Rheumatology, Thyroid Dysfunction and the Eye

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Learning Objectives

- Enhance clinical understanding of rheumatology and thyroid dysfunction and their ocular associations
- Enhance clinical diagnosis of ocular manifestations of rheumatologic diseases and thyroid disease
- Enhance clinical management and treatment of ocular manifestations of rheumatologic diseases and thyroid eye disease
- Increase comfort level when ordering or interpreting laboratory tests in rheumatologic and thyroid diseases
- Gain confidence in working closer with rheumatology and endocrinology

Thyroid Disease and Thyroid Eye Disease

Thyroid

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

  - Hypothalamus
  - Pituitary gland
  - Thyroid
  - Parathyroid glands

- Exocrine glands contain ducts. Ducts are tubes leading from a gland to its target organ
  - Digestive 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 (ducted gland) secreting digestive enzymes into the small intestine.
  - Endocrine (ductless gland) in that the islets of Langerhans secrete insulin and glucagon to regulate the blood sugar levels.
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

Thyroid regulates: heart rate, ventilation rate, metabolic rate, and development of cells

Thyroid disorder: approx 1 in 13 or 7.35% or 20 million people in USA, estimated 2 million undiagnosed

Diabetes: approx 1 in 13 or 7.8% or 17.9 million people in USA, 5.7 million undiagnosed

Pathophysiology: >40 postulates (thyroid)

Normal Thyroid Function

Discussion

Thyroid Dysfunction

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
Antibodies of Thyroid Dysfunction

- **TSH Receptor Antibodies**
  - Stimulating TSH receptor antibody
  - Thyroid Stimulating Immunoglobulin (TSI)
  - Thyroid blocking antibody (TBAb)

- **Thyroid Peroxidase Antibodies (TPOAb)**
  - TPO is found in thyroid follicle cells where it converts the thyroid hormone T4 to T3
  - TPOAb contributes to thyroid cell destruction.

- 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.

Hyperthyroid

- TSI attacks the thyroid
- T3 and T4 increase
- TSH decreases

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 T8 recp ab present

Hyperthyroidism (Thyrotoxicosis)

- **Primary autoimmune**
  - Graves
    - Goiter formation or von Basedow’s

- **Secondary/Tertiary**
  - Excess thyroid medication for treatment of hypo or goiter
  - Toxic multinodular goiter
  - Toxic adenoma
  - Excess iodine
  - Thyroiditis (inflammatory induced)
  - Excess hormone production ectopic tissue
  - Thyroid carcinoma

Hypothyroidism (most common organ-specific autoimmune disorder)

- **Primary autoimmune**
  - Chronic autoimmune thyroiditis
    - Autoimmune atrophic thyroiditis
  - Autoimmune thyroiditis
    - Primary myxedema
  - Opposite of Graves disease
  - Postpartum Thyroiditis

- **Secondary/Tertiary**
  - Lithium medication
  - Pregnancy
  - Surgically induced
  - Disorders of the pituitary gland or hypothalamus
Autoimmune atrophic thyroiditis (Hypothyroidism)

- Atrophic 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

Systemic Manifestations of Hyperthyroid (Primary or Secondary)

- Symptoms
  - Nervousness
  - Heat intolerance
  - Sweating
  - Fatigue
  - Polyphagia
  - Anorexia
  - Early satiety
  - Alopecia
  - Vitiligo
  - Brittle nails

- Signs
  - Sweating
  - Muscle Weakness
  - Emotional lability
  - Tachycardia
  - Tachypeaia
  - Arrhythmia
  - Hypermetabolism
  - Bruised tendon reflex
  - Diabetes
  - ↑ Triglycerides & Ca, ↓ CHO
  - ↑ Microcytosis
  - Possible goiter
  - Myxedema

Systemic Manifestations of Hypothyroid (Primary or Secondary)

- Symptoms
  - Cold intolerance
  - Weakness
  - Reduced energy
  - Lethargy
  - Muscle cramps
  - Constipation
  - Increased sleeping
  - Weight gain
  - Reduced appetite
  - Joint stiffness

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

Thyroid Eye Disease (TED)

- Other names used
  - Grave's disease
  - Grave's ophthalmopathy
  - Grave'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?

The eye symptoms usually occur at the same time as thyroid disease
- However they may precede or follow the obvious symptoms of the thyroid abnormality
- The incidence of thyroid eye disease associated with thyroid dysfunction is higher and more severe in smokers
- There is no way to predict which thyroid patients will be affected

Why is this so confusing?

While eye disease may be brought on by thyroid dysfunction
- Successful 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, 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 subclinical, hypothyroidism, either Hashimoto's thyroiditis, simple 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 hormone levels are normal. Most people with euthyroid Graves' disease develop eye disorder within eighteen months of the emergence of the eye disorder
- But some people with euthyroid Graves' disease never develop thyroid dysfunction

Why is this so confusing?

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

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
  - Periocular edema, decreased FT3 and FT4 levels
  - Resolution phase: symptoms regress and eyes return to normal

Phase secondary to abnormal thyroid hormone levels (T3 & T4) (Thyroid Eye Disease)

Thyroid Eye Disease

Hyperthyroidism eye symptoms
- Excess hormone acting on the nerves that supply the eye
- Usually specific and include:
  - Joidose
  - Dryness
  - Eyelid retraction

Hypothyroidism eye symptoms
- 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 (T3 and T4) 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
- TSH also lags at least 6 weeks behind thyroid hormone levels and often remains elevated longer in people who have been hyperthyroid
- Relying on the TSH level can be misleading and not treating TED

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Congestive Autoimmune form of Thyroid Eye Disease
(Active phase, Plateau phase, Resolution phase)
- Caused by both stimulating and blocking TSH receptor antibodies (TRAbs) and also immune system chemicals known as cytokines.
- Secondary targets appear to be TSH receptor antigens located on orbital fibroblasts as well as dermal fibroblasts.
- Active “inflammatory” phase of TED varies
  - Symptoms resolve quickly although no evidence the active phase lasts about 12-18 months.
  - TRAb levels are high, patients are smokers, nutrient deficiencies are present, or the patient continues to be exposed to environmental triggers such as excess dietary iodine, 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 epiphora, proptosis, diplopia, and in some cases, double vision.
- There are conservative procedures that can be performed to address these problems.

Similar receptors are found in the skin, fat and muscle of the orbit.

Euthyroid Graves’ disease
- If thyroid function is normal. How does one develop thyroid eye disease?

General Ocular Symptoms
- Prominent eyes, stare
- Pain
- Lacrimation
- Eyelid swelling
- Foreign-body sensation
- Double vision
- Photophobia
- Decreased vision in one or both eyes

You’re in the Know
Normal Values
Thyroglobulin <20 IU/ml
Peroxidase <35 IU/ml
TSH 1.75 IU/ml
It does work!

NOSPECS: Grading System
- Class 0: No signs or symptoms
- Class 1: Upper lid retraction
- Class 2: Soft tissue involvement
- Class 3: Proptosis
- Class 4: Optic nerve involvement
- Class 5: Corneal involvement
- Class 6: Sight 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 vs 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 (tissue laxation, sneeze sensation, retrobulbar discomfort)
  A. Grade 0: absent
  B. Grade A: minimal (edema of lids, injection, sandy feeling)
  C. Grade B: moderate (edema of lids, injection, chemosis, PFS, pain, behind lenses)
- 3: Proptosis associated with classes 2-6 only
  A. Grade 0: absent
  B. Grade A: minimal (21mm - 23mm)
  C. Grade B: moderate (24mm - 27mm)
  D. Grade C: marked (28mm or more)

Specify if inequality of >3 mm between eyes, or if progression of >3 mm under observation

4: EOM involvement (usually with diplopia)
- 0: absent
- A: minimal (limited motion, patient reports diplopia but no obvious restriction)
- B: moderate (evident restriction of motion)
- C: marked (position of globe is fixed)

5: Corneal involvement (due to proptosis, incomplete closure, lagophthalmos)
- 0: absent
- A: minimal (staining)
- B: moderate (ulceration)
- C: marked (clouding, necrosis, perforation)

6: Sight loss (due to optic nerve involvement)
- 0: absent
- A: minimal (disc pallor or edema, or VF defect, vision 20/20 - 20/60)
- B: moderate (same as A but VA 20/70 - 20/200)
- C: marked (blindness, VA < 20/200)

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

- 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

Endocrine ophthalmopathy with lid edema, exophthalmos, pseudoparesis of external eye muscle, and no optic nerve involvement

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
Lid Involvement
- Lid Retraction
- Lid Lag
- Lagophthalmus

Lid Retraction
- Scleral show in primary gaze
- Occurs in ~90% of Grave’s patients
- Excess stimulation of Muller’s muscle
- Fibrosis inferior rectus
- Mechanical restriction or infiltration of levator
- Increased orbital volume causes exophthalmos

Normal Lid Position
- Upper lid intersects cornea at the 2 and 10 o’clock positions
- 2-3 mm below the limbus
- Lower lid coincident or 1-2mm below the limbus

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 muscle insertions
- Chemosis
- Edema of the conjunctival and corneal epithelium
- Superior Limbal Keratoconjunctivitis
- 65% correlation between HT and systemic thyroid disease
- Rheumatoid arthritis
- Sjögren’s syndrome
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 if 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
Rheumatology, Thyroid Dysfunction and the Eye

Exophthalmometry

- Is race dependent? (Asians versus black men is statistically significant)
- Hertel or Luedde results
- Adults
  - Average reading 17 mm
  - 95% of population have readings between 13-21 mm
- General concepts
  - A difference of 2 mm or more between the eyes
  - A measurement of more than 24 mm

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<tr>
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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 30% 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

Optic Neuropathy

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

Corneal Exposure

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

Exposures keratopathy secondary to exophthalmos and lagophthalmos

Significant threat to visual function

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Treatment of Thyroid Eye Disease
- Depends on what phase of the disease we are in:
  - Phase secondary to abnormal thyroid hormone levels
  - Active "Inflammatory" phase
  - Plateau 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 cosmetic disfigurement
- Patient education is essential
- Communication with an endocrinologist or internist will ensure proper patient care

Palliative (hormone imbalance, active, passive)
- Lubricants
- Topical anti-inflammatory (Lotemax/Restasis)
- Prisms
- Steroids (active phase)
  - Oral
  - Periocular injections
  - IV with oral steroid taper
- Orbital radiotherapy (active phase)
- Orbital Decompression (passive phase)
  - Fat removal orbital decompression (FROD)
  - Large orbit
  - Bone removal orbital decompression (BROD)
  - Small orbit
  - Both FROD and BROD

Smoking causes the thyroid eye disease to be more severe
Smoking causes treatments to be less effective

Paradigm shifts
- Decrease in orbital radiotherapy
- Waiting for passive stage but doing surgery
- Increase usage of fat removal orbital decompression as first approach
- Preorbital injection of steroids for recurrent disease after oral

Looking for better or different ways to treat the active phase of this disease

Lid Retraction, Eyelid Lag, Lagophthalmos
- Must treat underlying thyroid dysfunction
- Altered hormone levels and active phase
  - Treat the exposure keratitis with lubricants
  - Tape eyelids shut at night
  - Lid weight
  - Moisture chamber at night
  - Antibiotic ointments
- Passive Phase
  - Surgical Management
  - Inferior rectus recession
  - Mullerotomy
  - Recession of lower lid retractors

Topical lubricants
- Artificial tears
- Ointments at night
- Topical steroids
- Restasis
- Tape eyelids closed at night or use mask
- Elevate head at night to decrease lid edema
- Oral diuretics: Acetazolamide
- Oral steroids: 60-80mg/day for 3 months
- IV steroids
- Periorbital steroids: Running 60-80mg/day

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- Artificial tears
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**Infiltrative Orbitopathy**

*Exophthalms/Proptosis*

- Orbital Disease Consult:
  - Systemic steroids to reduce inflammation
  - Low dose radiotherapy
  - Surgical orbital decompression

**Restrictive Myopathy**

- Non-surgical (while waiting for stability):
  - Teach proper head positions to alleviate diplopia
  - Prism in spectacle correction (fisheye or ground/s)
  - Oral steroids
  - Botulinum toxin injection

- Surgical Consult:
  - Recession of the rectus muscles involved
  - Diplopia in primary gaze, reading gaze or both
  - Stable angle of deviation for at least 6 months
  - No evidence of active disease
  - Binocular vision in at least primary and reading positions

**Corneal Exposure**

- Manage the corneal defect as first line:
  - Lubricating and antibiotic
  - Lid taping
  - Moisture barrier

- Orbital Disease Consult:
  - High dose oral steroids:
    - 120-140mg/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 d/c within 3 mo

- IV Methylprednisolone

- Orbital Decompression

**Orbital Decompression**

- Not effective if no medical treatment:
  - Two-wall decompression
    - 3-6 mm retroplacement of the globe
  - Three-wall decompression:
    - 6-10mm retroplacement
  - Four-wall decompression:
    - 10-16mm 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)

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. Let's discuss.

Laboratory Testing

- Hypothyroid
  - Low FT4, High TSH, indicates primary check antibodies
  - Low FT4, Low TSH, indicates secondary or tertiary, TSH stimulation, MRI
- Hashimoto's (primary disease)
  - Most common
  - Low FT4, High TSH, High Anti TPO Ab, High levels of Thyroglobulin (Tg) Antibodies (Right, anti Tg Resp Ab (Approx 10% present)
  - Autoimmune atrophic thyroiditis
  - Low FT4, High TSH, Low Anti TPO Ab, Low levels of Thyroglobulin (Tg) Antibodies (Right, anti Tg Resp Ab (Approx 60% present)
- Hyperthyroid
  - High FT4, Low TSH
  - Tg present

IOP in Thyroid Eye Disease

- Commonly used thyroid tests
  - Serum TSH concentration Serum total T4 (Thyroxine)
  - Serum total T3 (Thyroid hormone)
  - Estimation of the serum free T4 (or T3) concentration
  - Thyroglobulin (Tg) level
  - Anti-thyroid antibodies
    - Thyroglobulin receptor antibodies (TSI)
    - TSH binding inhibiting (TBI)
    - Anti-TPO antibodies
    - Thyroglobulin (Tg) Antibodies
- Commonly used thyroid tests
  - Serum T3 uptake test
  - Sensitivity serum TSH test (Thyroid stimulating hormones)
  - TRH stimulation test (Thyroid releasing hormones)
  - Thyroid (T3) suppression test
  - Scintigraphy
  - Needle biopsy
  - Thyroid scan
Signs in Thyroid Eye Disease

- **Dalrymple's sign:** Lid retraction
- **von Graefe's sign:** Upper lid lag on downward gaze
- **Griffith's sign:** Lower lid lag on downward gaze
- **Boston's sign:** Jerky irregular movement of the upper lid on downward gaze
- **Jellinek's sign:** Increased ptosis on downward gaze
- **Stellwag's sign:** Infrequent blinking
- **Kocher's sign:** Increased full retraction with visual fixation
- **Enroth's sign:** Puffy swelling of the lids
- **Rosenbach's sign:** Tumor of closed lids
- **Mobius' sign:** Wheelman-off convergence
- **Baklini's sign:** Palsy of one or more extraocular muscles
- **Baker's sign:** Weakness of fixation on lateral gaze
- **Ehren's sign:** Jerky papillary contraction to consensual light
- **Roses' sign:** Vascular dilation of the pupils
- **Jaffe's sign:** Absence of forehead wrinkling on upward gaze
- **Jeffrey's sign:** Absence of forehead wrinkling on upward gaze

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: Muscles, veins, and blood vessels
    - Connective tissue: Tendons, ligaments, fascia, fibrous tissues, fat, and synovial membranes
- 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
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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 numerous genes
    - 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
- Sjogrens Syndrome
- Systemic Sclerosis
- Polymyositis / Dermatomyositis
- Mixed Connective Tissue Disease
- Wegener’s Granulomatosis

Connective Tissue Diseases

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Similar Structures

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

- Synovial membrane: A layer of connective tissue that lines the cavities of joints, tendon sheaths, and bursae and makes synovial fluid, which has a lubricating function.

- Ténon’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**

- Do you smoke?
- Do you currently have a chronic illness?
- Do you have any eye problems?
- Do you have any skin problems?
- Do you have any joint problems?
- Do you have any pet hair allergies?
- Do you have any other allergies?

**Knuckles**

- Patient has severe arthritis in the knuckles.
- No definite diagnosis at this time.
- Blood work? If so, what test?
- Antinuclear antibody (ANA) and rheumatoid factor (RF)

**Treatment**

- Lotemax qid OS
- Ibuprofen 400 mg qid PO
- Artificial tears

- Educate patient on finding and possible underlying etiologies
  - This reveals an uncle with severe arthritis, no definite diagnosis
  - Blood work? If so, what test?
  - Antinuclear antibody (ANA) and rheumatoid factor (RF)

**6 days later**

- Lotemax TID=1 week
- Lotemax BID=1 week
- Lotemax 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 occurs in exposure zones
- Inflammation localized to episclera:
  - Vessels are moveable
  - 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.
- Systemic conditions:
  - Osteoporosis medications: Bisphosphonates:
    - Fosamax (Alendronate), Actonel (Risedronate)
    - Episcleritis, uveitis, iritis
- Testing for systemic disease indicated:
  - Multiple reoccurrences
  - Bilateral
  - History and exam suspicious for systemic association
- Possible systemic medications:
  - Systemic steroids
  - Non-steroidal anti inflammatories
  - Immunosuppression
  - Splint
  - Glaucoma

48 year old woman

- My OD eye has severe pain, it started as an ache about 1 week ago, but now it 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
- EOMs full, but pain on movement OD
- PERRL (P)
- Confrontation fields: full OU
- Let's take a look.

Diagnosis and Treatment?

- 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 1: male.
- Greater than 50% are bilateral.

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.
    - Communication/consult with rheumatologist.
    - Sub-Tenon's steroid injection is contraindicated.

Scleritis
Scleritis

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

**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**

<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>6%</td>
</tr>
<tr>
<td></td>
<td>with Inflammation</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>Necrotizing Anterior Scleritis</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>without Inflammation</td>
<td>2%</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

- Begin as localized patch of inflammation
- May present as avascular patch of sclera surrounded by injection
- Inflammation spreads to involve entire globe without appropriate treatment
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 sclera
- 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
  - Wegener
  - Gout
  - Polyarteritis nodosa
  - 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 Nuine’s ineffective
- 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
Rheumatoid Arthritis

- 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 (proximal interphalangeal, metacarpophalangeal, 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

Vasculitis

Rheumatoid Arthritis: Digital Necrosis
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)
  - 50-100 mg SQ q week
- Remicade (chimeric MAB)
  - 3 mg/kg - 10 mg/kg Q 4-8 weeks
- Humira (humanized MAB)
  - 40 mg SQ qow

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)
  - Anemia

- Sed rate: 48 (high)
- ANA: 1:640 (speckled pattern)
- Rheumatoid factor: negative
- ACE: normal
- HLA-B27: negative
- Fasting blood glucose (FBG): normal
- Lipid profile: 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
- Female to male (1 in 700)
- Peak age 15-25
- Immune complex deposition
- Photosensitive skin eruptions, serositis, pneumonitis, myocarditis, nephritis, CNS involvement

Anti-Nuclear Antibodies (ANA) positive

Specific labs
- dsDNA antibodies
- Anti-Sm antibody
- Anti-SSA and Anti-SSB - may also be positive

Systemic Lupus Erythematosus: Diagnostic Criteria

<table>
<thead>
<tr>
<th>Diagnostic criteria*</th>
<th>Percent/Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malar rash</td>
<td>64</td>
</tr>
<tr>
<td>Discoid rash</td>
<td>17</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>37</td>
</tr>
<tr>
<td>Oral ulcers</td>
<td>15</td>
</tr>
<tr>
<td>Arthritis</td>
<td>9%</td>
</tr>
<tr>
<td>Proteinuria (0.5 g/dl) or cellular casts</td>
<td>20</td>
</tr>
<tr>
<td>Serositis or pleurisy</td>
<td>19</td>
</tr>
<tr>
<td>Pleuritis or pericarditis</td>
<td>19</td>
</tr>
<tr>
<td>Hemolytic anemia, leukopenia, lymphopenia, or thrombocytopenia</td>
<td>11-40</td>
</tr>
<tr>
<td>Antibody to DNA or Sm antigen</td>
<td>15-60</td>
</tr>
<tr>
<td>Anti-ENA or anti-SB1</td>
<td>95</td>
</tr>
</tbody>
</table>

*The diagnosis of SLE requires the presence of four of the 11 criteria (90% sensitivity, 90% specificity).
*Increased antibodies to double-stranded DNA are pathognomonic.
Systemic lupus erythematosus
1982 classification criteria definitions

- **Malar rash**
  Fixed erythema, flat or raised, sparing the nasolabial folds

- **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
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 or positive serologic test for syphilis)

  - Antinuclear antibody test: Positive

Systemic Lupus Erythematosus

- **Discoid Lupus: Cutaneous manifestations**

- **Scarring**

- **Butterfly rash, discoid type**

Systemic lupus erythematosus
photosensitivity

- **Butterfly rash, discoid type**

- **Photosensitivity**
Systemic lupus erythematosus
interarticular dermatitis

Systemic lupus erythematosus
retinal vasculitis

Systemic Lupus Erythematosus

Treatment: Rheumatologist involvement
Avoidance of sun
Use of sunscreens
DMARDs

Systemic Lupus Erythematosus
Disease Modifying Anti-rheumatic Drugs (DMARDs)

- Methotrexate (MTX)
- Hydroxychloroquine
- Leflunomide
- Sulfasalazine
- Cytoxin
- 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:
    - Systane q4h OU
    - Restasis bid OU
    - Systane night PRN
- She wants plugs to help decrease her usage of lubricants
- SLE: confirms almost absent tear prism and mild to moderate Lissamine 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 RLL/LLL
- ESR: 33 mm/hr
- CRP: 1.7
- ANA: 1:320
- 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.

1-2 million Americans affected
- 90% women
- 2nd most common autoimmune rheumatic disease
- A major women’s health problem

Sjögren’s Syndrome

- 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
Rheumatology, Thyroid Dysfunction and the Eye

February 24, 2018

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**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**

---

**Sjögren’s Syndrome**
(Oral features)

---

**Sjögren’s Syndrome**

**Dental Caries ( Decay) in Sjögren’s Syndrome Patients**

---

**Salivary Glands**
Sjögren’s Syndrome

---

**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 receptors and stimulates exocrine glands
- Muscarinic receptor subtypes
  - Evoxac has high affinity for M1 and M3 subtype
  - Secretion from salivary glands and stomach
  - Slow heart rate, Reduce contractile forces of atrium, reduce conduction velocity of AV nodes
- Sufficient dosages, muscarinic agonists can increase secretion of exocrine glands

---

**Connective tissue diseases secondary to autoimmunity**

**Common Ocular Involvement**
- Systemic Lupus Erythematosus
- Rheumatoid Arthritis
- Sjogrens Syndrome

**Potential Ocular Involvement**
- Systemic Sclerosis
- Polymyositis/Dermatomyositis
- Mixed Connective Tissue Disease
- Wegner’s Granulomatosis
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**
**Sjogrens Syndrome**
**Systemic Sclerosis**
**Polymyositis / Dermatomyositis**
**Mixed Connective Tissue**
**Wegner’s Granulomatosis**

Vasculitides

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

**Vasculitides**

- Polyarteritis Nodosa
- Churg-Strauss Syndrome
- Hypersensitivity Vasculitis
- Wegener’s Granulomatosis
- Giant Cell Arteritis
- Behcet’s Disease
- Cogan’s Disease
- Kawasaki Disease

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

Fundus Reveals

![Ocular Images]

Work Up

- CBC/diff: normal
- ACE: normal
- FTA ABS: negative
- VDRL: negative
- HLA-B27: negative
- PPD: normal
- ANA: negative
- RF: negative
Refer to Rheumatologist

- Testing and examination reviews Behcet’s diagnosis
  - Vasculitis with triad of oral and genital ulcer and uveitis or iritis
  - Ulcers, covered in pale pseudomembrane
    - Painful, on lips, gingiva, buccal mucosa, tongue, palate and oropharynx
    - Central ulcer similar in appearance
  - Ulcers heal in days to weeks with scarring
- 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
Spondyloarthropathy

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
  - Bilateral
  - 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.
- What was once referred to as “Baker’s syndrome” and is now referred to as reactive arthritis.
- Described as a triad of arthritis, nonspecific urethritis, and conjunctivitis, often accompanied by uveitis.
- 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 50-60% of patients with spondyloarthritis 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 Spondyloarthropathy (USpA)

- To describe symptoms and signs of spondyloarthritis in someone who does not meet the criteria for a definitive diagnosis of AS or related disease
  - Unrecognized by many physicians
  - Initial diagnosis of Spondyloarthropathy or Undifferentiated Spondyloarthropathy if certain symptoms are present but are not enough to make a specific diagnosis
- Some times, most people with USpA will develop a well-defined form of spondyloarthritis such as enthesitis-related spondyloarthritis

What Drug Do Rheumatologists Use Quite Often?

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
- About 5-10% of people taking chloroquine or hydroxychloroquine will develop retinopathy
- There is no treatment for this condition
- Therefore must be caught early
- Screening for the earliest signs of functional or anatomic change
- Plaquenil toxicity is not well understood

Revised Again

- Background: The American Academy of Ophthalmology’s recommendations on screening for chloroquine (CQ) and hydroxychloroquine (HCQ) retinopathy are revised in light of new information about the prevalence of toxicity and patterns of retinopathy seen in patients treated with these medications.
  - HCQ toxicity is a serious and preventable problem, and early detection of toxicity is essential to prevent or minimize visual loss.
  - Suggested Screening Schedule: Patients taking CQ or HCQ for systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA) should undergo baseline screening and yearly examinations for the first 5 years of therapy, then every 2 years for up to 10 years, then annually.
  - Risk factors: Age >65 years, female sex, and greater than 5 years of therapy increase the risk of toxicity.
  - Screening tools: Best-corrected visual acuity, Goldmann visual field, Color Vision, Amsler Grid, and dark adaptation tests are recommended for baseline and annual screening.
  - Retinal Imaging: Fundus photography and spectral-domain optical coherence tomography (SD-OCT) are recommended for baseline and annual screening.
  - Treatment: Chloroquine is not reversible, and there is no current treatment. Recognition at an early stage before irreversible vision loss is important to prevent permanent visual loss.

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Plaquenil Toxicity

Oh Boy!

Plaquenil Zone

With all testing for Plaquenil toxicity... focus on the "5.0-1.0 mm radius Plaquenil Zone."

Symmetrical and nothing obvious

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 PII
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
D. A AND C

Figure 1. The flying saucer sign representing compromise of the perifoveal retinal tissue with maintenance of the foveal retinal tissue. From Chen E, Brown DM, Barl VE, et al. Spectral domain optical coherence tomography as an effective screening test for hydroxychloroquine retinopathy (the “flying saucer” sign). Clin Ophthalmol 2010; 4: 1151–1158. Published online 2010 October 21. doi: 10.2147/OPTh.S14257
71 yo woman

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

2016

WAY OUTTA THE BARN

THE END GAME...ONCE YOU DISCONTINUE PLAQUENIL IT STAYS AROUND A WHILE TO CREATE DAMAGE..LONG ½ LIFE
Thank You!

Questions