagophthalmos
- Significant threat to visual function

Optic Neuropathy

- Affects 5% of patients
- Usually mild to moderate exophthalmos and shallow orbits
- Enlargement of the recti muscles compresses ONH on its blood supply at the apex of the orbit
- Compression MAY occur without significant proptosis
- Compressive and/or ischemic and/or toxic

Treatment of Thyroid Eye Disease

Depends on what phase of the disease we are in:
- Phase secondary to abnormal thyroid hormone levels
- Active or inflammatory phase
- Relapse phase and Resolution "Passive" phase
- Depends on what orbital tissue or structures are involved
- Depends on the risk of vision loss
- Depends if primary, secondary or tertiary thyroid dysfunction
- Management consists of:
  - Control of inflammation
  - Prevention of ocular and visual damage
  - Addressing ocular motility abnormalities
  - Improving corneal alignment
- Patient education is essential
- Communication with an endocrinologist or internist will ensure proper patient care

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- Significant threat to visual function

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- Enlargement of the recti muscles compresses ONH on its blood supply at the apex of the orbit
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- Compressive and/or ischemic and/or toxic

Treatment of Thyroid Eye Disease

Palliative (hormone imbalance, active, passive):
- Lubricants
- Topical anti-inflammatory (Lotemax/Restasis)
- Prisms
- Steroids (active phase)
- Orals
- Periocular injections
- IV with oral steroid taper
- Orbital radiotherapy (active phase)
- Orbital Decompression (passive phase)
  - For removal, orbital decompression (FROD)
  - Orbital decompression (BROD)
  - Smoking causes the thyroid eye disease to be more severe
  - Smoking causes treatments to be less effective

Treatment of Thyroid Eye Disease

- Palliative (hormone imbalance, active, passive)
  - Lubricants
  - Topical anti-inflammatory (Lotemax/Restasis)
  - Prisms
  - Steroids (active phase)
  - Orals
  - Periocular injections
  - IV with oral steroid taper
  - Orbital radiotherapy (active phase)
  - Orbital Decompression (passive phase)
    - For removal, orbital decompression (FROD)
    - Large orbits
    - Bone removal orbital decompression (BROD)
    - Local steroids
  - Smoking causes the thyroid eye disease to be more severe
  - Smoking causes treatments to be less effective

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Rheumatology, Thyroid Dysfunction and the Eye

February 11, 2022

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**Rheumatology, Thyroid Dysfunction and the Eye**

**February 11, 2022**

**Corneal Exposure**
- Manage the corneal defect at first line
  - Lubricating and antibiotic
  - Lid taping
  - Moisture barrier
- Orbital Disease Consult
  - High dose oral steroids
  - 100mg/day x 7 days
  - Orbital decompression

**Optic Neuropathy**
- Systemic Steroids
  - If rapidly progressive and painful in the early stage of the disease
  - Only if no contraindications
  - Prednisolone 80-100mg, expect results within 48hrs. Taper dose and discontinue in 3 mo
  - IV Methylprednisolone
  - Radiotherapy if contraindication to steroid
  - Orbital decompression

**Orbital Decompression**
- Not effective if no medical treatment
  - Two-wall decompression
    - 2-3 mm retroplacement of the globe
  - Three-wall decompression
    - 3-6 mm retroplacement
  - Four-wall decompression
    - 10-16 mm retroplacement

**Orbital Decompression (Surgical/Cosmetic)**

**Thyroid Eye Disease and Depression**
- When facial disfigurement occurs, thyroid eye disease is equivalent to the diagnosis of cancer and AIDS

**Orbital Decompression (Medical/Vision Threatened)**

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A rise in IOP has been reported with TED
I would have higher suspicion when you see
- Periorbital edema
- Exophthalmos, proptosis
- Restrictive myopathy
Some literature reports IOP in up gaze to be part of the diagnoses of thyroid dysfunction...let’s discuss.

Laboratory Testing
- Thyroid Hormone Levels
  - Serum total T4 (Thyroxine)
  - Serum total T3 (Triiodothyronine)
  - Estimation of the serum free T4 (or T3) concentration
  - Thyroglobulin (Tg) level
- Anti-thyroid antibodies
  - Thyroperoxidase antibody (TPO)
  - TSH-releasing hormone stimulating antibodies (TSH-RhAs)
  - Antibodies to TSH receptor (TSH-R)
  - Thyroglobulin (Tg) Antibodies (TgA)
- Commonly used Thyroid tests
  - TSH stimulation test
  - Radioactive iodine uptake test
  - Serum free T3 and T4
  - T3 suppression test
  - Sonography
  - Needle Biopsy
  - Thyroid scan

Hypothyroid
- Low FT4, High TSH, indicates primary check antibodies
- Low FT4, Low TSH, indicates secondary or tertiary, TRH stimulation, MRI
- Hashimoto’s (primary disease)
- Most common
- Low FT4, High TSH, Low Anti-TPO Abs, Low levels of Thyroglobulin (Tg) Antibodies (TgAb), Anti-TB Recp AB (approx. 10% present)
- Autoimmune atrophic thyroiditis
- Low FT4, High TSH, Low Anti-TPO Abs, Low levels of Thyroglobulin (Tg) Antibodies (TgAb), Anti-TB Recp AB (approx. 60% present)
- Treatment: Levothyroxine (Synthroid, Levothroid, Levoxyl, Unithroid)

Hyperthyroid
- High FT4, Low TSH
- TSH present

February 25, 2019
“Nothing Else Can Be Done”
Rheumatology, Thyroid Dysfunction and the Eye

April 22, 2019

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Teprotumumab-trbw (Tepezza)

- Horizon Therapeutics – HQ Dublin, Ireland and US based Chicago
- Biologic pharmaceutical
- Chinese Hamster Ovary
- Infusion, 8 total, every 3 weeks
- Treated eye disease
- IGF-1 receptor (Insulin like growth factor 1) and TSH receptors are overexpressed
- On the orbital fibroblasts
- Inhibiting downstream inflammatory cascades
- Cytokines, hyaluronan, leukotriene
- Differentiation into adipocytes and myofibroblasts
- Phase 2 and published in New England Journal of Medicine
- Phase 3 completed
- Not published
- PDUFA - March 2020, was approved early in 2020

https://www.tepezza.com/hcp/tepezza-moa/

Teprotumumab-trbw (Tepezza)
Teprotumumab (Tepezza)

- Infusion center
  - Go to Horizon website
  - Contact Us
  - Type in your question
    - Looking for infusion center

- Infusion Reactions (mild/moderate): approximately 4% of patients
  - Transient increases in blood pressure, flushing, heat, tachypnea, dyspnea, headache, and muscle pain
  - Consideration should be given to premedicating with an antihistamine, antipyretic, or corticosteroid and/or administering at a slower infusion rate.

- Hyperglycemia: Increased blood glucose or hyperglycemia
  - In clinical trials, 10% of patients experienced hyperglycemia
  - Monitor patients for elevated blood glucose and symptoms of hyperglycemia while on treatment with teprotumumab.
  - Patients with preexisting diabetes should be euglycemic before beginning treatment.

- Signs in Thyroid Eye Disease
  - "Dysiopsia" sign: lid retraction
    -von Graefe's sign: lid retraction on downward gaze
  - Grinno sign: lower lid lag on downward gaze
  - Asthenopic sign: irregular movement of the upper lid on downward gaze
  - Jeppson's sign: increased palpebral fissure of the eye
  - Swinging sign: intermittent blepharospasm
  - Kuster's sign: increased lid retraction on cross fixation

- Enroth's sign: Puffy swelling of the lid
  - Rosenbach's sign: Lid retraction with visual fixation
  - Mobius sign: Weakness of convergence
  - Ballet's sign: Palsy of one or more extraocular muscles
  - Suker's sign: Weakness of fixation on lateral gaze
  - Cowen's sign: Jerky papillary contraction to consensual light
  - Knies' sign: Unequal dilatation of the pupils
  - Jeffrey's sign: Absence of forehead wrinkling on upward gaze

Teprotumumab-trbw (Tepezza)

- Clinical Activity Score
  - Spontaneous pain, gaze evoked pain, eyelid erythema, chemosis, inflammation
  - Scale of 0-7, needed 4 to be in the study
  - 78% improved to 0 or 1, 7% improved 0 or 1 with placebo

- Proptosis
  - Improvement of 2 mm or better
  - 83% had 2 mm or better, 10% with placebo
  - Average was 3.2 mm at week 24

- Diplopia
  - Scale of 0, 1, 2, or 3
  - 68% improved 1 point, 29% with placebo

- Grave's Ophthalmopathy - Quality of Life Score
  - Scale 0-100
  - 17.28 point improved, 1.80 with placebo

Teprotumumab-trbw (Tepezza)

- Optics and Optic X Studies
  - 3 infusions, every 3 weeks, 24 weeks
  - Optics - acute, less than 9 months of disease
  - Optics X - chronic, 12-16 months disease

- Clinical Activity Score
  - Spontaneous pain, gaze evoked pain, eyelid erythema, chemosis, inflammation
  - Score of 7, needed 4 to be in the study
  - Proptosis
    - Improvement of 2 mm or better
    - 83% had 2 mm or better, 10% with placebo
  - Diplopia
    - Score of 0, 1, 2, or 3
    - 87% had 3-5 points, 23% with placebo

- Grave's Ophthalmopathy - Quality of Life Score
  - Scale 0-100
  - 17.28 point improved, 1.80 with placebo

Teprotumumab-trbw (Tepezza)

- Adverse Reactions
  - Very well tolerated
  - The most common adverse reactions (incidence ≥ 5% and greater than placebo) are muscle spasm, nausea, alopecia, diarrhea, fatigue, hyperglycemia, hearing impairment, dysgeusia, headache, and dry skin.

- Infusion center
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February 11, 2022

Questions

Rheumatology and the Eye

Rheumatology

- Specializes in the diagnosis and therapy of clinical problems involving
  - Joints
  - Osteoporosis
  - Musculoskeletal pain disorders
  - Soft tissues
    - Not connective tissue
      - Bones, cartilage, and blood vessels
    - Connective tissue
      - Tendons, ligaments, fascia, fibrous tissues, fat, and synovial membrane
- There are more than 200 types of these diseases, including rheumatoid arthritis, osteoarthritis, gout, lupus, back pain, osteoporosis, fibromyalgia, and tendinitis.

Where the Eye and Rheumatology Overlap

- Connective Tissue Disease
- Vasculitides
- Spondyloarthropathies

Connective Tissue Disease

- Connective tissue disease is any disease that has the connective tissues of the body as a primary target of pathology
- The connective tissues are composed of two major structural protein molecules
  - Collagen
  - Elastin
- The collagen and elastin become injured by inflammation
  - Typically due to autoimmunity
- "Collagen vascular disease" is an antiquated term used to describe diseases of the connective tissues

Connective tissue diseases secondary to gene abnormalities

- Connective tissue diseases that are strictly due to genetic inheritance include
  - Marfan syndrome
    - Gene FBN1 on chromosome 15
    - Can have tissue abnormalities in the heart, aorta, lungs, eyes, and skeleton
  - Ehlers-Danlos syndrome
    - Many types with autosomal gene
    - Typically have loose, fragile skin and hyperextensible joints, depending on type
Connective tissue diseases secondary to autoimmunity

- Cannot be regularly defined by gene abnormalities
- The spontaneous over activity of the immune system
  - Results in the production of extra antibodies into the circulation
  - Systemic Lupus Erythematosus
  - Rheumatoid Arthritis
  - Sjogren Syndrome
  - Systemic Sclerosis
  - Polymyositis/Dermatomyositis
  - Mixed Connective Tissue
  - Wegner’s Granulomatosis

Connective Tissue Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Auto-antibody</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic Lupus Erythematosus</td>
<td>Anti-dsDNA, Anti-Scl</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>Anti-RA33, Anti-ccp</td>
</tr>
<tr>
<td>Sjogren Syndrome</td>
<td>Anti-Ro52(S), Anti-La58(B)</td>
</tr>
<tr>
<td>Systemic Sclerosis</td>
<td>Anti-Scl 70, Anti-centromere</td>
</tr>
<tr>
<td>Polymyositis/Dermatomyositis</td>
<td>Anti-Jo-1</td>
</tr>
<tr>
<td>Mixed Connective Tissue Disease</td>
<td>Anti-U1-RNP</td>
</tr>
<tr>
<td>Wegner’s Granulomatosis</td>
<td>c-ANCA</td>
</tr>
</tbody>
</table>

Similar Structures

- The connective tissues are composed of two major structural protein molecules
  - Collagen
  - Elastin

  - Synovial membrane: A layer of synovium (white, fibrous, protective, outer layer of the eye containing collagen and elastic fibers)

  - Tenon’s capsule – a layer of connective tissue which forms a thin membrane that envelops the eyeball from the optic nerve to the limbus, separating it from the orbital fat and forming a socket.

53 year old woman

- Referred for treatment for a red OS
- 3 weeks ago sudden onset of red eye
- No pain, just feels like eyestrain
- At times it’s worse at times it’s better
- 5 years ago same eye was red, it resolved without treatment

Discussion

OD OS

Review of Systems
Knuckles

Treatment
- Lotemax qid OS
- Ibuprofen 400 mg qid PO
- Artificial tears
- Educate patient on finding and possible underlying etiologies
  - The patient was found to have arthritis, no definite diagnosis
  - Blood work? if so what test?
    - Antinuclear antibody (ANA) and rheumatoid factor (RF)

6 days later
- Treatment
  - Lotemax
    - TID=1 week
    - BID=1 week
    - QD=1 week
  - Ibuprofen 200mg QID
  - D/C
  - Review of lab results

Lab Results
- Referral to Rheumatologist

Final Outcome
- Diagnosed with rheumatoid arthritis
- Current treatment successful
- No ocular occurrence since treatment of rheumatoid arthritis

Episcleritis
- Typically occur in exposure zone
- Inflammation localized to episclera
  - Radiate posterior from limbus
  - Vessels are movable
  - Vessels blanch with sympatomimetics
- Types
  - Simple episcleritis: 80%
  - Nodular episcleritis: localized with variable tenderness
- Clinical Evaluation:
  - Sectoral injection 70%
  - Diffuse injection 30%
Episcleritis
- 70% of the cases are idiopathic
- 15-20% are due to allergy
- 5-10% are due to systemic disease
- Diagnosis:
  - Vision change: blurred or increased sensitivity to light
  - Redness
  - Pain
  - Sensation of foreign body

48 year old woman
- My OD eye has severe pain, it started as an ache about 1 week ago, but now is a throbbing pain
- It hurts to move my eye or touch my eye
- The pain is radiating to my cheek
- Patient does suffer from rheumatoid arthritis
- VA 20/20 OU
- IOMs full, but pain on movement OD
- PERRL (RAPD)
- Confrontation fields: full OU
- Let’s take a look

Diagnosis and Treatment?

Episcleritis, uveitis, iritis
- Systemic medications
  - Osteoporosis Medications
    - Bisphosphonates:
      - Fosamax (Alendronate), Actonel (Risedronate)

Testing for systemic disease indicated
- Multiple reoccurrences
- Bilateral
- History and exam are suspicious for systemic association
- Possible systemic etiologies
  - Rheumatoid arthritis
  - Lupus
  - Ankylosing spondylitis
  - Sarcoid
  - Tuberculosis
  - Gout
  - Syphilis
  - Wegeners

My OD eye has severe pain, it started as an ache about 1 week ago, but now is a throbbing pain.
It hurts to move my eye or touch my eye.
The pain is radiating to my cheek.
Patient does suffer from rheumatoid arthritis.
VA 20/20 OU.
IOMs full, but pain on movement OD.
PERRL (RAPD).
Confrontation fields: full OU.
Let’s take a look.

Non-Necrotizing Scleritis
- Depending on severity, one or combination of:
  - Oral Non Steroidal Anti Inflammatory agents
    - Ibuprofen or indomethacin (50 mg po bid)
  - Oral steroids
  - Communication/consult with rheumatologist
  - Sub Tenon’s steroid injection is contraindicated

Scleritis
- Severe inflammatory condition
- An immune mediated inflammation and destruction of the sclera
- Commonly associated with underlying systemic disease
- 4th to 6th decade of life
- Rare in children
- Female > male
- Greater than 50% are bilateral

Scleritis
- Symptoms
  - Gradual presentation (days)
  - Deep boring pain
  - May worsen at night
  - Referred pain to head and jaw
  - Eye is tender to the touch
Scleritis

Clinical Evaluation
- Sectoral or diffuse injection at all levels of vessels
- Blue hue in natural light
- Vessels do not blanch or move

Classification of Scleritis

Classified by location and appearance of inflammation

<table>
<thead>
<tr>
<th>Location</th>
<th>Subtype</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior Sclera</td>
<td>Diffuse Anterior Scleritis</td>
<td>40%</td>
</tr>
<tr>
<td></td>
<td>Nodular Anterior Scleritis</td>
<td>44%</td>
</tr>
<tr>
<td></td>
<td>Necrotizing Anterior Scleritis</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>w/ inflammation</td>
<td>3%</td>
</tr>
<tr>
<td></td>
<td>w/o inflammation</td>
<td>4%</td>
</tr>
<tr>
<td>Posterior Sclera</td>
<td>Posterior Scleritis</td>
<td>2%</td>
</tr>
</tbody>
</table>

Non Necrotizing Scleritis

- Diffuse
  - Portion involved in 60%
  - Entire sclera involved in 40%
  - Red/blue hue

- Nodular
  - Scleral nodule
  - Deep red-purple
  - Nodule is immobile and separate from episclera

Necrotizing Scleritis

- Most destructive form
- 60% develop ocular/systemic complications
- 40% have vision loss
- 30% mortality rate at 5 years

Necrotizing Scleritis Without Signs of Inflammation

(Scleromalacia Perforans)

- Predominantly seen in patients with rheumatoid arthritis (55%)
- Signs of inflammation are minimal
- No pain
- Progressive scleral thinning
- Uvea becomes visible
- Eye may rupture
Posterior Scleritis

May occur in isolation or with associated anterior involvement

Presentation:
- Pain (ocular/head)
- Proptosis
- Visual loss
- Restricted motility

Posterior Findings:
- Choroidal folds
- Exudative retinal detachment
- Papilledema

Easily missed if no associated anterior scleritis

Diagnosis confirmed with ultrasound, CT, or MRI

Hallmark: thickened striae

Most have no identifiable related systemic disease

Management

- Laboratory evaluation warranted
- Scleritis is often associated with systemic disease (some fatal)
- Common etiologies
  - Rheumatoid Arthritis
  - Systemic Lupus Erythematosus
  - Ankylosing spondylitis
  - Gout
  - Polyarteritis nodosum
  - Hansen disease

Treatment

- Non-Necrotizing Scleritis
  - Depending on severity, one or combination of:
    - Oral Non Steroidal Anti Inflammatory agents
      - Ibuprofen or indomethacin (50 mg po bid)
    - Oral steroids
    - Topical steroids and NSAID

- Necrotizing Scleritis
  - Oral/IV steroids
  - Immunosuppressive/ cytotoxic agents
  - "Sub-Tenon's steroid" injection is contraindicated

Rheumatoid Arthritis

- 1% of the population
- Women affected 2-3 X more than men
- Age of onset is 40-50
- Juvenile form

- Inflammation of the synovial tissue (lymphocytic) with synovial proliferation
- Symmetric involvement of peripheral joints, hands, feet and wrists
- Occasional systemic effects: vasculitis, visceral nodules, Sjogren syndrome, pulmonary fibrosis
- Anti-RA-33 autoantibodies
- RA associated nuclear antigen (RANA)
Rheumatoid Arthritis: Diagnostic Criteria

1. Morning stiffness (>1h)
2. Swelling of three or more joints
3. Swelling of hand joints (prox interphalangeal, metacarpophalyngeal, or wrist)
4. Symmetric joint swelling
5. Subcutaneous nodules
6. Serum Rheumatoid Factor
7. Radiographic evidence of erosions or periarticular osteopenia in hand or wrists

Criteria 1–4 must have been present continuously for 6 weeks or longer and must be observed by a physician. A diagnosis of rheumatoid arthritis requires that 4 of the 7 criteria are fulfilled.

Rheumatoid Arthritis fusiform synovitis

Rheumatoid Arthritis Vasculitis

Rheumatoid Arthritis Disease Modifying Anti-rheumatic Drugs (DMARDs)

- Methotrexate (MTX)
- Hydroxychloroquine
- Leflunomide
- Sulfasalazine

- Cyclosporine
- Parenteral/oral gold
- Azathioprine
- D-penicillamine
- Minocycline*

* Not approved by the FDA for the treatment of RA.

Rheumatoid Arthritis (Biologic DMARDs)
- Enbrel (Fusion Protein)
  - 50-100mg SQ q week
- Remicade (chimeric MAB)
  - 2mg/kg -10mg/kg Q 4-8 weeks
- Humira (humanized MAB)
  - 40mg SQ qwow

45 year old woman
- Reports a black line in her vision OD
- “The line in my vision does not move like a floater”
- Vision 20/20 OU
- Externals: unremarkable
- SLE: unremarkable

Fundus Photo OD

Cotton Wool Spots
- Non-specific finding
  - Hypertension
  - Diabetes
  - Connective Tissue Disease
  - HIV Retinopathy
  - Blood dyscrasia
    - Leukemia
    - Anemia

Many Faces of CWS
- No underlying etiology
- History of uncontrolled HTN and DM

Laboratory Work-Up
- Sed rate
- ANA
- Rheumatoid factor
- ACE
- HLA-B27
- Fasting blood glucose (FBG)
- Lipid profile
- Complete blood count (CBC)
Results

- Complete blood count (CBC):
  - WBC: 2.9 low
  - Hemoglobin: 9.1 low
  - Hematocrit: 33.9% low
  - Platelet count: 110 low
- Sed rate: 48 high
- ANA: 1:640 speckled pattern
- Rheumatoid factor: negative
- ACE: normal
- HLA-B27: negative
- Fasting blood glucose (FBG): normal

Referred to Rheumatologist

- Patient diagnosed with systemic lupus erythematosus (SLE) and treated with an immunosuppressant
- CWS have resolved and no other occurrences

Systemic Lupus Erythematosus

- General
  - autoimmune multisystem disease
  - prevalence 1 in 2,000
  - 9 to 1: female to male (1 in 700)
  - peak age 15-25
  - immune complex deposition
  - photosensitive skin eruptions, serositis, pneumonitis, myocarditis, nephritis, CNS involvement

Systemic Lupus Erythematosus: Diagnostic Criteria

<table>
<thead>
<tr>
<th>Diagnostic criteria</th>
<th>1982 classification criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malar rash</td>
<td>Prevalence 1%</td>
</tr>
<tr>
<td>Discoid rash</td>
<td>Prevalence 1%</td>
</tr>
<tr>
<td>Oral ulcers</td>
<td>Prevalence 1%</td>
</tr>
<tr>
<td>Arthritis</td>
<td>Prevalence 1%</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>Prevalence 1%</td>
</tr>
<tr>
<td>Nephritis</td>
<td>Prevalence 1%</td>
</tr>
<tr>
<td>CNS involvement</td>
<td>Prevalence 1%</td>
</tr>
</tbody>
</table>

Systemic lupus erythematosus: Diagnostic criteria definitions

- Malar rash: Fixed erythema, flat or raised, sparing the nasolabial fold.
- Discoid rash: Raised patches, adherent keratotic scaling, follicular plugging; older lesions may cause scarring.
- Photosensitivity: Skin rash from sunlight.
- Oral ulcers: Usually painless.
- Arthritis: Nonerosive, inflammatory in two or more peripheral joints.
- Serositis: Pleuritis or pericarditis.
Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects multiple organ systems.

### 1982 classification criteria definitions

- **Renal disorder**: Persistent proteinuria or cellular casts
- **Neurologic disorder**: Seizures or psychosis
- **Hematologic**: Hemolytic anemia, leukopenia (<4,000/mm³), lymphopenia (<1,500/mm³), or thrombocytopenia (<100,000/mm³)
- **Immunologic disorder**: Antibodies to dsDNA or Sm or positive antiphospholipid antibodies (IgG or IgM antibodies, lupus anticoagulant, or false positive serologic test positive serologic test for syphilis)
- **Antinuclear antibody test**: Positive

### Skin manifestations

- **Discoid Lupus**: Cutaneous manifestations
  - Scar upon healing

- **Butterfly rash**: Discoid type

- **Photosensitivity**

- **Interarticular dermatitis**
Systemic lupus erythematosus
retinal vasculitis

Treatment: Rheumatologist involvement
Avoidance of sun
Use of sunscreens
DMARDs

Systemic Lupus Erythematosus

Methotrexate (MTX)
Hydroxychloroquine
Leflunomide
Sulfasalazine
Cytosine
Cellcept
Cyclosporine
Parenteral/oral gold
Azathioprine
D-penicillamine
Minocycline*

* Not approved by the FDA for the treatment of RA.

37 year old woman

Referred in for punctal plug insertion due to dry eyes; temporary plug outcome was successful
Currently using
System q2-d OU
Restasis bid OU
System right PRN
She wants plugs to help decrease her usage of lubricants
SLE: confirms almost absent tear prism and mild to moderate Lisamine green staining
Anything suspicious here?

Treatment

Permanent plugs: RUL/RLL
Labs ordered:
- ESR, CRP, ANA, RF, SS-A, SS-B and thyroid panel

Results

Excellent outcome to permanent plugs: RUL/LLL
- ESR: 33 mm/hr
- CRP: 1.7
- ANA: 1:120
- RF: positive
- SS-A: positive
- SS-B: positive
- Thyroid panel: normal

Referral to rheumatologist for diagnosis and treatment
Diagnosis

- Sjögren’s Syndrome

Definition of Sjögren’s Syndrome

A chronic systemic autoimmune disease characterized by lymphocytic infiltration of salivary and lacrimal glands, leading to dry mouth (xerostomia) and dry eyes (keratoconjunctivitis sicca) as a consequence of progressive glandular destruction and dysfunction.

Sjögren’s Syndrome

- 1.2 million Americans affected
- 90% women
- 2nd most common autoimmune rheumatic disease
- A major women’s health problem

Sjögren’s Syndrome

Common features

- Primary or secondary
- Dry mouth and dry eyes
- Serum autoantibodies - RF, anti-Ro/SSA, anti-La/SSB
- Glandular and extraglandular manifestations
- Overlap with other autoimmune rheumatic diseases
- Women > Men (9:1)

Sjögren’s Syndrome

(Ocular signs)

- Reduced tear production
- Measured by Schirmer test
- Decreased tear breakup time
- Epithelial staining with diagnostic dye
- Filamentary keratitis by biomicroscopy

Sjögren’s Syndrome

(Oral features)

- Dry mouth
- Sore or burning mouth
- Intolerance to acidic or spicy foods
- Abnormalities of taste
- Difficulty with chewing and swallowing dry foods
- Difficulty with phonation (speaking)
- Difficulty wearing dentures
**Dental Caries (Decay) in Sjögren’s Syndrome Patients**

**Salivary Glands**

**Why Can Muscarinic Agonists Be Used to Stimulate Saliva?**

- The severity of salivary dysfunction is disproportionate to the amount of lymphocyte infiltration.
- Most Sjögren’s syndrome patients have remaining acinar cells in their salivary glands.
- Muscarinic receptors on these cells are still capable of responding to stimulation.
- In sufficient dosages, muscarinic agonists can increase secretion of exocrine glands.

**Evoxac**

- **Mechanism of Action**
  - A cholinergic agonist that binds to muscarinic receptor and stimulates exocrine glands.
  - **Muscarinic receptor subtypes**
    - Evoxac has high affinity for M1 and M3 subtype.
    - Selective from salivary glands and stomach.
    - Slow heart rate, reduce contractile forces of atrium, reduce conduction velocity of AV node.
  - Sufficient dosages, muscarinic agonists can increase secretion of exocrine glands.

**Connective tissue diseases secondary to autoimmunity**

**Potential Ocular Involvement**

- Systemic Lupus Erythematosus
- Rheumatoid Arthritis
- Sjögren Syndrome

**Cannot be regularly defined by gene abnormalities**

- The spontaneous over activity of the immune system results in the production of extra antibodies into the circulation.
Vasculitides

The vasculitides are a group of diseases characterized by non-infectious necrotizing vasculitis and resultant ischemia.

32 year old man

"I have bleeding in my eyes", patient requests 3rd opinion
"I have been tested for high blood pressure and diabetes 4 times, I don’t have either one"
Vision 20/20 OU

Work Up

- CBC/diff normal
- ACE normal
- FTA ABS negative
- VDRL negative
- HLA B27 negative
- PPD normal
- ANA negative
- RF negative

Results and Fundus 3 Weeks Later

Vasculitides

- Polyarteritis Nodosa
- Churg Strauss Syndrome
- Hypersensitivity Vasculitis
- Wegener’s Granulomatosis
- Giant Cell Arteritis
- Behcet’s Disease
- Cogan’s Disease
- Kawasaki Disease
Rheumatology, Thyroid Dysfunction and the Eye

February 11, 2022

Ask and You Shall Receive

Refer to Rheumatologist

Testing and examination reviews Behcet’s diagnosis
- Ulcers, covered in pale pseudomembrane
- Punctate oral, gingival, basilar, mucosal, tongue, palate and oropharynx
- Central ulcer similar in appearance
- Heat is chronic with remission
- The treatment of Behcet’s syndrome depends on the severity and the location of its manifestations in an individual patient
- This patient oral steroids and Remicade

Spondyloarthropathies

Prevalence is similar to Rheumatoid Arthritis, 1-2%
- Share similar clinical, radiographic, and genetic features
- A cluster of overlapping forms of inflammatory arthritis
  - Are distinct from rheumatoid arthritis
  - Affect the spine
  - Affect the entheses (insertions of tendons and ligaments)
- The syndromes include
  - Ankylosing spondylitis
  - Reactive arthritis (Reiter’s syndrome)
  - Psoriatic arthritis
  - Enteropathic arthritis
- Syndromes sometimes included (controversial)
  - Whipple’s disease
  - Behcet’s syndrome

Seronegative Spondyloarthropathy

Seronegative refers to the absence of the specific antibodies (or substance) that were being tested for
- Rheumatoid factor
- Spondyloarthropathies are inflammatory joint diseases of the vertebral column associated with the major histocompatibility complex (MHC) Class I molecule
- HLA-B27
HLA B27

- The major histocompatibility complex is encoded by several genes located on human chromosome 6
- Most (but not all) patients with spondylitis carry a gene called HLA-B27
- People carrying the HLA B27 gene
  - are at increased risk of developing spondylitis
  - The majority (over 75%) will never develop the disease
- HLA-B27 is not helpful in prognosis

HLA-B27 & Uveitis

- Features:
  - Marked or severe presentation
  - Anterior uveitis
  - Unilateral
  - Acute onset, <3 months
- Can occur as a HLA B27 uveitis
- Can occur with a spondyloarthropathy

Ankylosing Spondylitis

- Ankylosing spondylitis is a chronic, usually progressive, disease involving the articulations of the spine and adjacent soft tissues
- HLA B27 positive 90%
- Uveitis 20-40% chance

Reactive Arthritis

- A spondyloarthropathy following enteric (GI tract) or urogenital infections and occurring in individuals who are HLA-B27 positive
  - Usually also referred to as “Reiter syndrome” and is now referred to as reactive arthritis
  - May be described as a triad of arthritis, nonspecific urethritis, and conjunctivitis, often accompanied by iritis
  - Can cause inflammation in the joints of the spine, legs and arms and in other parts of the body
  - The syndrome usually begins with urethritis followed by conjunctivitis and rheumatological findings
    - Arthritis begins within 1 month of infection in 80% of patients
    - HLA B27 positive 40-80%
    - Uveitis 20-40% chance

Psoriatic Arthritis

- Patients with psoriasis have a 5-42% chance of developing psoriatic arthritis
- About 20% of people who develop PsA will eventually have psoriatic spondylitis
  - The inflammation in the spine can lead to complete fusion
  - Spondylitis associated with psoriasis
    - 60-70% are HLA-B27 positive
    - Psoriatic arthritis without spondylitis 15% HLA B27 positive
  - Uveitis 7% chance

Enteropathic Arthritis

- A form of chronic, inflammatory arthritis associated with the occurrence of an inflammatory bowel disease (IBD)
  - Ulcerative colitis
  - Crohn’s disease
- About one in five people with Crohn’s or ulcerative colitis will develop enteropathic arthritis
  - Approximately 33-60% of patients with spondylitis in association with IBD have HLA-B27
  - The most common areas affected are the peripheral (limb) joints
    - In some cases, the entire spine can become involved as well
  - Uveitis 3-11% chance
Undifferentiated Spondyloarthritis (USpA)

- To describe symptoms and signs of spondylitis in someone who does not meet the criteria for a definitive diagnosis of AS or related disease

- Underrecognized by many physicians
- Initial diagnosis of Spondyloarthritis or Undifferentiated Spondyloarthritis if certain symptoms are present but are not enough to make a specific diagnosis
- Some times, more people with USpA will develop a well-defined form of spondylitis such as ankylosing spondylitis

Revised Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy

- Recommendations were 2002 by the American Academy of Ophthalmology
- Improved screening tools and new knowledge about prevalence of toxicity have prompted the change
- Th e revised criteria for any RPE loss is important to prevent central visual loss. However, questionable test results should be repeated or reviewed for more sensitive tools
- Screening for the earliest hint of fundus or retinal change
- Plaquenil toxicity is not well understood

Background: Plaquenil toxicity is not well understood. The American Academy of Ophthalmology recommends screening for chloroquine and hydroxychloroquine retinopathy. Although the issue of visual damage is protracted in many years, most patients show signs of toxic retinopathy by the first year of use. The American Academy of Ophthalmology (AAO) recommends annual screening, which correlates better with risk than ideal weight. Treatment is estimated to be for 5 years, and most patients will show functional or anatomic change. Improved screening tools and new generations for the American Academy of Ophthalmology (AAO) recommendations for screening that were published in 2011.

Risk of Toxicity: Chloroquine toxicity remains a problem in many parts of the world, but is seen less frequently in the United States.

Major Risk Factors: The risk of toxicity is dependent on daily dose and duration of use. At recommended doses, the risk of toxicity up to 5 years is under 1% and up to 10 years is under 2%, but it rises to almost 20% after 20 years of use. The American Academy of Ophthalmology recommends screening for chloroquine and hydroxychloroquine retinopathy. Begin annual screening after 5 years for patients on acceptable doses and without major risk factors.

Retinal toxicity from chloroquine (CQ) and its analogue hydroxychloroquine (HCQ) has been recognized for many years. Chloroquine is used widely for the treatment of amebic dysentery and other inflammatory and dermatologic conditions. It is not known how many patients on CQ and HCQ show an extramacular pattern of damage.

Counseling: There is no treatment for this toxicity. Screening is the only preventive measure.

What Drug Do Rheumatologists Use Quite Often?

Hydroxychloroquine is used widely for the treatment of rheumatoid arthritis and related inflammatory conditions. It is estimated to be for 5 years, and most patients will show functional or anatomic change. Improved screening tools and new generations for the American Academy of Ophthalmology (AAO) recommendations for screening that were published in 2011.
Rheumatology, Thyroid Dysfunction and the Eye

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February 11, 2022

PLAQUENIL ZONE

WITH ALL TESTING FOR PLAQUENIL TOXICITY—FOCUS ON THE "1.0-1.5 MM RADIUS PLAQUENIL ZONE"  

1-1.5 MM PERIMACULAR GCC THINNING THE FIRST SIGN OF PLAQUENIL TOXICITY

WHY? THICKEST LAYER OF GANGLION CELLS AND SMALLEST GANGLION CELLS AT THAT LOCATION. VERY SENSITIVE TO TOXICITY

WHAT DO YOU SEE ON THE SCANS?
A. THINNING OF THE GCC IN THE PLAQUENIL ZONE
B. MACULAR EDEMA
C. COMPROMISED PIL
D. NOTHING OF IMPORT

DO YOU SEE ANY PROBLEM IN THE PLAQUENIL ZONE?

WHAT DO YOU SEE ON THE SCANS?
A. THINNING OF THE GCC IN THE PLAQUENIL ZONE
B. MACULAR EDEMA
C. COMPROMISED PIL
D. NOTHING OF IMPORT

DO YOU SEE ANY PROBLEM IN THE PLAQUENIL ZONE?
WHAT DO YOU SEE ON THE SCANS?

A. THE FLYING SAUCER SIGN
B. MACULAR EDEMA
C. INCREASED PERIMACULAR RETINAL THINNING

BILATERAL COMPROMISE OF THE PIL (WHITE ARROWS) AFTER COLLAPSE OF PERIFOveal RETINA (RED DASHED ARROWS) WITH FLYING SAUCER ATTACK (BLUE ARROWS)
THE END GAME...ONCE YOU DISCONTINUE PLAQUENIL IT STAYS AROUND A WHILE TO CREATE DAMAGE...LONG ½ LIFE

WAY OUTTA THE BARN

71 yo woman

- With Lupus and hypertension
- Medications:
  - Colazapam
  - Plaquenil 200 mg BID, 15 years
  - 81 mg ASA
  - Prednisone
  - Losartin
- VA 20/25 OD/OS (mild cataracts)
- Patient was told to see an ophthalmologist in 2013

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2016

2016

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Thank you!

Rheumatology, Thyroid Dysfunction and the Eye

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