Rheumatology, Thyroid Dysfunction and the Eye

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South Dakota Optometric Society
September 18, 20/20

Disclosure Statement
(next slide)

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Disclosures- Greg Caldwell, OD, FAAO

- Will mention many products, instruments and companies during our discussion
  - I don't have any financial interest in any of these products, instruments or companies
- Pennsylvania Optometric Association –President 2010
  - POA Board of Directors 2006-2011
- American Optometric Association, Trustee 2013-2016
- I never used or will use my volunteer positions to further my lecturing career
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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

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Thyroid Disease and Thyroid Eye Disease

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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 messenger) that circulate within the body via the bloodstream or lymph system to affect distant organs
  - Hypothalamus
  - Pituitary gland
  - Thyroid
  - Parathyroid glands
  - Pancreas
  - Adrenal glands
  - Gonads (testes and ovaries)
  - Pineal gland

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Thyroid

- 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 level.

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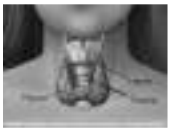
Thyroid



- 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

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Thyroid

- 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)

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Normal Thyroid Function

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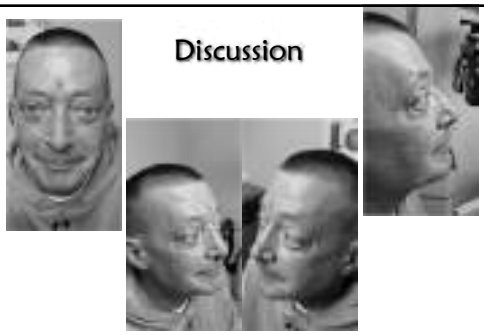
Discussion



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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

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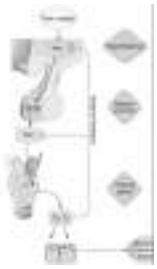
Thyroid Dysfunction

- Primary=Thyroid gland
- Secondary= Pituitary failure
- Tertiary= Hypothalamic



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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 cellular 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

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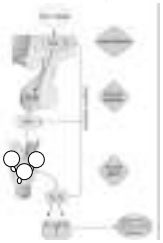
Hyperthyroid



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

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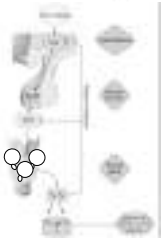
Hypothyroid



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

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Thyroid Dysfunction

Hyperthyroidism
(Thyrotoxicosis)

- Primary-autoimmune
  - Graves
    - Graves-Basedow 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
    - Hashimoto's thyroiditis
  - Autoimmune atrophic thyroiditis
    - Primary myxedema
    - Opposite of Graves disease
  - Postpartum thyroiditis
- Secondary/Tertiary
  - Lithium medication
  - Pregnancy
  - Surgically induced
  - Disorders of the pituitary gland or hypothalamus

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GRAVE' S
(Hyperthyoidism)

- 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)

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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 recp ab present

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Autoimmune atrophic thyroiditis
(Hypothyroidism)

- Atrophic thyroiditis is similar to Hashimoto's thyroiditis
- A goiter is not present

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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
  - Arrhythmia
  - Hypertension
  - Brisk tendon reflex
  - Diabetes
  - ↑Triglycerides & Ca, ↓CHO
  - Microcyticanemia
  - Possible goiter
  - Myxedema

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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
  - Myotonia
  - Delirium
  - Bradycardia
  - Slow reflexes
  - Obesity
  - Hypothermia
  - Myxedema

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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

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Why is this so confusing?

- Thyroid Eye Disease
  - Is often seen in conjunction with Graves' 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

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Why is this so confusing?

- The eye symptoms usually occur at the same time as the 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

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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 eyes 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

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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

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Thyroid Eye Disease

- 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

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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
    - Plateau phase-reduced activity
    - Resolution phase-symptoms regress and eyes return to normal

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Phase secondary to abnormal thyroid hormone levels (T_3/T_4)
(Thyroid Eye Disease)

- Hyperthyroidism eye symptoms
  - Excess hormone acting on the nerves that supply the eye
  - Usually spastic and include staring
  - 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 (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
- TSH also lags at least 6 weeks behind thyroid hormone levels and often remains elevated longer in people who have been hypothyroid
- Relying on the TSH level can be misleading and in 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 (TRAb) and also immune system chemicals known as cytokines
- Secondary targets appear to be TSH receptor antigens (epitopes) located on orbital fibroblasts as well as dermal fibroblasts
- Active "inflammatory" phase of TED varies
  - Symptoms resolve quickly although on average 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 eye protrusion, eyelid retraction, and in some cases, double vision
  - There are corrective procedures that can be performed to address these problems

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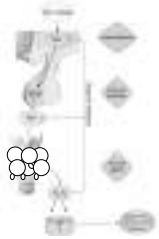
Euthyroid Graves' disease

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



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

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You're in the Know

Normal Values
Thyroglobulin 20 IU/ml
Peroidase <35 IU/ml
TSI 1.75 IU/ml

It does work!

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General Ocular Symptoms

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

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NOSPECS: Grading System

- 1969 by S.C. Werner
  - **Class 0: No signs or symptoms**
  - **Class 1: Only signs, upper lid retraction**
  - **Class 2: Soft Tissue involvement with symptoms**
  - **Class 3: Proptosis**
  - **Class 4: EOM involvement**
  - **Class 5: Corneal involvement**
  - **Class 6: Sight Loss**
- Class 2-6 document severity
  - 0: absent
  - A: minimal
  - B: moderate
  - C: marked
- Within classes 2 to 6 the investigator has to differentiate the severity grades 0, A, B, C
- NOSPECS, classifies severity but not the activity or stage (active/inflammatory or passive/congestive)

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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 (excess lacrimation, sandy sensation, retrobulbar discomfort)
  - Grade 0: absent
  - Grade A: minimal (edema of lids, injection, sandy feeling)
  - Grade B: moderate (edema of lids, injection, chemosis, FBS, pain behind eyes)
  - Grade C: marked
- 3: Proptosis associated with classes 2-6 only
  - Grade 0: absent
  - Grade A: minimal: 21mm -23mm
  - Grade B: moderate: 24mm -27mm
  - Grade C: marked: 28mm or more
  - Specify if inequality of ≥3 mm between eyes, or if progression of ≥3 mm under observation

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NOSPECS: Grading System

- 4: EOM involvement (usually with diplopia)
  - 0: absent
  - A: minimal (limitation of 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)

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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 closing)
- 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

L1E1M2O0
Endocrine ophthalmopathy with lid edema, exophthalmos , pseudoparesis of external eye muscles, and no optic nerve involvement

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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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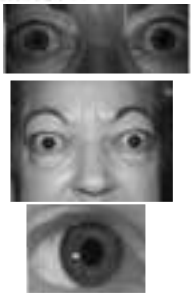
Lid Retraction

- Scleral show in primary gaze
- Occurs in ~90% of Grave's patients
  - Excess stimulation of Muller's muscle
  - Fibrotic 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 mm below the limbus
  - Lower lid coincident or 1-2mm below the limbus



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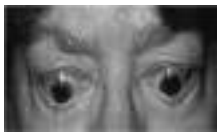
Eyelid Lag: von Graefe's Sign

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



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Lagophthalmos

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

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Soft Tissue Involvement

- Conjunctiva
- Chemosis
- Periorbital edema

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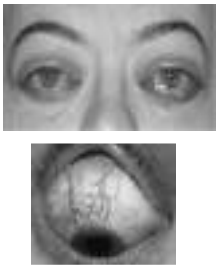
Conjunctiva

- Conjunctival and episcleral injection
  - Especially near the horizontal recti insertions
- Chemosis
  - Edema of the conjunctiva and caruncle
- Superior Limbic Keratoconjunctivitis
  - 65% correlation between SLK and systemic thyroid disease
  - Rheumatoid arthritis
  - Sjögren's syndrome



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Periorbital Edema

- Inflammation of the subcutaneous connective tissue
- May be first sign of thyroid eye disease
- Greatest in the morning

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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

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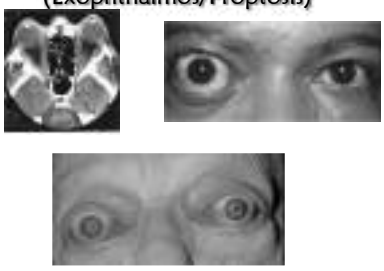
Infiltrative Orbitopathy
(Exophthalmos/Proptosis)



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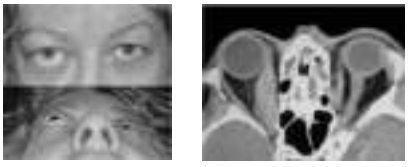
Infiltrative Orbitopathy
(Exophthalmos/Proptosis)



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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 13-21mm
- General concerns
  - A difference of 2 mm or more between the eyes
  - A measurement of more than 24 mm

Race	Mean Normal Value	Upper Limits
	mm	mm
White women	15.4	20.1
White men	16.5	21.7
Black women	17.8	23.1
Black men	18.5	24.7
Asians	----	18.0

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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

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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

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Restrictive Myopathy

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

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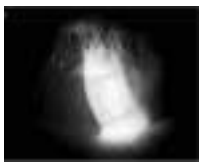
Corneal Exposure

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



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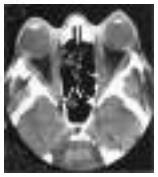
Optic Neuropathy

- 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



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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 motor abnormalities
  - Improving cosmetic disfigurement
- Patient education is essential
- Communication with an endocrinologist or internist will ensure proper patient care

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Treatment of Thyroid Eye Disease

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

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

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Treatment of Thyroid Eye Disease

- Paradigm shifts
  - Decrease in orbital radiotherapy
  - Waiting for passive stage but doing surgery
  - Increase usage of fat removal orbital decompression as first approach
  - Peri-orbital injection of steroids for recurrent disease after orals
- Future
  - Looking for better or different ways to treat the active phase of this disease

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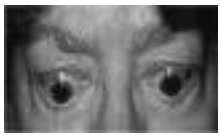
Lid Retraction, Eyelid Lag, Lagophthalmos

- Must treat underlying thyroid dysfunction
- Abnormal hormone level 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



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Lid Retractor Surgery

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Conjunctiva, Periorbital edema

- 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
  - Kenalog last 1 month

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Infiltrative Orbitopathy (Exophthalmos/Proptosis)

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

67

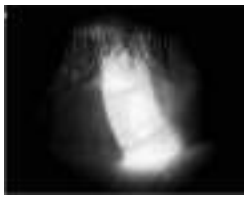
Restrictive Myopathy

- Non-surgical (while waiting for stability)
  - Teach proper head position to alleviate diplopia
  - Prism in spectacle correction (Fresnel or ground in)
  - Oral steroids
  - Botulinum toxin injection
- Surgical Consult
  - Recession of the rectus muscle/s 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

68

Corneal Exposure

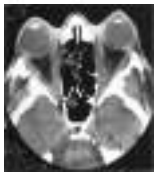
- Manage the corneal defect as first line
  - Lubricating and antibiotic
  - Lid taping
  - Moisture barrier
- Orbital Disease Consult
  - High dose oral steroids
    - 120-140mg /day x 7 days
  - Orbital decompression



69

Optic Neuropathy

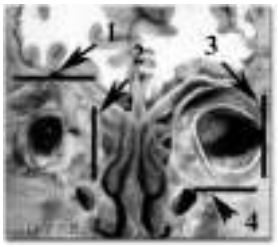
- Systemic Steroids
  - If rapidly progressive and painful in the early stage of the disease
  - Only if no contraindications
  - Prednisolone 80-100mg, expect results within 48hrs. Taper dose and d/c within 3 mo
- IV Methylprednisolone
- Radiotherapy: if contraindication to steroid
- Orbital decompression



70

Orbital Decompression

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



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Orbital Decompression (Surgical/Cosmetic)

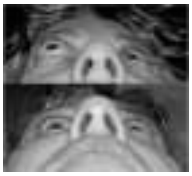
72

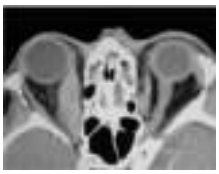
Thyroid Eye Disease and Depression

- When facial disfigurement occurs, thyroid eye disease is equivalent to the diagnosis of cancer and AIDS

73

Orbital Decompression
(Medical/Vision Threatened)





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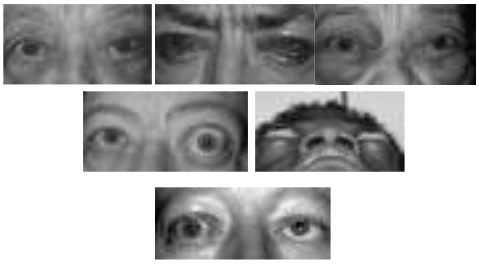
IOP in Thyroid Eye Disease

- 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

75

IOP in Thyroid Eye Disease



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Laboratory Testing

- Thyroid Hormone Levels
  - Serum TSH concentration Serum total T4 (Thyroxine)
  - Serum total T3 (Triiodithyronine)
  - Estimation of the serum free T4 (or T3) concentration
  - Thyroglobulin (Tg) level
- Anti-thyroid antibodies
  - Thyrotropin receptor antibodies (TSI)
  - TSH binding inhibiting immunoglobulins (TBII)
  - Anti-TPO antibodies
  - Thyroglobulin (Tg) Antibodies (TgAb)
- Commonly used thyroid tests
  - Resin T3 uptake test
  - Sensitive serum TSH test (Thyroid stimulating hormone)
  - TRH stimulation test (Thyroid releasing hormone)
  - Thyroid (T3) suppression test
  - Sonography
  - Needle Biopsy
  - Thyroid Scan

77

Laboratory Testing

- 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, High Anti-TPO Ab, High levels of Thyroglobulin (Tg) Antibodies (TgAb), Anti-TB Recp Ab (approx 10% present)
  - Autoimmune atrophic thyroiditis
    - Low FT4, High TSH, Low Anti-TPO Ab, 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
  - TSI present

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February 25, 2019
"Nothing Else Can Be Done"

79

February 25, 2019
"Nothing Else Can Be Done"

80

February 25, 2019
"Nothing Else Can Be Done"

81

March 1, 2019 (4 days later)
Oral and Topical Steroids

82

March 1, 2019 (4 days later)
Oral and Topical Steroids

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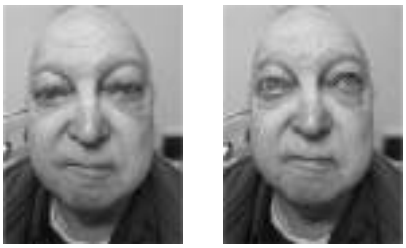
March 1, 2019 (4 days later)
Oral and Topical Steroids

84

March 25, 2019



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March 25, 2019

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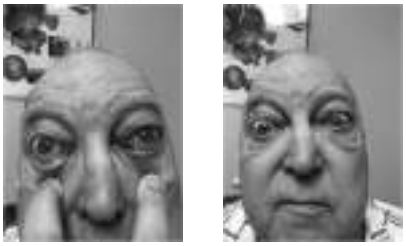
April 22, 2019



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April 22, 2019

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Teprotumumab-trbw (Tepezza)

- Horizon Therapeutics – HQ Dublin, Ireland and US based Chicago
- Biologic pharmaceutical
  - Human
  - Infusion, 8 total, every 3 weeks
- IGF-1 receptor inhibitor monoclonal antibody
  - On the orbital fibroblasts
    - Inhibiting downstream inflammatory cascade
      - Cytokines, hyaluran, 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

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Sign's 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 pigmentation of the lids
- Stellwag's sign: Infrequent blinking
- Kocher's sign: Increased lid retraction with visual fixation
- Enroth's sign: Puffy swelling of the lids
- Rosenbach's sign: Tremor of closed lids
- 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

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Questions

93

Rheumatology and the Eye

94

Rheumatology

- Specializes in the diagnosis and therapy of clinical problems involving
  - Joints
  - Osteoporosis
  - Musculoskeletal pain disorders
  - Soft tissues
    - Not connective tissue
      - Muscle, nerve, 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

95

Where the Eye and Rheumatology Overlap

- Connective Tissue Disease
- Vasculitides
- Spondyloarthropathies

96

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 autoimmune
- "Collagen vascular disease" is an ***antiquated*** term used to describe diseases of the connective tissues

97

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

98

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 Granulomatous

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Connective Tissue Diseases

Disease	Auto-antibody
Systemic Lupus Erythematosus	Anti-dsDNA, Anti-SM
Rheumatoid Arthritis	RF, Anti-RA33
Sjogrens Syndrome	Anti-Ro(SS-A),Anti-La(SS-B)
Systemic Sclerosis	Anti-Scl-70, Anti-centromere
Polymyositis/Dermatomyositis	Anti-Jo-1
Mixed Connective Tissue Disease	Anti-U1-RNP
Wegener's Granulomatosus	c-ANCA

100

Similar Structures

- The connective tissues are composed of two major structural protein molecules
  - Collagen
  - Elastin
- Sclera- the opaque, white, fibrous, protective, outer layer of the eye containing collagen and elastin fibers
- 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.
- 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

101

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

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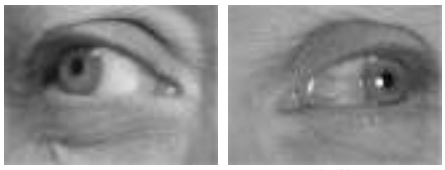
Discussion



OD OS

103

Review of Systems

104

Knuckles

105

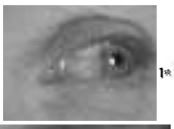
Treatment

- 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)

106

6 days later

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



1st Day

Day 6

107

Lab Results

Referral to Rheumatologist

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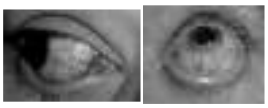
Final Outcome

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

109

Episcleritis

- Typically occurs in exposure zones
- Inflammation localized to episclera:
  - Radiate posterior from limbus
  - 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%



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Episcleritis

- 70% of the cases are idiopathic
  - 15-20% are due to allergy
  - 5-10% are due to systemic disease
- Systemic medications
  - Osteoporosis Medications- Bisphosphonates:
    - Fosamax (Alendronate), Actonel (Risedronate)
      - Episcleritis, uveitis, iritis
- 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

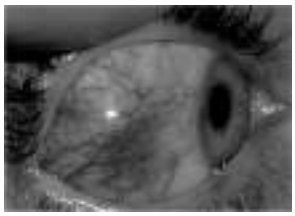
111

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
- EOMs full, but pain on movement OD
- PERRL (-)APD
- Confrontation fields: full OU
- Let's take a look

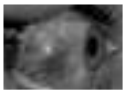
112

Diagnosis and Treatment?



113

Treatment

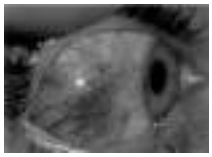


- Non-Necrotizing Scleritis
  - Depending on severity, one or combination of:
    - Oral Non Steroidal Anti Inflammatory agents
      - Ibuprofen or indomethacin (50 mg po bid)
    - Oral steroids
- Communication/consult with rheumatologist
- Sub-Tenon's steroid injection is contraindicated

114

Scleritis

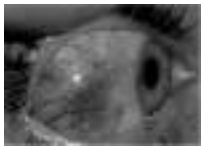
- Severe inflammatory condition
- An immune mediated inflammation and destruction of the sclera
- Commonly associated with underlying systemic disease
- 4th to 6th decade of life
- Rare in children
- Female > male
- Greater than 50% are bilateral



115

Scleritis

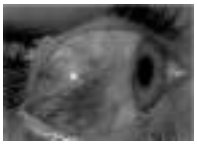
- Symptoms
  - Gradual presentation (days)
  - Deep boring pain
    - May worsen at night
  - Referred pain to head and jaw
  - Eye is tender to the touch



116

Scleritis

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



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Classification of Scleritis

Classified by location and appearance of inflammation

Location	Subtype	Prevalence
Anterior Sclera	Diffuse Anterior Scleritis	40%
	Nodular Anterior Scleritis	44%
	Necrotizing Anterior Scleritis with Inflammation	10%
	Necrotizing Anterior Scleritis w/out Inflammation	4%
Posterior Sclera	Posterior Scleritis	2%

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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

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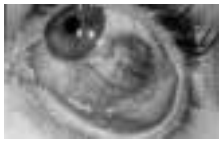
Necrotizing Scleritis

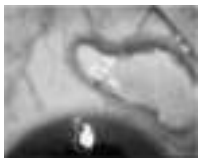
- Most destructive form
- 60% develop ocular/systemic complications
- 40% have vision loss
- 30% mortality rate at 5 years



120

Necrotizing Scleritis

- Begin as localized patch of inflammation
- Symptoms>>>findings
- May present as avascular patch of sclera surrounded by injection
- Inflammation spreads to involve entire globe without appropriate treatment



121

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

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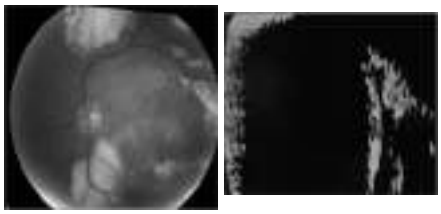
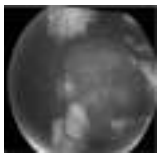
Posterior Scleritis



123

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



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Management

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

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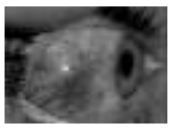
Treatment

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



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Rheumatoid Arthritis

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

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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)

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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.

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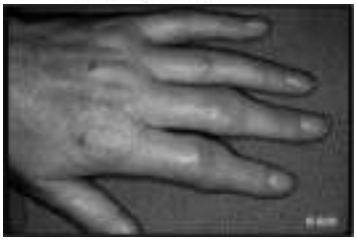
Rheumatoid Arthritis

fusiform synovitis



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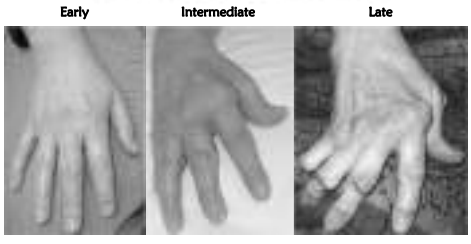
Rheumatoid Arthritis



Courtesy of J. Cush, 2002.

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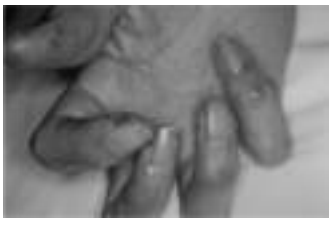
Rheumatoid Arthritis

Vasculitis



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Rheumatoid Arthritis

Vasculitis / Digital Necrosis

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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.
ACR guidelines for the management of rheumatoid arthritis. *Arthritis Rheum* 2002;46:328-346.

134

Rheumatoid Arthritis
(Biologic DMARDs)

- Enbrel (Fusion Protein)
  - 50-100mg SQ q week
- Remicade (chimeric MAB)
  - 3mg/kg -10mg/kg Q 4-8weeks
- Humira (humanized MAB)
  - 40mg SQ qow

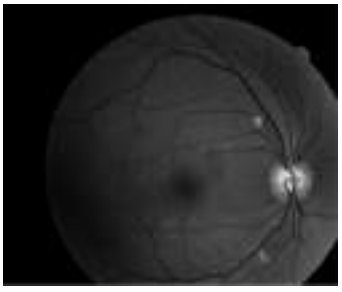
135

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

136

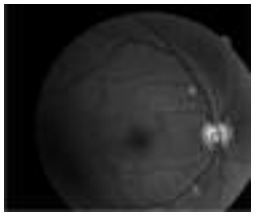
Fundus Photo OD



137

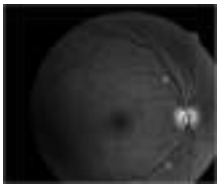
Cotton Wool Spots

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

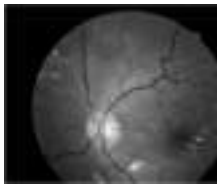


138

Many Faces of CWS



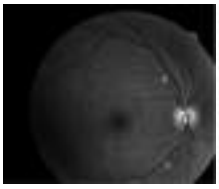
No under lying etiology



History of uncontrolled HTN and DM

139

Laboratory Work-Up



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

140

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

141

Referred to Rheumatologist

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

142

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

143

Systemic Lupus Erythematosus

- Anti-Nuclear Antibodies (ANA)-positive
- Specific labs
  - dsDNA antibodies
  - Anti-Sm antibody
  - Anti-SSA and Anti-SSB – may also be positive

144

Systemic Lupus Erythematosus: Diagnostic Criteria

Diagnostic criteria*	Percent/Incidence
Malar rash	64
Discoid rash	17
Photosensitivity	37
Oral ulcers	16
Arthritis	84
Proteinuria (0.5 g/d) or cellular casts	31
Seizures or psychosis	15
Pleuritis or pericarditis	18
Hemolytic anemia, leukopenia, lymphopenia, or thrombocytopenia	17–43
Antibody to DNA or Sm antigen, + LE prep, or false +RPR†	16–68
Positive ß-dependent antinuclear antibody*	95

*The diagnosis of SLE requires the presence of four of the 11 criteria (98% sensitivity, 96% specificity).
†Anti-exact antibodies to double-stranded DNA are pathognomonic.

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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

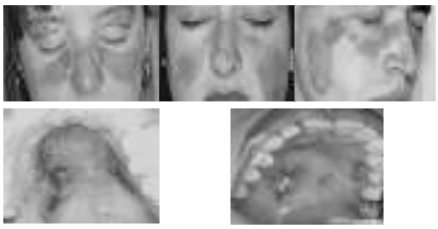
146

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 (<100,00/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

147

Systemic Lupus Erythematosus



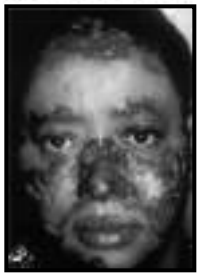
148

Systemic Lupus Erythematosus

- Discoid Lupus: Cutaneous manifestations
- Scar upon healing

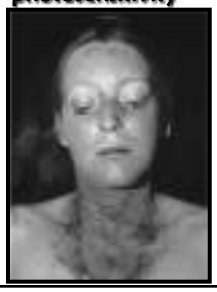
149

Systemic lupus erythematosus
butterfly rash, discoid type



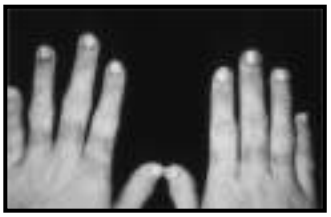
150

Systemic lupus erythematosus
photosensitivity



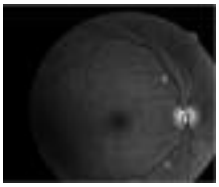
151

Systemic lupus erythematosus
interarticular dermatitis



152

Systemic lupus erythematosus
retinal vasculitis



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Systemic Lupus Erythematosus

- Treatment: Rheumatologist involvement
- Avoidance of sun
- Use of sunscreens
- DMARDs

154

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.
ACR guidelines for the management of rheumatoid arthritis. *Arthritis Rheum.* 2002;46:328-346.

155

37 year old woman

- Referred in for punctal plug insertion due to dry eyes, temporary plug outcome was successful
  - Currently using
    - Systane q1-2h 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 Lisamine green staining
- Anything suspicious here?

156

Treatment

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

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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

158

Diagnosis

- Sjögren's Syndrome

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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

160

Sjögren's Syndrome

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

161

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)

162

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

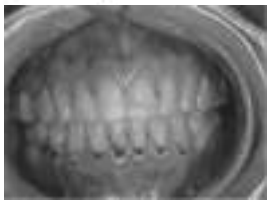
163

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

164

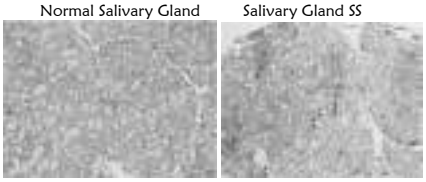
Dental Caries (Decay) in Sjögren's Syndrome Patients



165

Salivary Glands
Sjögren's Syndrome

Normal Salivary Gland | Salivary Gland SS



166

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

167

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
  - Evoxac has a lower affinity for the M2 subtype
    - Slow heart rate. Reduce contractile forces of atrium, reduce conduction velocity of AV node
- Sufficient dosages, muscarinic agonists can increase secretion of exocrine glands

168

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
- Wegner's Granulomatous

169

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 Granulomatous

170

Vasculitides

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

171

Vasculitides

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

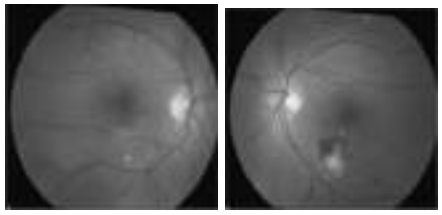
172

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

173

Fundus Reveals



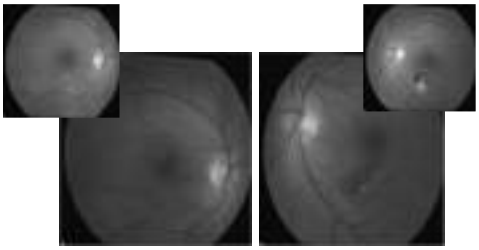
174

Work Up

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

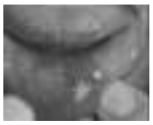
175

Results and Fundus 3 Weeks Later



176

Ask and You Shall Receive



177

Refer to Rheumatologist

- Testing and examination reviews Behcet's diagnosis
  - Vasculitis with triad of oral and genital ulcers and uveitis or iritis
  - Ulcers, covered in pale pseudomembrane
    - Painful, on lips, gingiva, buccal mucosa, tongue, palate and oropharynx
    - Genital ulcers similar in appearance
    - 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

178

Spondyloarthropathies

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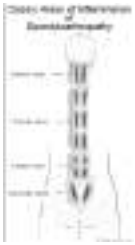
Spondyloarthropathies

- 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

180

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

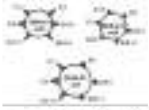


181

Spondyloarthropathy

182

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

183

HLA-B27 & Uveitis

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

184

Ankylosing Spondylitis

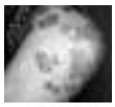
- Ankylosing spondylitis is a chronic, usually progressive, disease involving the articulations of the spine and adjacent soft tissues
- HLA B27 positive 90%
- Uveitis 20-40% chance

185

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 "Reiter syndrome" and is now referred to as reactive arthritis
    - Was 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

186



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

187

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 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

188

Undifferentiated Spondyloarthropathy (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
  - Unrecognized by many physicians
  - Initial diagnosis of Spondyloarthropathy or Unclassified Spondyloarthropathy if certain symptoms are present but are not enough to make a specific diagnosis
    - Over time, most people with USpA will develop a well-defined form of spondylitis such as ankylosing spondylitis

189

What Drug Do Rheumatologists Use Quite Often?

190

Revised Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy

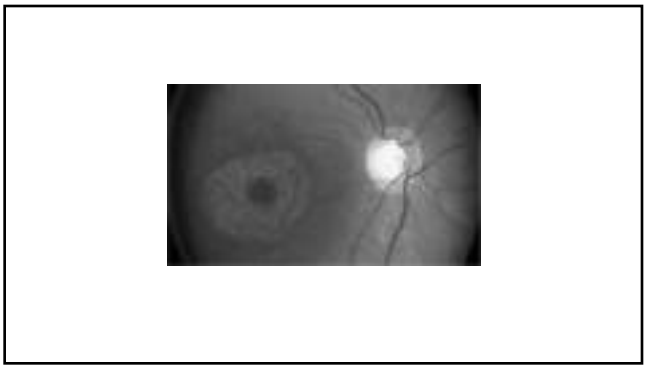
- Recommendations were 2002 by the American Academy of Ophthalmology
- Improved screening tools and new knowledge about prevalence of toxicity have prompt the change
  - 1% after 5-7 years of use or a cumulative dose of 1000 grams (plaquenil)
- There is no treatment for this condition
  - Therefore must be caught early
- Screening for the earliest hints of functional or anatomic change
- Plaquenil toxicity is not well understood

191

Revised Again

192

193



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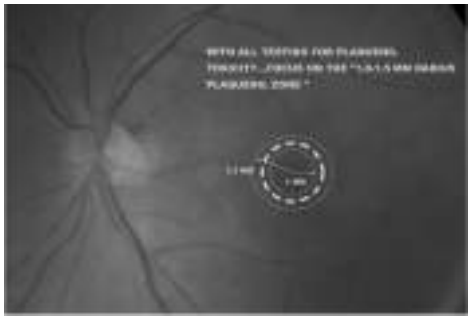
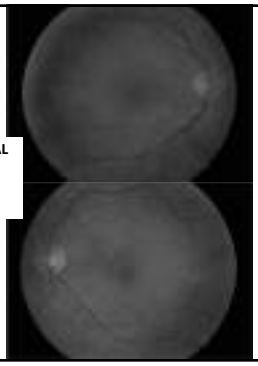
PLAQUENIL ZONE



195

SYMMETRICAL AND NOTHING OBVIOUS

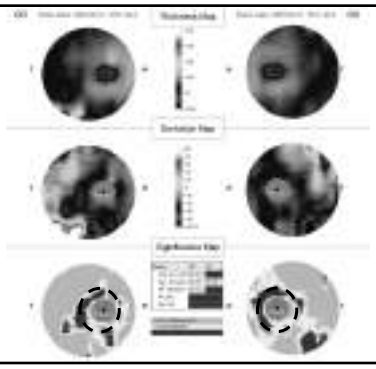


196

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

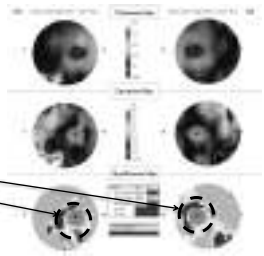
197



198

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

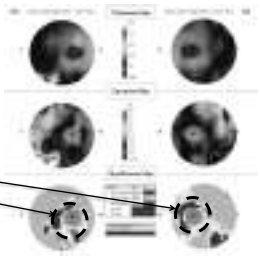


DO YOU SEE ANY PROBLEM IN THE PLAQUENIL ZONE?

199

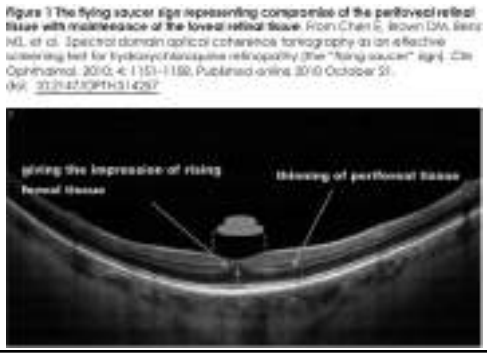
WHAT DO YOU SEE ON THE SCANS?

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?

200



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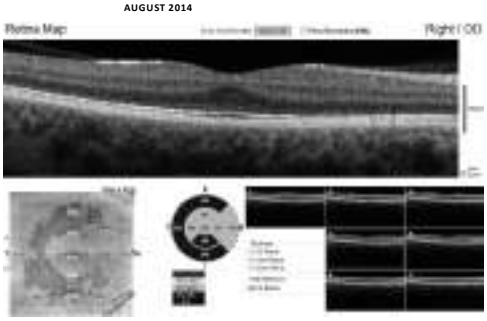

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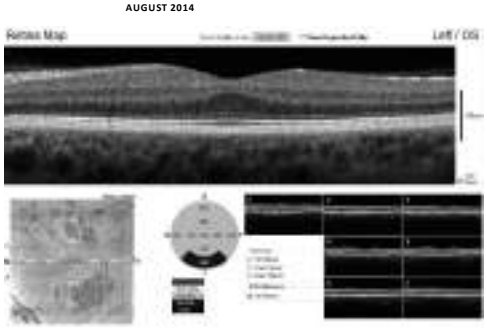
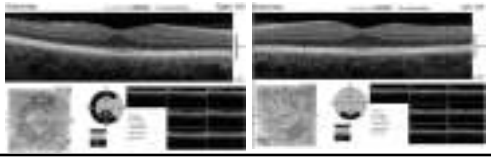


203

WHAT DO YOU SEE ON THE SCANS?

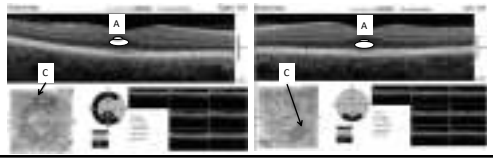
A. THE FLYING SAUCER SIGN
B. MACULAR EDEMA
C. INCREASED PERIMACULAR RETINAL THINNING
D. A AND C



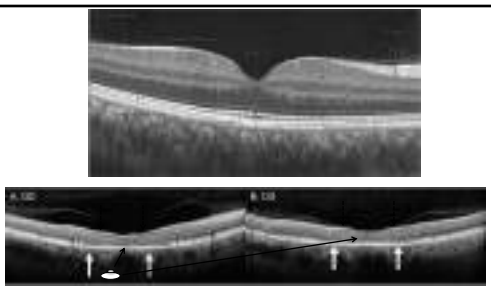
204

WHAT DO YOU SEE ON THE SCANS?

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



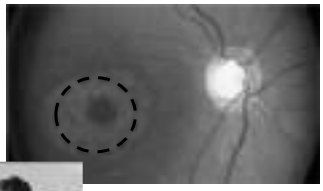
205

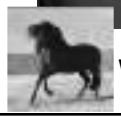


BILATERAL COMPROMISE OF THE PIL (WHITE ARROWS) AFTER COLLAPSE OF PERIFOVEAL RETINA (RED DASHED ARROWS) WITH FLYING SAUCER ATTACK (BLUE ARROWS)

206

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





WAY OUTTA THE BARN

207

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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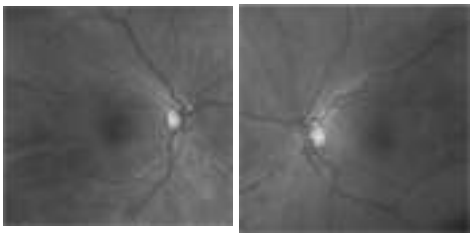
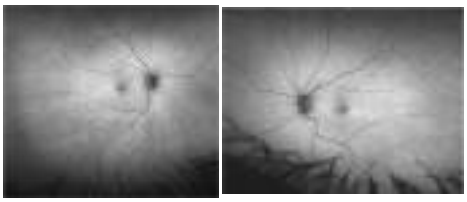
2016

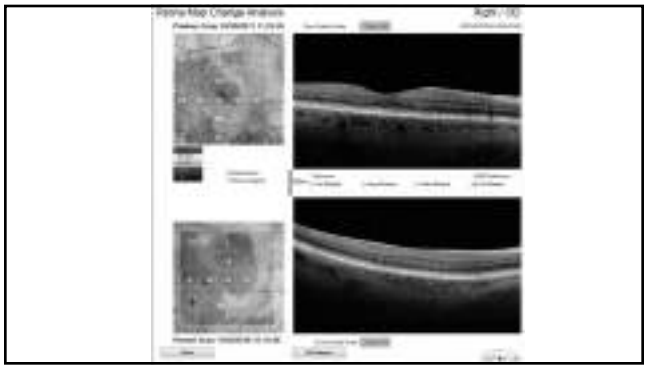


209

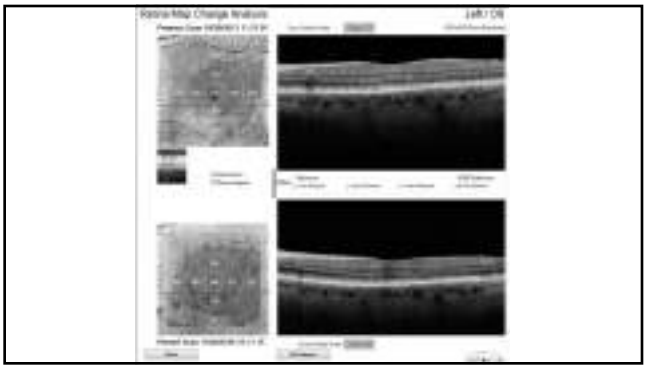
2016



210



211



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Thank You!

814-931-2030
grubod@gmail.com

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