THYROID DISEASE AND THE EYE: WHAT WE MUST KNOW

William D. Townsend, O.D., F.A.A.O.
Advanced Eye Care, Canyon, TX
Adjunct Professor, UHCO

Disclaimer

- My lectures and research have been sponsored by or I am a consultant to:

Alcon	Allergan
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Odyssey Medical	TearLab
VSP	NovaBay

Why ?

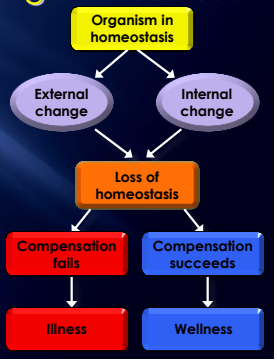
- …are the vast majority of patients w/ thyroid disease women?
- …do patients with hyperthyroidism usually end up converting to hypothyroid disease?
- …do people who are hyperthyroid or hypothyroid end up developing dry eye?
- … do individuals with thyroid disease often have other immune-related diseases?

Endocrine System: Basic Science

The Goal of the Endocrine System: Maintaining Homeostasis

- Organisms are constantly exposed to change
- Capacity to respond to change is inherent to living things

Maintenance of homeostasis is vital to well being & survival, but it requires communication



Implications for Communication: Simple to Complex

- One celled organisms - minimal communication
- Complex organisms - limited communication
- Very comple ophisticated communicati

Communication and Homeostasis

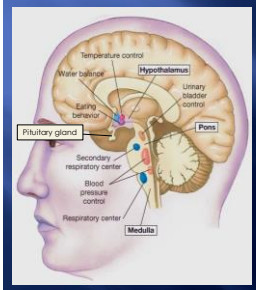
- When situations require a focal, rapid response
  - Speed is critical
  - Utilization of resources - minimal importance
  - Hard wired "point-to-point"
  - Impulses travel along nerves

Nervous System

- When situations demand widespread reaction
  - Speed is not critical
  - Reaching multiple target tissues is crucial
  - Resources need to be conserved
  - Potential to reach every cell

Endocrine System

Endocrine Regulation is Vital

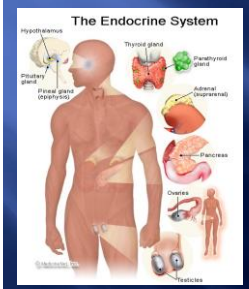


- Growth
- Development
- Metabolism
- Electrolyte balances
- Reproduction

Central Control Centers

- Hypothalamus – region not gland
  - Releasing & inhibiting hormones
- Pituitary gland- endocrine gland
  - Hormones reach circulation, act on:
    - Other glands
    - Target organs

Hormones Regulate Many Vital Body Functions

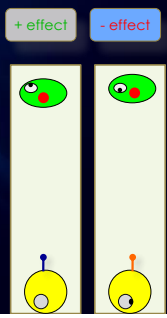


- Adrenal glands- andrenaline, cortisol, aldosterone
- Gonads- sex hormones
- Parathyroid- parathyroid hormone
  - Calcium metabolism
- Pancreas- insulin, glucagon
  - Carbohydrate, lipid metabolism
- Thyroid- T3 & T4 hormones
  - Impact metabolism of entire

Hormonal Receptor Selectivity

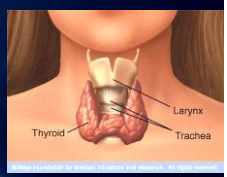
- A hormone only affects a target cell when receptors specific for that hormone are on the cell membrane
- Cells lacking receptors to a specific hormone will not react to it, regardless of concentration

Hormonal selectivity is crucial to proper functioning of the endocrine system



Thyroid Gland

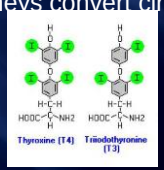
- Butterfly-shaped gland overlying larynx
  - Overlies recurrent laryngeal nerve
- Structure
  - Follicular cells + colloid
  - Follicles- synthesize thyroid hormones
- Iodine
  - Essential to hormone synthesis*
  - Thyroid gland contains 30% of body's iodine
- Hormone synthesis
  - Follicles absorb iodine from circulation
  - Colloid, site of hormone synthesis



Thyroid follicles

Thyroid Gland Hormones

- Thyroid produces two hormones:
  - Thyroxine (T4) 90% - 4 iodine molecules
  - Triiodothyronine (T3) 10% - 3 iodine molecules
    - T3 more biologically powerful & rapidly acting
- Liver & kidneys convert circulating T4 into T3



Functions of Thyroid Hormones

- Support growth & development
  - Especially in CNS of embryo & neonate
- Regulate internal thermostasis, particularly in infants
- Maintain metabolic energy balance
  - Increase basal metabolic rate
  - Augment energy production
  - Increase number & size of mitochondria
  - Increase production of ATP
  - Promote sodium-potassium pump activity
    - Critical in cells, especially neurons

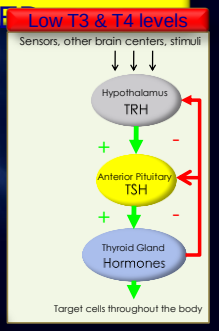
Effects of Thyroid Hormones

- Increase heart rate, cardiac contractility & output
- Increase alertness, positive mental state
- Stimulate carbohydrate metabolism
- Stimulate protein synthesis
- Stimulate fat mobilization
  - Increase plasma concentrations of fatty acids
  - Reduce cholesterol levels
- Generally excitatory for cellular functions

Thyroid hormones are very powerful molecules!

THE POWER OF HORMONES MUST BE CLOSELY CONTROLLED

- Receptors detect low hormone levels & stimulates production
- Adequate or excessive hormone levels trigger negative feedback loop
- Feedback system prevents effects of excessive or deficient hormones levels



Failure to regulate hormone release results in hyper-abundance of hormones

- Overall prevalence: 1 in 13 persons (7.35% or 22M)
- Undiagnosed prevalence in USA: 1 in 20 or 13 M

Risk Factors for Thyroid Disorders

- Gender: females
  - 13% lifetime risk for developing a thyroid disorder (1 in 8)
  - Five to eight times greater risk than males
- Age:
  - Individuals over 50 have a higher risk of thyroid disease
  - Males' risk for thyroid disease increases after age 60
- Radiation exposure
  - Increases risk of thyroid disease
  - Highest risk in radiation of head and neck region
  - During childhood
- Diet: deficiency or absence of dietary iodine

Thyroid- associated Disorders

- Hypothyroidism
- Hyperthyroidism
- Thyroid cancer
- Thyroid nodules
- Thyroid associated eye disease (TAED)
- Euthyroid Grave's Disease

Hypothyroidism

What other autoimmune condition does this patient have?

Hypothyroidism

- #2 endocrine disorder in US
- Reduced or no production of thyroid hormones

Associated Conditions

- Goiter- enlarged thyroid gland
  - Compensates for □ thyroid hormone levels by growing-goiter
  - Worldwide: 90% of goiter caused by iodine deficiency
- Weight increase @ onset of disease

When Thyroid Hormone Levels Fall, Body Functions Decline

- Reduced overall metabolic rate
  - Slower heart rate (bradycardi
  - Reduced body temperature
  - Mood, alertness (lethargy, reduced mentation)
  - Reduced protein production
    - Skin, hair changes
- Lipid metabolism (elevated LDL)
  - Females w hypothyroid = 2x risk for cardiac

OD's can test for or recognize many of these attributes

Hypothyroidism: Symptoms

EARLY SYMPTOMS: PRE-TREATMENT

- Hard stools or constipation
- Increased sensitivity to cold
- Fatigue or feeling tired
- Heavier menstrual periods
- Joint or muscle pain
- Paleness or dry skin
- Sadness or depression
- Thin, brittle hair or fingernails
- Weakness
- Weight gain without trying

LATE SYMPTOMS: UNTREATED

- Decreased taste and smell
- Hoarseness
- Puffy face, hands, and feet
- Slow speech
- Thickening of the skin
- Hair loss

Etiologies of Hypothyroidism

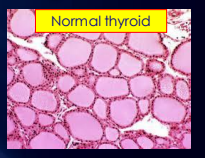
- Autoimmune- chronic inflammation, destruction
- Thyroidectomy- 1º for thyroid cancer, nodules
  - Radioactive iodine therapy for hyperthyroidism
  - Head, neck radiation for unrelated conditions
- Disorders of thyroid hormone synthesis
  - Congenital (1 in 3000 infants defective, a
  - # 1 med for arrhythmia
  - Medication-induced

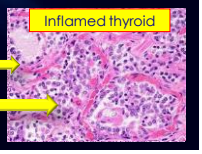
Hashimoto's Thyroiditis

- Most common cause of hypothyroidism
- Described in 1912 by Japanese physician Hakaru Hashimoto. MD
- Autoimmune disease
  - Antibodies bind to, mark TSH receptors
  - Lymphocytic infiltration of thyroid ultimately destroy the gland
- Gender: 5-10x more common in females
  - 3.5 females and 0.8 males per 1000 per year
- Mean age @ onset- 47.8 years

Hashimoto's Thyroiditis: Histological Findings

- Lymphocytic infiltration of the thyroid
  - Destruction of follicular epithelial cells, colloid
  - Reduction in colloid volume
  - Process eventually "burns out,"
  - Minimal, no functional thyroid remains
- Triggers- iodine, medications, infection, smoking, possibly stress





Signs & Symptoms Hashimoto's Disease

- Fatigue
- Depression
- Modest weight gain
- Cold intolerance
- Excessive sleepiness
- Dry, coarse hair
- Constipation

Hashimoto's: Understanding Laboratory Testing Results

- Lab Tests
  - T3 &T4 levels reduced

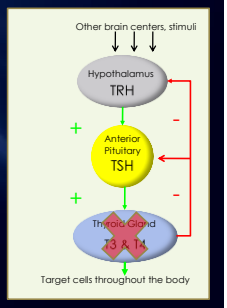
Why? Because inflamed thyroid tissues cannot meet the demand for T3, T4 hormones

  - Thyroid stimulating hormone (TSH) elevated

Why? Because the feedback loop demands more thyroid hormones

  - Serum anti-thyroid antibodies target

Why? Because the immune system produces antibodies that direct T-cells to attack thyroid follicular cells



Protein Binding, Hormones, & Medications

- Circulating blood proteins reversibly bind to hormones & some medications
- Any molecule (hormone, drug) bound to protein is INACTIVE ∴ it cannot exert an effect
- Conditions that alter blood protein levels influence the active fraction of meds or hormones

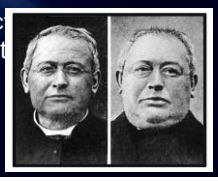
Thyroid Test Interpretation

Test / Name	Normal Range	Interpretation
TSH- Thyroid stimulating hormone (serum thyrotropin)	0.3 to 3.0 (as of 2003)	Under .4 can indicate possible hyperthyroidism. Over 6 is considered indicative of hypothyroidism.
Total T4 (serum thyroxine)	4.5 to 12.5	Less than 4.5 can be indicative of an underfunctioning thyroid when TSH is also elevated. Over 12.5 can indicate hyperthyroidism. Low T4 with low TSH can sometimes indicate a pituitary problem
Free T4 / (free thyroxine)	0.7 to 2.0	Less than 0.7 considered indicative of possible hypothyroidism
T3 / (serum Triiodothyronine)	80 to 220	Less than 80 can indicate hypothyroidism.

Hypothyroidism- Etiologies

- Iodine deficiency disorders – rare in USA today
  - Before the 1920s, common in the Great Lakes, Appalachians, Northwest, and Canada- soil iodine
  - Endemic goiter- enlargement 2nd to iodine deficiency
- educ
- aut

Goiter and thyroid cancers are potential causes of Horner's Syndrome



Goiter 2nd to Chronic Iodine Deficiency

Signs & Symptoms of Hypothyroidism by Incidence

Sign or symptom	Affected patients (%)
Weakness	99
Dry or coarse skin	97
Lethargy	91
Slow speech	91
Eyelid edema	90
Cold intolerance	89
Decreased sweating	89
Cold skin	83
Thick tongue	82
Facial edema	79
Coarse hair	76

Management of Hypothyroidism

- Thyroid hormone replacement therapy (levothyroxine)
  - Synthroid. Levoxyl
  - Generics
- PCP, internist, endocrinologist titrate dosing based on serum levels of unbound (free) T3, T4 hormone
- Treatment may initially cause increased

Important Signs of Hypothyroidism for OD's to Recognize

- Lid edema, pretibial edema
- Changes in mentation, personality
- Moderate weight gain
- Changes in skin, hair

Often reversible

Still Awake?

Thyroid Diseases: Hyperthyroidism

- Hyperthyroidism- excessive production T3 & T4
  - Increases overall metabolic rate
  - Incidence- 0.8 females/1000/year, 0.1males/1000/year
- Graves disease (autoimmune thyrotoxicosis)
  - Most common cause of hyperthyroid & diffuse goiter
  - Mediated by autoimmunity to thyrotropin (TSH) receptor
    - First described 1835- Dr. Robert Graves
      - Goiter- enlarged thyroid gland
      - Exophthalmos
      - Hyperthyroidism
  - Selenium deficiency*
  - Thyrotoxicosis of pregnancy (5-10% of females postpartum)- self limiting

Signs & Symptoms of Hyperthyroidism

- **Palpitations**
- **Heat intolerance**
- **Nervousness**
- **Insomnia**
- **Breathlessness**
- **Increased bowel movements**
- **Light or absent menses**
- **Fatigue**
- **Tachycardia**
- **Tremor**
- **Weight loss**
- **Muscle weakness**
- **Warm moist skin**
- **Hair loss**
- **Staring gaze**

Signs of Hyperthyroidism

- Warm, moist skin
- Tachycardia (heart rate >85)
- Tremor
- Irregular heartbeat (atrial fibrillation)
- Muscle weakness
- Extraocular tissue inflammation*
- Proptosis*
- Pretibial myxedema*

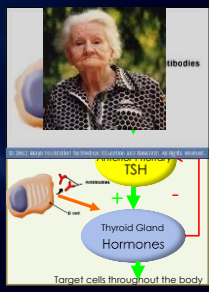
Most common

Least common

* Graves disease only

Pathogenesis of Graves' Disease

- Genetic predisposition a major factor!
- A thyroid-specific autoimmune disorder
- Plasma cells produce antibodies to the thyroid stimulating hormone receptor
- Antibodies bind to & stimulate thyroid gland to produce hormones
- Exogenous antibodies are not subject to negative feedback
- Unrestrained supply of thyroid hormones are produced, released



Management of Hyperthyroidism

- Anti-thyroid medicines-work best in mild cases
  - Mechanism: reduce production of T3, T4
  - Methimazole (Tapazole)
  - Propylthiouracil (Propyl-Thyracil or PTU)
- Selenium supplementation
- Radioactive iodine (I-131) thyroid & radiation!
- Surgical ablation of thyroid
  - 1800s- mortality rate from thyroid surgery was @ 40%.
  - Injury to the recurrent laryngeal nerve

Thyroid Associated Eye Disease (TAED)

- Dry eye (85%-95%)
- Thyroid-associated eye disease
  - Upper lid retraction (Dalrymple sign) #1 sign
  - Lower lid retraction
  - Proptosis
  - Compressive neuropathy
  - Visual field loss
  - Diplopia
  - Increased IOP – especially in up gaze
  - Reduction in venous flow to EOMs

A small percentage of thyroid patients have TAED

Ocular manifestations of Graves' disease more common & severe in smokers ✪

Patients w/ hypothyroidism have dry eye!

Patients w/ hyperthyroidism have dry eye!

How can that be?

What do These Patients Have In Common?

- Both have significant dry eye symptoms
- Both have significant staining with lissamine green

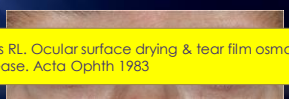
- 70 y/o male with history of hyperthyroid
- Optic n. neur… retraction, myopathy, visual field loss- smoker!

Thyroid-associated dry eye is no respecter of age

- 9 y/o female confirmed …hyroidism
- …ts with symptoms of burning, blurring, stinging with near work

Thyroid Associated Dry Eye

- Evaluated 17 patients w/ Graves' D…
- 94% had dry eye symptoms
- 42% had increased tear film osmolarity
- Increased palpebral fissure width (lid retraction)
  - Rose bengal staining ≈ palpebral fissure width
  - Increased blink rate associated w/ Rose bengal staining



Gilbard JP, Farris RL. Ocular surface drying & tear film osmolarity in thyroid eye disease. Acta Ophth 1983

Thyroid Disease-Related Dry Eye

- Compared 48 subjects w/ thyroid-associated ophthalmopathy to 26 controls
- Tests
  - Tear production- Schirmer test
  - Tear stability- TFBUT
  - Ocular surface health- Rose Bengal staining
  - Ocular surface health- fluorescein staining
  - Ocular surface health- impression cytology (conjunctiva)
  - Blinking- lid width, closure, ocular surface, upward excursion
  - Lacrimal gland- expression of TSH receptors

Eckstein AK et al. Dry eye syndrome in thyroid-associated opthalmopathy: lacrimal expression of TSH receptor suggests involvement of TSHR-specific antibodies. Acta Ophth 2004

Thyroid Disease Related Dry Eye

Test	TAO Patients	Controls	Significance
Schirmer	10 mm	17 mm	p < 0.001
TFBUT	3 seconds	19.5 seconds	P < 0.001
Rose bengal	2	0	p < 0.001
Fluorescein	2	0	p < 0.001
Impression cytology	3	0	
Blinking alteration sum	0.39	0	p < 0.05

"A pathological engagement by autoantibodies of lacrimar TSH receptor could be an important factor in the alteration of the gland's function and contribute to TAO and dry eye syndrome"

Eckstein AK et al. Dry eye syndrome in thyroid-associated opthalmopathy: lacrimal expression of TSH receptor suggests involvement of TSHR-specific antibodies. Acta Ophth 2004

Thyroid Disease & MGD

- 80% of all DES probably associated w/ MGD
- PubMed search = 5 articles
- T3 concentrates in MG

Managing Thyroid-Associated Dry Eye

- Well designed artificial tears
- Manage accompanying meibomian gland dysfunction
- Punctal occlusion
- Restasis- Excellent front line therapy for thyroid-associated dry eye
  - Expect a three month lag between TX & imp
- Lacrisert- methylcellulose inplant
- Omega-3 + GLA fatty acids PO
- Meibomian gland heat (Bruder Mask) +

Current OTC Dry Eye Therapy

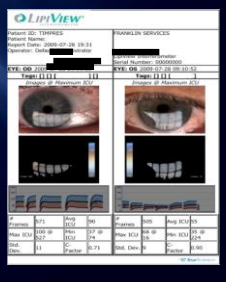
- Contain various active and inactive agents
- Many preserved w/ BAK
- Patients view products as interchangeable
- Differing mechanisms of action and efficacies
- A need exists for clear

What Works for My Patients W/Thyroid-Associated Dry Eye + MGD

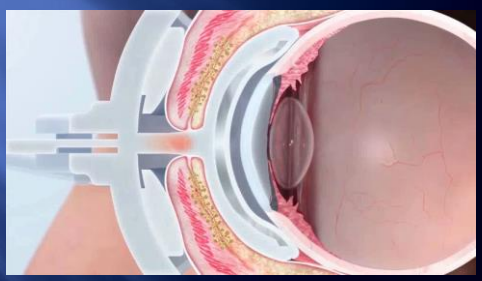
Lipid-Based Products

What Works for My Patients W/Thyroid-Associated Dry Eye + MGD

Procedures & Products



LipiFlow: Pressure + Pulsation for MGD



Korb, DR, Blackie, CA. Meibomian gland therapeutic expression: quantifying the applied pressure and the limitation of resulting pain. Eye&Contact Lens. 2011 Sep;37(5):298-301.

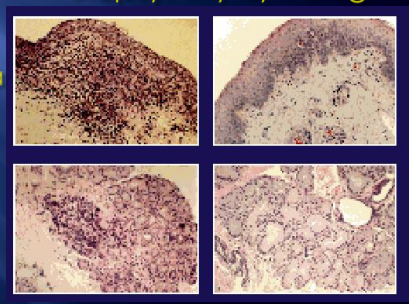
What Works For My Patients W/ Thyroid-Associated Dry Eye

Polyethylene Glycol and Propylene Glycol Products

Hypo-osmolar Products

Thyroid Associated Eye Disease and Cyclosporine A

Biopsy: Dry Eye Dog



Cyclosporine

- Initially isolated from *Tolypocladium inflatum* soil sample obtained Norway
- Cyclosporine thought to act as a partial immunomodulator
  - Not an immunosuppressant as in corticosteroids
- Binds to the immunophilin of immunocompetent lymphocytes, especially T-lymphocytes
- Inhibits calcineurin, which is responsible for activating the transcription of interleukin 2.

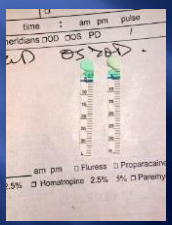
Restasis Case Study: Sue

Sue, 65 yo female

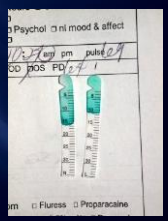
- Hyperthyroidism
- Va 20/20 – OU
- Meds: Synthroid
- External
  - Lissamine green stain OU

Restasis Case Study: Sue

Baseline Schirmer's



3 month Schirmer's



"a significant decrease ($P < 0.01$) in the mean score of the CsA group has also been shown at the end of the course."

Wang J, et al. Immunosuppressive therapies in patients with Graves' ophthalmopathy. Chinese Journ Int Med 2004

Restasis: Patient Education

- Minimum time for clinical effect = 3 months
- Benefit may increase for up to 6 months
- Same vial for both am and pm dosing
- Does not help all patients w/ OSD
  - Minimal benefit- medication-induced OSD
  - Not effective on "burned out" lacrimal glands
- Small studies demonstrate benefit in MGD
- New delivery systems may allow Q 24 hr do
- Consider Q 24 or 6 hr. dosing
- Rx to enable patient to get two trays with one co-pay
- Does not replace artificial tears (patients do not

Thyroid-associated Dry Eye & Punctal Occlusion

- Positive prognostic indicators
  - Moderate to adequate aqueous layer
  - Minimal inflammatory indicators
    - Anterior blepharitis and or posterior blepharitis
    - Meibomian gland & lid margin scarring
- Negative prognostic indicators
  - Minimal to no aqueous layer
  - Significant inflammatory indicators
    - Anterior blepharitis and or posterior blepharitis
    - Meibomian gland & lid margin scarring
    - Lid configuration issues
      - Punctal ectropion

Punctal Occlusion

Temporary Collagen Implants

- *Excellent diagnostic tool*
- Available in 0.3 and 0.4 diameters
- Use the largest size possible; dilate puncta if necessary to get maximum occlusion
- Dissolve in 3-5 days
- Occlude both lowers and uppers
- Phone progress 3-5 days- staff

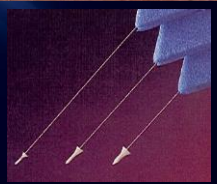
Punctal Occlusion

Parasol Style Plugs

- Available in bulk, non-sterile
- Can be loaded and disinfected prior to insertion
- Cost makes them very attractive
- 30-day replacement policy
- Design prevents rubbing of dome against conjunctiva in most cases.
- Available in small, medium, & large

Complications of Punctal Plugs

- Epiphoria
  - Remove one
  - Try flow restrictors
- Extrusion
- Canaliculitis
  - Dilation, irrigation, antimicrobial therapy
- Irritation
- Rubbing on conjunctiva



LACRISERT (hydroxypropyl cellulose ophthalmic insert)

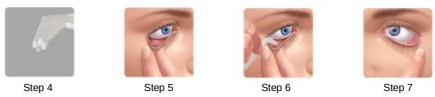
Indicated in patients with moderate to severe dry eye syndrome (DES), including keratoconjunctivitis sicca.

Indicated especially in patients who remain symptomatic after an adequate trial of therapy with artificial tear solutions.

Indicated for patients with exposure keratitis, decreased corneal sensitivity, and recurrent corneal erosions.

Lacrisert [package insert]. Aton Pharma, Inc.: Lawrenceville, NJ; 2007.

LACRISERT Insertion (cont'd)

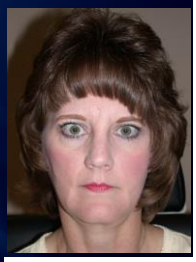


See www.lacrisert.com for an insertion guide and instructional video.

Instructions for using Lacrisert. Aton Pharma, Inc. Lawrenceville, NJ; 2007.

Lacriserts

- Gail- 48 y/o female with Graves disease, severe DES
  - Lissamine green staining cornea & conjunctiva
  - Severely reduced TBUT
- "Nothing really helped"
  - Artificial tears
  - Restasis
  - Punctal plugs
- 1 month trial of Lacriserts
  - "The best they have felt in yrs."
  - SLE: minimal staining,



Thyroid Associated Eye Disease (TAED)

- Characterized by inflammation in orbital tissues
  - Infiltration, edema
  - Impaired glandular function
  - Compression, scarring of ocular structures
- Target tissues for thyroid autoimmune disease:
  - Thyroid gland
  - Extraocular muscles, orbital fat
  - Lacrimal gland
  - Pretibial skin
- Thyroid gland does not cause TAED

Thyroid Associated Ophthalmopathy (TAO) Pathogenesis: Autoimmunity

Lymphocytic infiltration of orbital tissue

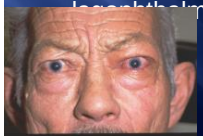
⇓

Release of cytokines primarily interleukin-1

- Cytokines activate quiescent fibroblasts ⇒ secrete hyaluronan (hyaluronic acid), a glycosaminoglycan
- Doubling hyaluronic acid content causes 5-fold increase in tissue osmotic load
  - Increased osmotic pressure results in muscle edema
- May occur despite well controlled hyperthyroidism

TAED: Lid Lag and Retraction

- Mechanisms:
  - Proptosis
  - Sympathetic drive of Müller muscle
  - Upgaze restriction
  - Fibrosis of the levator
  - Contralateral ptosis (myasthenia)
- ⇑ surface area ⇒ dry eye ⇒ lagophthalmos

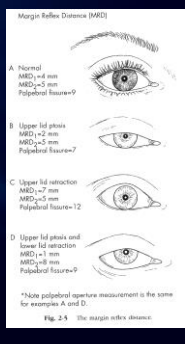


Recording these findings?

Defining Vertical Lid Position- MRD

- Margin Reflex Distance
  - Number of mm from the corneal light reflex to the lid margin
  - Upper lid – 4 to 5 mm (rests slightly below limbus)
  - Lower lid – 5 mm (rests at the lower limbus)
  - Reflex to lid margin 6.5 mm

Photo Biomicroscopy



Lid Lag and Retraction

- Lid lag on down gaze (von Graefe sign)
  - Slowly move fixation object from upward to downward
  - Observe whether or not eyelid lags behind the globe
- Retraction- may be upper, lower, or both
  - May change significantly over time
  - Obtain (and bill for) baseline photos
  - May eventually require surgery
    - Work with a competent and conservative lid specialist
- Dryness- protect the anterior surface from exposure- related changes, dryness

Medical-Surgical Management

- Botulinum toxin injections
  - Duration @ 3 months-40 months
  - Complications
    - Ptosis
    - Diplopia
- Surgery
  - Recession of the levator aponeurosis **and Mueller's muscle**
  - Relaxing procedure to reduce lid lag
  - Implantation of gold weights
  - Delay consultation until stable

Dwight

- Proptosis
- Lid lag
- Exophthalmos
- Big side burns
- Smoker

OD's have powerful influence on patients in helping them decide to stop smoking

Dwight

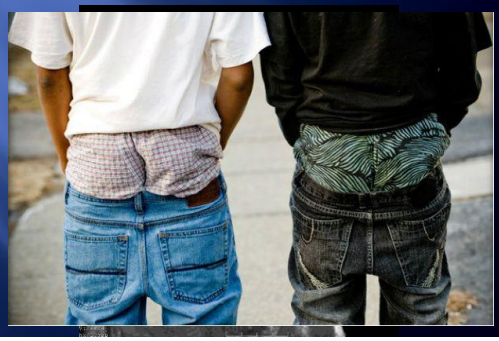
- Color plates- pass 1 of 12
- Turns out he is color blind
- What is your next move

TAO: Differentials & Dx

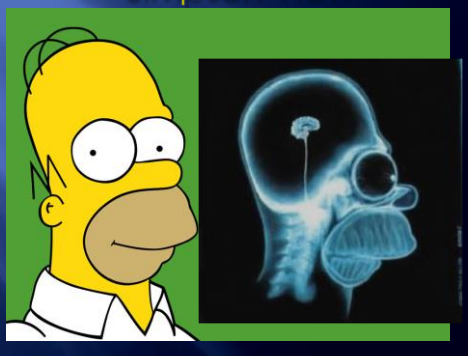
- Differentials:
  - Orbital cellulitis
  - Cavernous sinus fistula
  - Sarcoidosis
  - Space-occupying lesion
- CT and MRI
  - Not necessary if the Dx of TAO can be established clinically
  - If studies are indicated, obtain axial & coronal views.
  - If you order imaging, tell center purpose of scan

Coronal View

Sagital View



Simpson View



Thyroid Associated Ophthalmopathy (TAO)

- Goals of therapy
  - Cosmetic (disfiguring proptosis, exophthalmos, strabismus)
  - Functional (reduce dryness, diplopia)
  - Sight preservation (compressive optic neuropathy, ocular surface damage)
    - ODs can monitor for early ON changes VF, color vision
- Approx 5% of TAO patients require surgery

TAO & Strabismus

- Most common presentations: hypotropia, esotropia
  - Edema leads to shortening of muscle
  - EOMs most frequently affected; inferior rectus and medial rectus
- Surgical correction
  - Goal of surgery-to minimize diplopia in the primary and reading positions
  - Multiple strabismus surgeries and prisms may be required
  - Delay referal in active phase; wait until stable if

TAO & Lifestyle Changes

- Frequent use of artificial tears: NO BAK
  Smoking cessation ⇓ congestive orbitopathy
- Sleeping w/ the head of the bed elevated may ⇓ morning lid edema
- No ceiling fans while sleeping


Exophthalmopathy

- Compressive optic neuropathy
  - Blurred vision
  - Visual field loss
  - Dyschromatopsia
- Management: evaluate on regular basis,
  - Educate patient on possible complications
  - Monocular self VA check
  - Follow fields, serial photos
- Optic nerve decompression
  - History and approaches
  - Current preferred technique


Optic Nerve Decompression

- Surgery should generally delayed until post resolution of the inflammatory phase
  - May be forced to operate sooner if vision loss occurs secondary to compression of ON
- Two orbital walls decompressed
  - Traditionally, the medial wall and floor of the orbit
  - Decompression of the medial & lateral orbital walls is gaining popularity
- Three orbital walls decompressed
  - Medial, lateral walls and floor of orbit

Kallmann R, Mourits M. Prevalence and management of elevated IOP in patients with Graves' orbitopathy. Br J Ophth 1998.

Conclusions

- IOP elevated in Graves' in upgaze secondary to:
  - Fibrosis and enlargement of inferior rectus
  - Resulting compression elevates episcleral venous pressure
- Compressive neuropathy leads to ON-related VF loss; decompression is often beneficial
- Pre-op VF defects in this study regressed or disappeared after decompression
- Risk for elevated IOP: Graves 3.9% Non

Rituximab for TAED

- Assessed the efficacy & safety of rituximab-mediated B-lymphocyte depletion for TAED
- Rituximab (anti-monoclonal antibodies) used to treat lymphomas, leukemias, transplant rejection
- Small study: 12 patients
- CAS scores - a statistically significant decrease from baseline at each of the follow-up visits

Silkiss RZ, et al .Rituximab for thyroid eye disease. Ophthal Plast Reconstr Surg. 2010 Sep-Oct;26(5):310-4.

Cindy

- 38 year old female complains of recent onset:
  - Drooping eyelid OD
  - Discoloration of eyelid OS
  - Irritation OU
  - Mild weight gain
  - Hair loss
- Denies:
  - Diplopia
  - Field loss
  - Blurring of vision

Lab Tests for Thyroid Function: "Thyroid Profile"

- T3 and T4 are highly protein-bound ; only unbound fraction is active
- Normal findings for unbound fraction
  - Free T3 = 0.3%
  - Free T4 = 0.03%
- TSH- if low, = reduced synthesis of T3 and T4
- TRAb- thyroid receptor antibodies*

Cindy's thyroid profile was totally normal

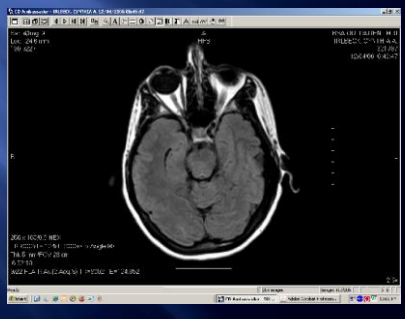
Tentative Diagnosis

1. Hypothyroidism
2. Hyperthyroidism
3. Euthyroid Grave's disease
4. Thyroid tumor

It might have something to do with thyroid!

Do you want to order any other tests?

Cindy's CT Scan



Cindy: Assessment

- Normal thyroid profile
- Lid lag and retraction OS
- Mild proptosis OS > OD
- EOM enlargement OS > OD
- Lid pigment changes OS
- Moderate dry eye OU

What is our diagnosis?

Euthyroid Graves Disease

- "an autoimmune disease characterized by the signs and symptoms of thyroid eye disease in the absence of thyroid dysfunction."
- Typically have high levels of both stimulating and blocking TSH receptor antibodies (TRAb)
- Most patients with euthyroid Graves' disease develop lab-confirmed thyroid disease within 12-18 months of onset of eye symptoms

CONCLUSION
Thyroid Disease: The OD's Role

- Detection
  - High index of suspicion especially in females
  - Recent onset severe dry eye- no other cause
  - Weight gain, loss, pretibial edema
  - Changes in mentation, personality
  - Obvious changes in lids, adnexae
- Consultation
  - Internist or endocrinologist
  - Send reports after your visits: (Forms in MS Word)
- Long-term care, reassurance, remediation

Conclusion

- OD's may be the first health care providers with the opportunity to detect thyroid disease
- ODs may be the first health care providers to diagnose TAED
- Management of most patients with these conditions within our scope and expertise
- Have an index of suspicion for any patient who presents with the diverse signs & symptoms of TAED