Optometric Education Consultants


# Thyroid Eye Disease
## What Every Clinician Needs to Know

Greg Caldwell, OD, FAAO

Music City Fall Classic
Optometric Education Consultants
Saturday, October 21, 2023

# Disclosures- Greg Caldwell, OD, FAAO

All relevant relationships have been mitigated

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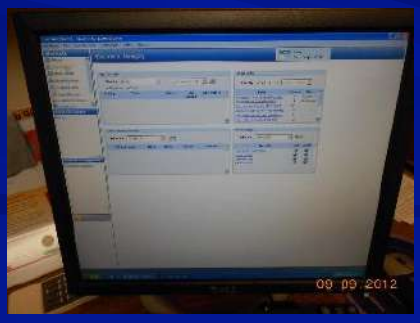
# My Practice

I am a clinician first then a scientist

- Some are scientists first then clinician
- I need to simplify for patient and patient care.
- Science is great, but not good if there isn't a clinical application.
- Some lectures are science based without clinical application.
- My lecture will be a hybrid. Showing clinical applications of the science

It is wonderful to have someone who's juggling so many aspects of optometry [scientific, clinical experience, teacher & lecturer]. It is refreshing and very informative. -Sarah

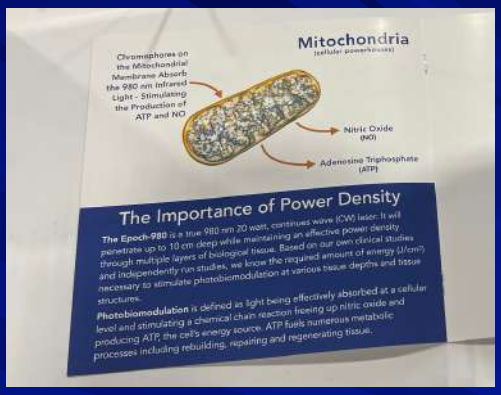





"The Comfort Zone"
Find purpose
Deal with challenges and problem
Live dreams
Lack of self-confidence
COMFORT ZONE
Feel safe and in control
FEAR ZONE
Find excuses
Be affected by others' opinions
LEARNING ZONE
Acquire new skills
GROWTH ZONE
Set new goals
Extend your comfort zone
Conquer objectives


Credit to: James LaValle, RPh, CCN


A4M
Longevity
FEST 2022
30TH ANNUAL WORLD CONGRESS
FRIDAY DECEMBER 9TH
10:30AM - 6:00PM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time—line
Mitochondrial health is key to healthy aging
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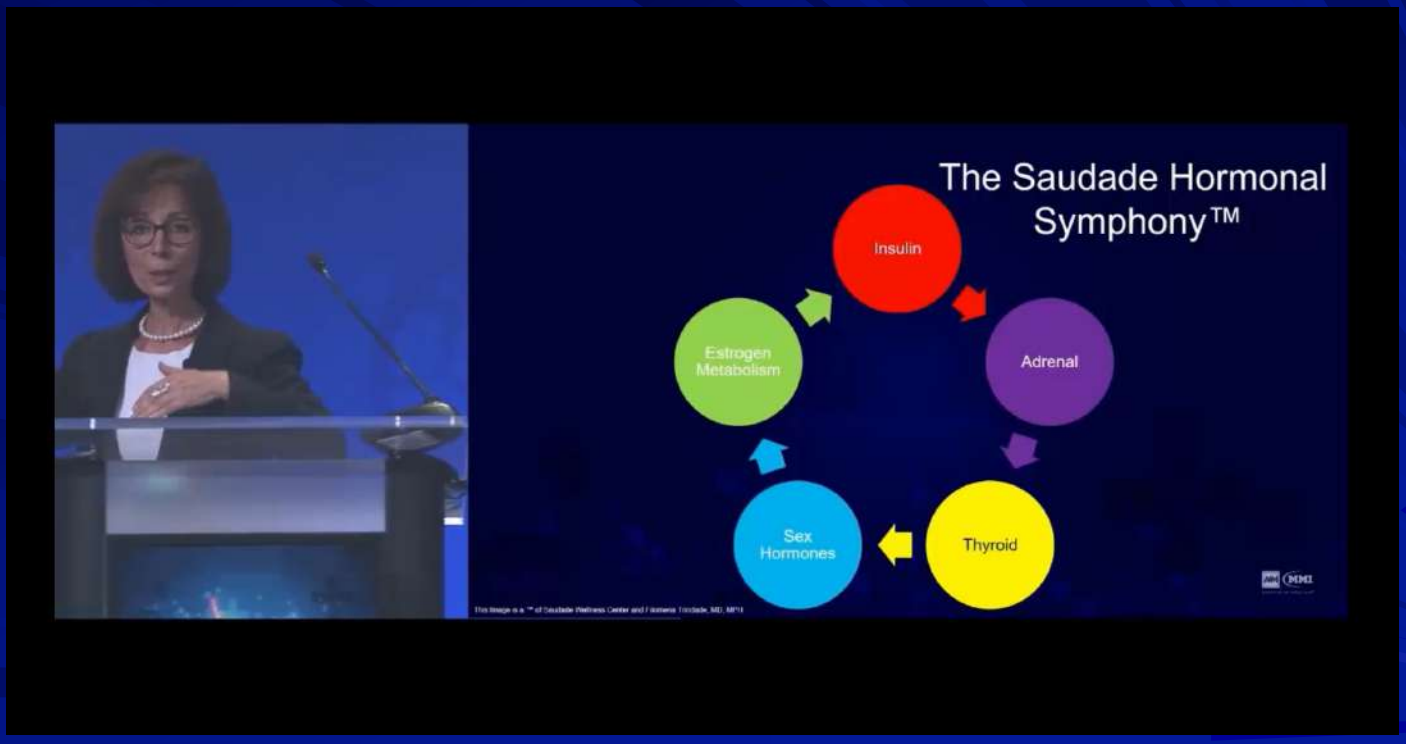



Credit to: Filomena Trindade, MD

# Thyroid Disease
# and
# Thyroid Eye Disease

# Questions

- Everyone on Synthroid is at risk for TED?
- What type of disease is TED?

# Thyroid

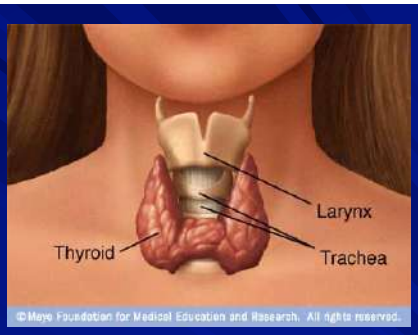
- Thyroid is an endocrine gland
- Two types of glands
  - Endocrine
  - Exocrine
- Endocrine system is a control system of ductless endocrine glands that secrete hormones (chemical messenger) that circulate within the body via the bloodstream or lymph system to affect distant organs

  - Hypothalamus
  - Pituitary gland
  - Thyroid
  - Parathyroid glands
  - Pancreas
  - Adrenal glands
  - Gonads (testes and ovaries)
  - Pineal gland

# Thyroid

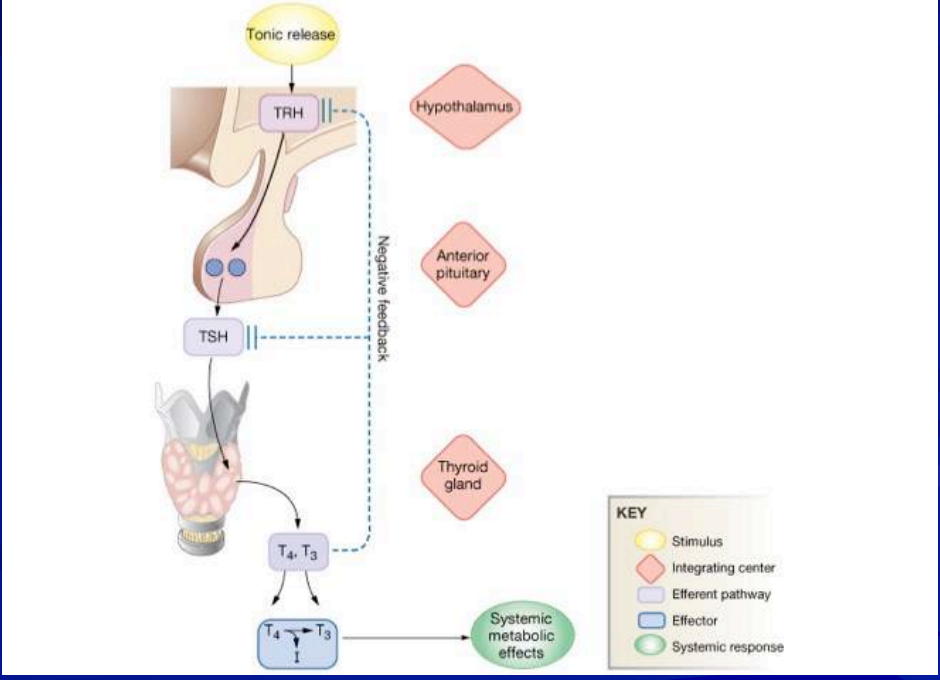
- Exocrine glands contain ducts. Ducts are tubes leading from a gland to its target organ
  - Digestive glands have ducts for releasing the digestive enzymes
  - Salivary glands, sweat glands and glands within the gastrointestinal tract
- Pancreas is both endocrine and exocrine
  - Exocrine (ducted gland) 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.

# 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

# Normal Thyroid Function



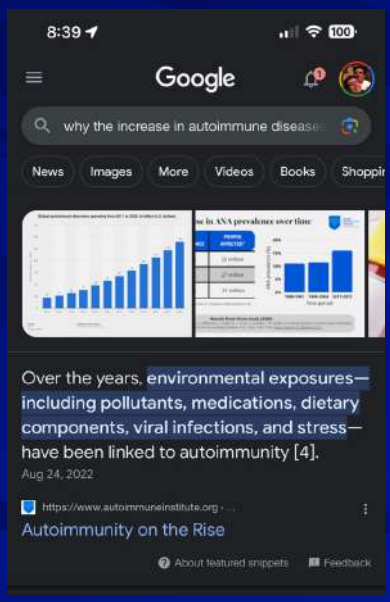
# Discussion

# Thyroid Dysfunction

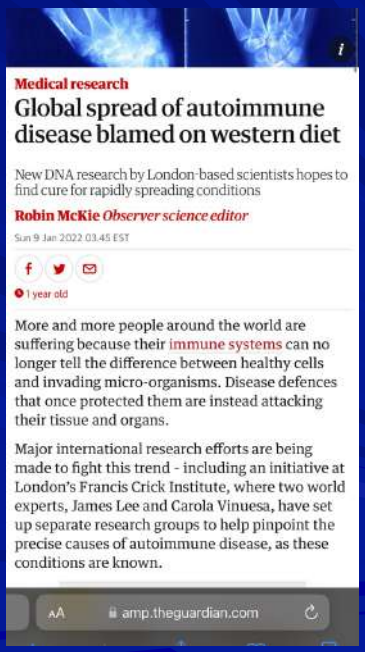
- What is the most common cause of thyroid dysfunction?
  A. Cancer
  B. Surgically induced
  C. Medication toxicity or side effect
  D. Pregnancy
  E. Autoimmune disease

- In autoimmune disease the body typically produces _____ that attacks itself, this can be systemic or organ specific
  - Antibodies, immunoglobulins

# Why Autoimmune Disease is on the Rise?







# Why Autoimmune Disease is on the Rise?

"Numbers of autoimmune cases began to incre about 40 years ago in the west," Lee told the *Observer*. "However, we are now seeing some emerge in countries that never had such diseas before.

For example, the biggest recent increase in inflammatory bowel disease cases has been in t Middle East and east Asia. Before that they had hardly seen the disease."

Autoimmune diseases range from type 1 diabet to rheumatoid arthritis, inflammatory bowel disease and multiple sclerosis. In each case, the immune system gets its wires crossed and turn on healthy tissue instead of infectious agents.

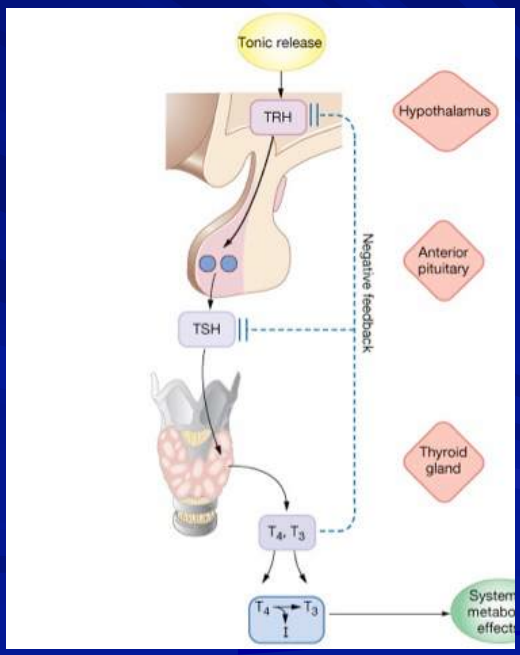
"Fast-food diets lack certain important ingredients, such as fibre, and evidence suggests this alteration affects a person's microbiome - the collection of micro-organisms that we have in our gut and which play a key role in controlling various bodily functions," Vinuesa said.

"These changes in our microbiomes are then triggering autoimmune diseases, of which more than 100 types have now been discovered."

Both scientists stressed that individual susceptibilities were involved in contracting such illnesses, ailments that also include celiac disease as well as lupus, which triggers inflammation and swelling and can cause damage to various organs, including the heart.

# Thyroid Dysfunction

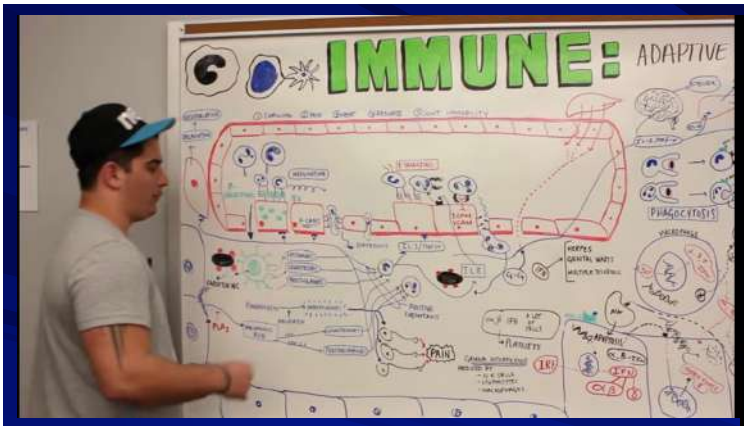
- Primary=Thyroid gland
- Secondary= Pituitary failure
- Tertiary= Hypothalamic

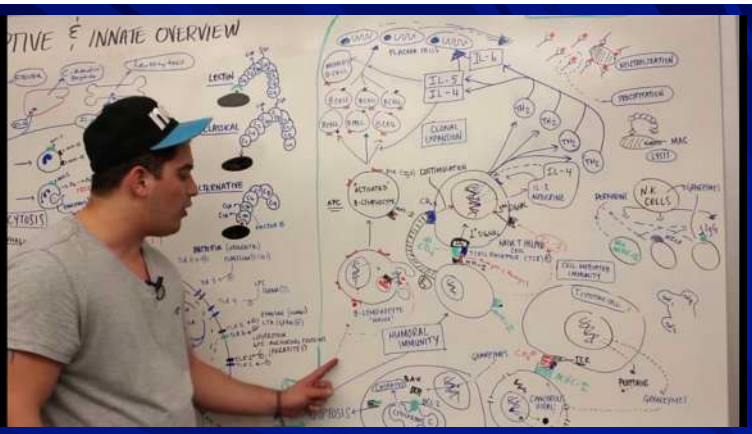


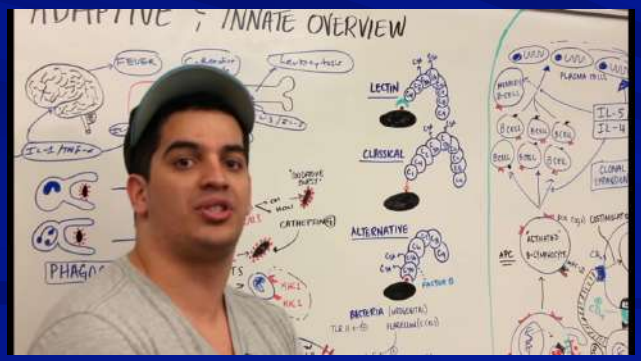
# Antibodies of Thyroid Dysfunction

- TSH Receptor Antibodies
  - Stimulating TSH receptor antibody
    - Thyroid Stimulating Immunoglobulin (TSI)
  - Thyroid blocking antibody (TBAb)
- Thyroid Peroxidase Antibodies (TPOAb)
  - TPO is found in thyroid follicle cells where it converts the thyroid hormone T4 to T3
  - TPOAb contributes to thyroid 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




Ninja Nerd Science
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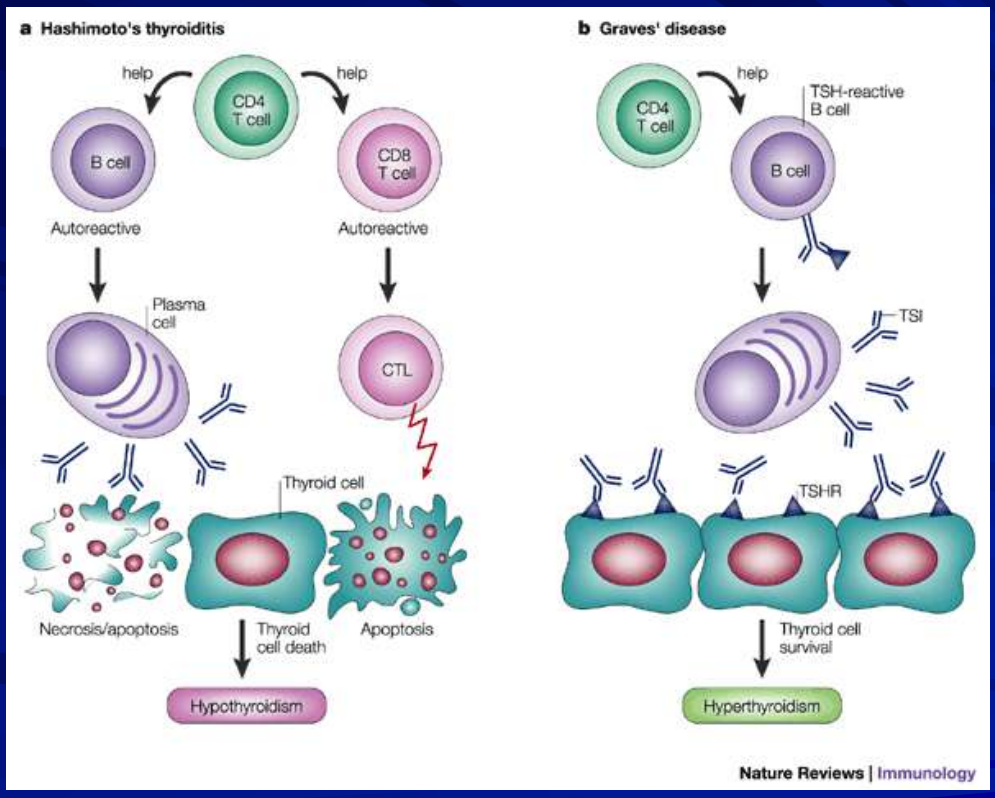
a Hashimoto's thyroiditis
help
CD4 T cell
help
B cell
CD8 T cell
Autoreactive
Autoreactive
Plasma cell
CTL
Thyroid cell
Necrosis/apoptosis
Thyroid cell death
Apoptosis
Hypothyroidism
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LOW
CONTRIBUTION TO RISK RESULTS
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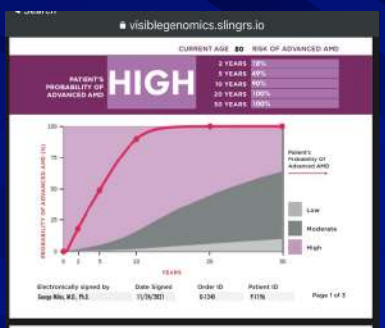
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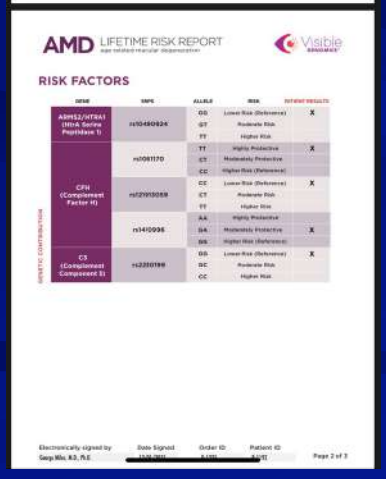
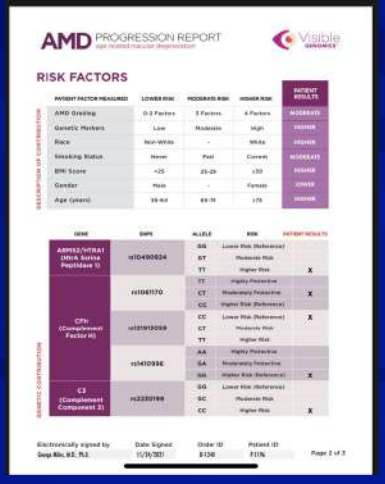

AMD LIFETIME RISK REPORT
RISK FACTORS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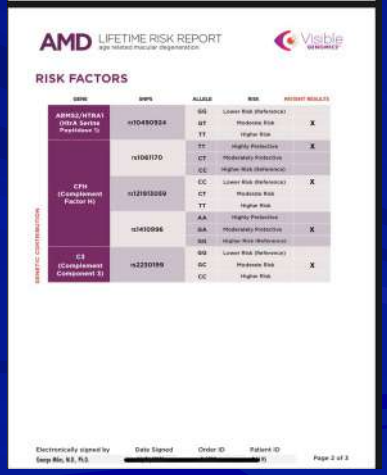
AMD LIFETIME RISK REPORT
RISK FACTORS

# Complement factor H in AMD: Bridging genetic associations and pathobiology

Christopher B. Toomey [a, b, 1], Catherine Bowes Rickman [a, b]

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https://doi.org/10.1016/j.preteyeres.2017.09.001

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## Abstract

Age-Related Macular Degeneration (AMD) is a complex multifactorial disease characterized in its early stages by lipoprotein accumulations in Bruch's Membrane (BrM), seen on fundoscopic exam as drusen, and in its late forms by neovascularization ("wet") or geographic atrophy of the Retinal Pigmented Epithelial (RPE) cell layer ("dry"). Genetic studies have strongly supported a relationship between the alternative complement cascade, in particular the common H402 variant in Complement Factor H (CFH) and development of AMD. However, the functional significance of the CFH Y402H polymorphism remains elusive. In thi

FEEDBACK

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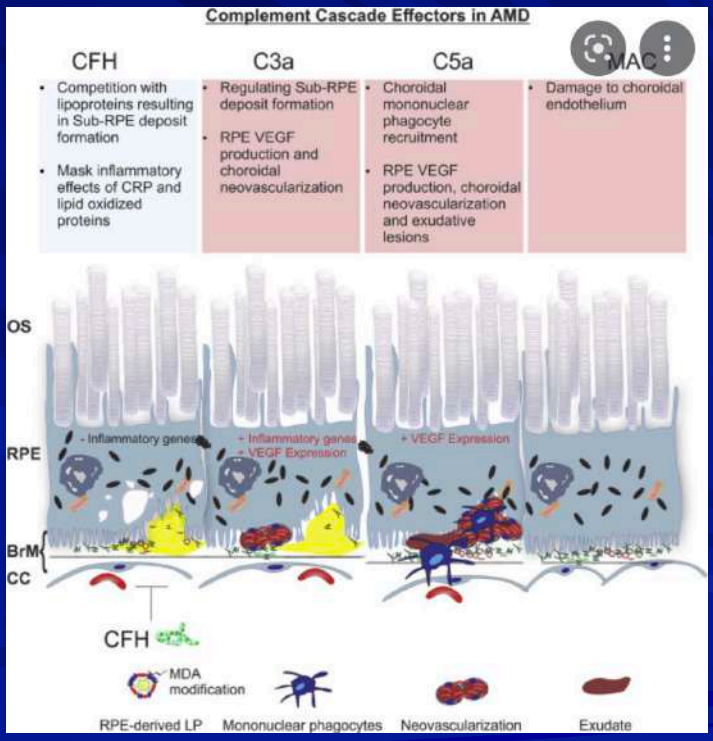
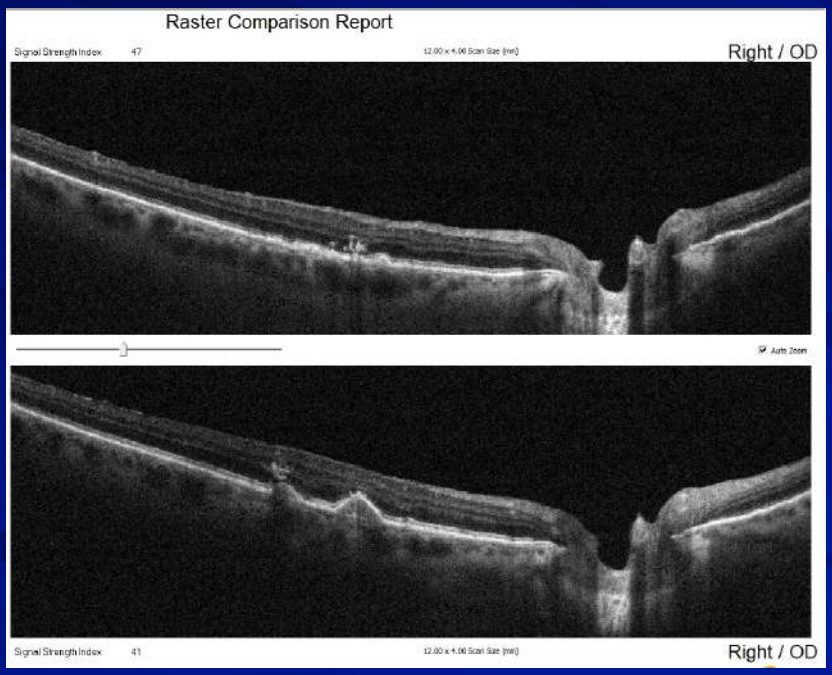


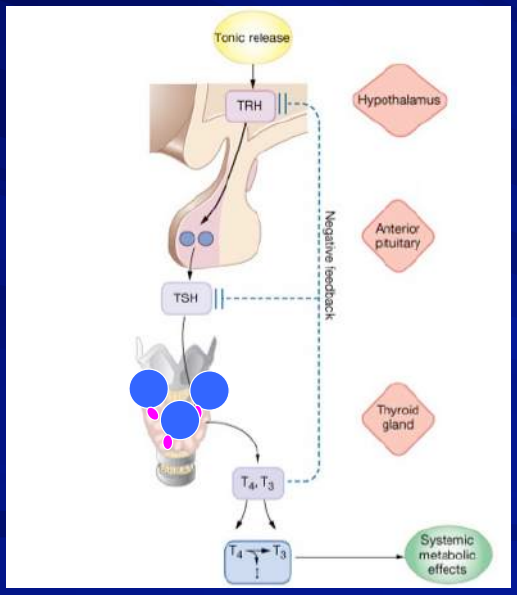
# April 27, 2021 – January 26, 2022 (9 months)





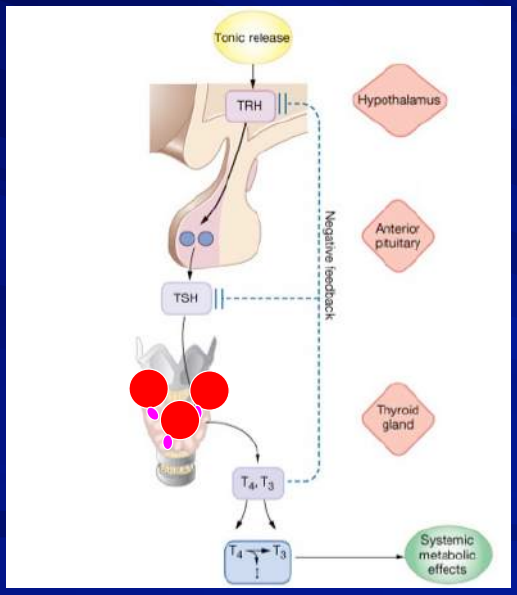
Melonie Clemmons, OD
May 20, 2022 AACO Nashville

# Hyperthyroid




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

# Hypothyroid




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

# 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

# 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)

# 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

# Autoimmune atrophic thyroiditis
## (Hypothyroidism)

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

# Postpartum Thyroiditis
## (Hypothyroidism)

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

# Systemic Manifestations of Hyperthyroid
## (Primary or Secondary)

### Symptoms
- Nervousness
- Heat intolerance
- Sweating
- Fatigue
- 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

# 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

# Thyroid Eye Disease (TED)

- Other names used
  - Grave's disease
  - Grave's ophthalmopathy
  - Grave's orbitopathy
  - Exophthalmos in Graves Disease
  - Thyroid Associated Orbitopathy (TAO)
  - Thyroid Orbitopathy
  - Ophthalmic Graves Disease
  - Inflammatory Eye Disease
  - Endocrine Orbitopathy

# Why is this so confusing?

- Thyroid Eye Disease
  - Is often seen in conjunction with 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

# 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

# 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

# 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

# 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

# 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

## 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

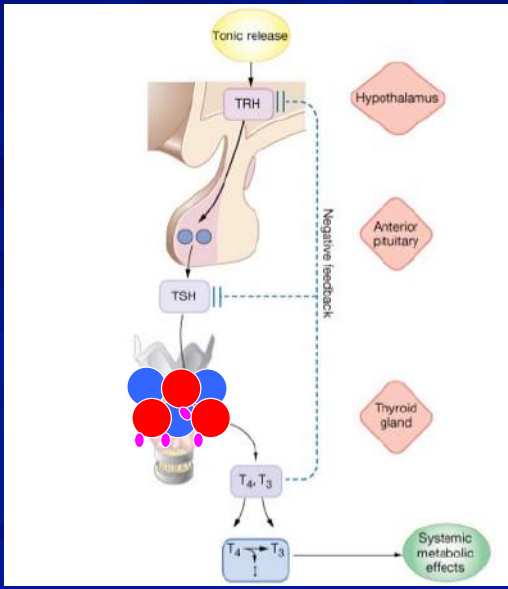
- This form of TED resolves within a few weeks after thyroid hormone levels (FT4 and FT3) are corrected and brought back into the normal range
- The pituitary hormone TSH can stay low or suppressed for many months during the course of treatment for hyperthyroidism and doesn't mean that the patient is 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

## Congestive Autoimmune form of Thyroid Eye Disease (Active phase, Plateau phase, Resolution phase)

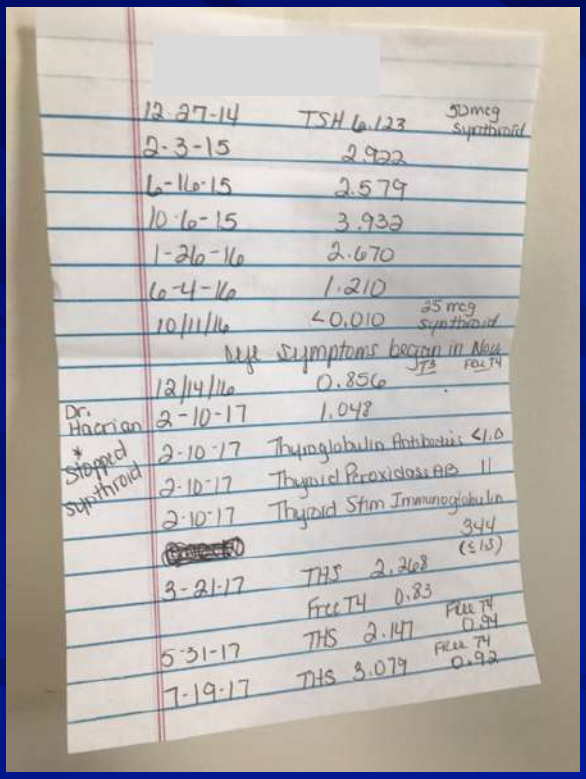
- Caused by both stimulating and blocking TSH receptor antibodies (TRAb) and also immune system chemicals known as cytokines
- Secondary targets appear to be TSH receptor antigens (epitopes) located on orbital fibroblasts as well as dermal fibroblasts
- Active "inflammatory" phase of TED varies
  - Symptoms 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

# Euthyroid Graves' disease

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



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




You're in the Know

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

It does work!

# General Ocular Symptoms

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

# 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)

# 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 $\geq$3 mm between eyes, or if progression of $\geq$3 mm under observation

# 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)

# 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)

# 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

# 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**

# Clinical Activity Score (CAS)

- Thyroid disease characterized by:
  - ★ Severity
  - ★ Activity – want 3 or above
    - CAS (1-7)
- Studies for Tepezza
- Payers using CAS for approval
  - ★ Due to wide open label
  - ★ Those infusing are charting the CAS

**Table 2** | Clinical Activity Score

| | Clinical Activity Score |
|---|---|
| 1 | Painful feeling behind globe |
| 2 | Pain on attempted gaze |
| 3 | Redness of eyelids |
| 4 | Redness of conjunctiva |
| 5 | Chemosis |
| 6 | Inflammatory eyelid swelling |
| 7 | Inflammation of caruncle or plica |
| 8 | Increase of ≥2 mm in proptosis in last 1–3 months |
| 9 | Decrease in visual acuity in last 1–3 months |
| 10 | Decrease in eye movements of ≥8° in last 1–3 months |

For initial CAS, items 1–7 are tallied at one point each for a final CAS based on a 7-point scale. On follow-up visits, the final three items are added for a CAS out of 10 points

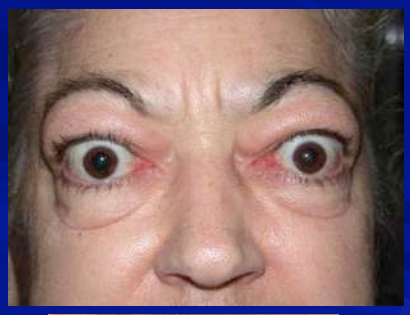
# Lid Involvement

- Lid Retraction
- Lid Lag
- Lagophthalmus

# Lid Retraction

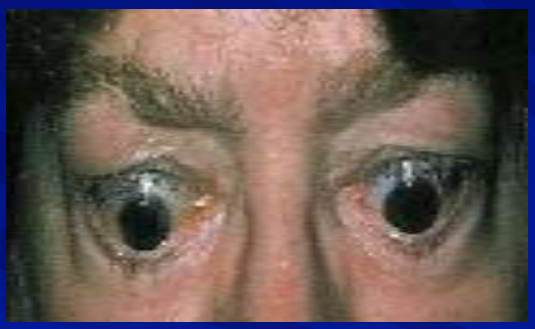
- Scleral show in primary gaze
- Most commonly seen complication
- Occurs in ~90% of Grave's patients
  - Excess stimulation of Muller's muscle
  - Fibrotic inferior rectus
  - Mechanical restriction or infiltration of levator
  - Increased orbital volume causes exophthalmos

- 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



# Eyelid Lag: von Graefe's Sign

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



# Lagophthalmos

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

# Soft Tissue Involvement

- Conjunctiva
- Chemosis
- Periorbital edema

# Conjunctiva

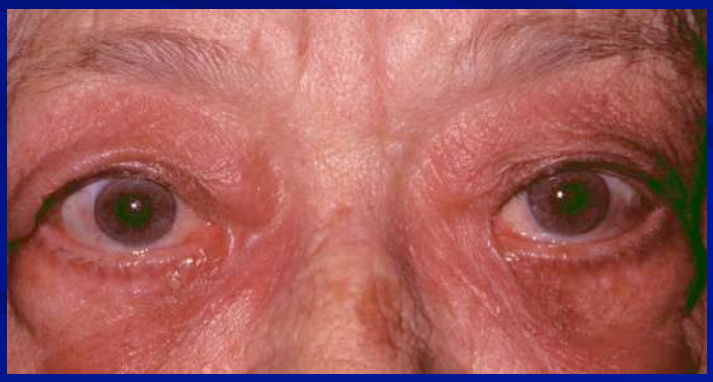
- Conjunctival and episcleral injection
  - Especially near the horizontal recti insertions
- Chemosis
  - Edema of the conjunctiva and caruncle
- Superior Limbic Keratoconjunctivitis
  - 65% correlation between SLK and systemic thyroid disease
  - Rheumatoid arthritis
  - Sjögren's syndrome

# "If it is Red think TED"

Dr. Andy Morgenstern 12-7-2013, OMS-Contemporary Resort

# Periorbital Edema

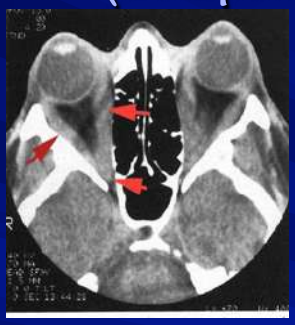
- Inflammation of the subcutaneous connective tissue
- May be first sign of thyroid eye disease
- Greatest in the morning

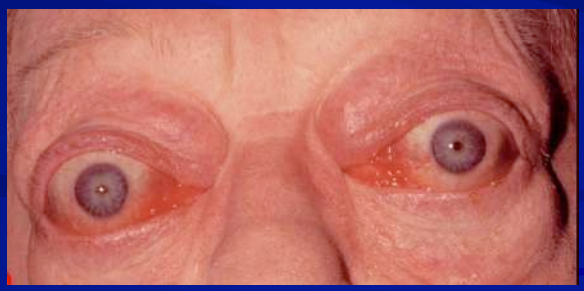


# Infiltrative Orbitopathy
## (Exophthalmos/Proptosis)

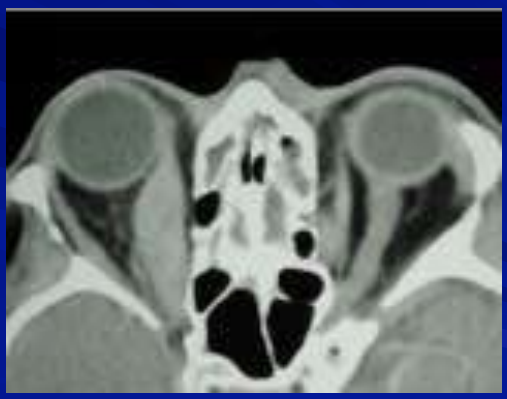
- Thyroid Eye Disease is most common cause of unilateral and bilateral exophthalmos
- The term exophthalmos is reserved for prominence of the eye secondary to thyroid disease
- May need MRI to determine or obvious exophthalmos may be present
- It is permanent in 70% of cases
- Caused by increased volume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

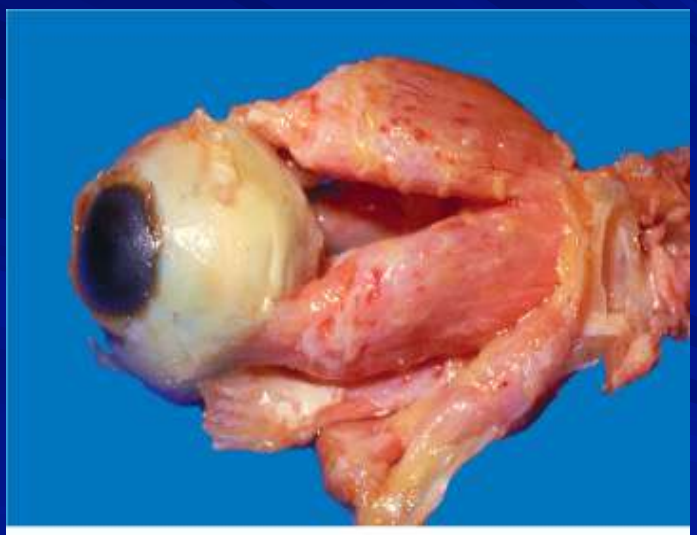
# Infiltrative Orbitopathy
## (Exophthalmos/Proptosis)





# Infiltrative Orbitopathy
## (Exophthalmos/Proptosis)





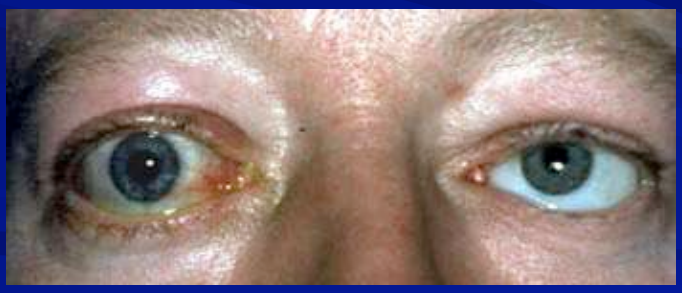
# Exophthalmometry

- 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 |

# Restrictive Myopathy

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



# IOP in Thyroid Eye Disease

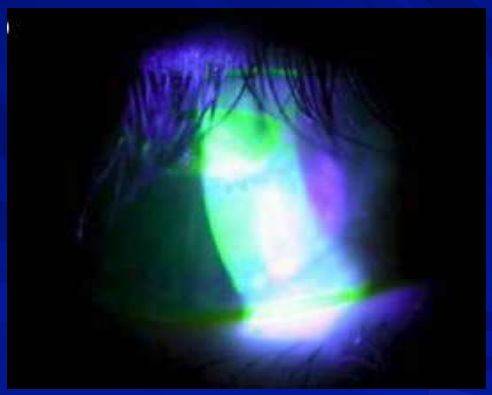
- A rise in IOP has been reported with TED
- I would have higher suspicion when you see
  - Periorbital edema
  - Exophthalmos, proptosis
  - Restrictive myopathy
- Some literature reports IOP in up gaze to be part of the diagnoses of thyroid dysfunction

# Restrictive Myopathy

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

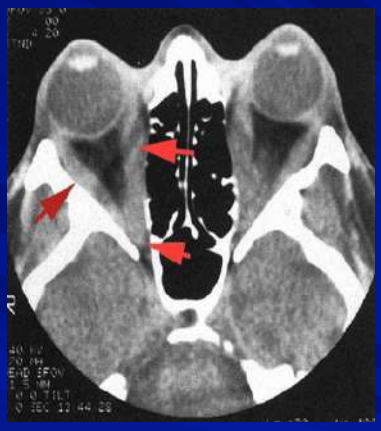
# Corneal Exposure

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



# Optic Neuropathy

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



# Treatment of Thyroid Eye Disease

- Depends on what phase of the disease we are in:
  - Phase secondary to abnormal thyroid hormone levels
  - Active "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

# 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

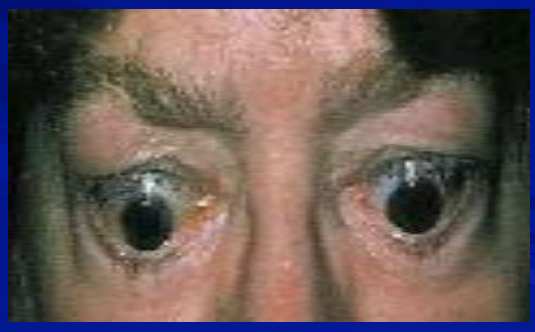
Smoking causes treatments to be less effective

# 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

# Lid Retraction, Eyelid Lag, Lagophthalmos

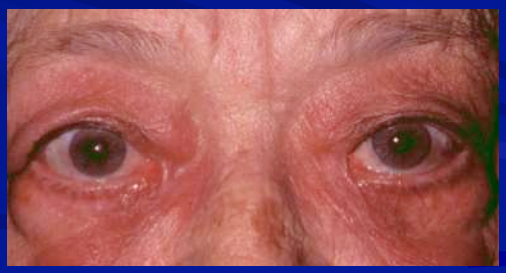
- Must treat underlying thyroid dysfunction
- Abnormal hormone level and Active phase
  - Treat the exposure keratitis with lubricants
  - Tape eyelids shut at night
  - Lid weight
  - Moisture chamber at night
  - Antibiotic ointments
- Passive Phase
  - Surgical Management
  - Inferior rectus recession
  - Mullerotomy
  - Recession of lower lid retractors



# Lid Retractor Surgery

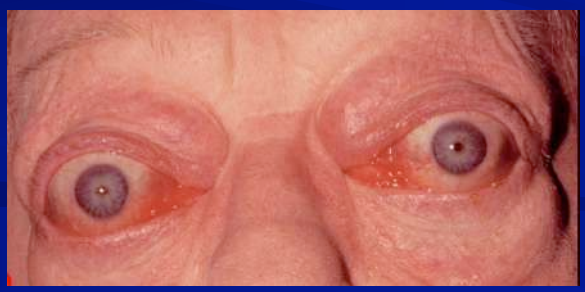
# Conjunctiva, Periorbital edema

- 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



# Infiltrative Orbitopathy
## (Exophthalmos/Proptosis)

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

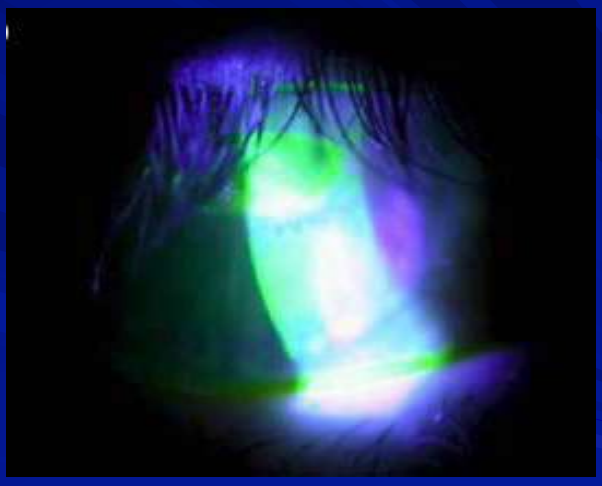


# Restrictive Myopathy

- Non-surgical (while waiting for stability)
  - Teach proper head 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

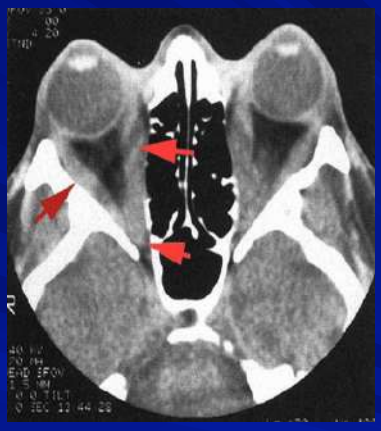
# Corneal Exposure

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



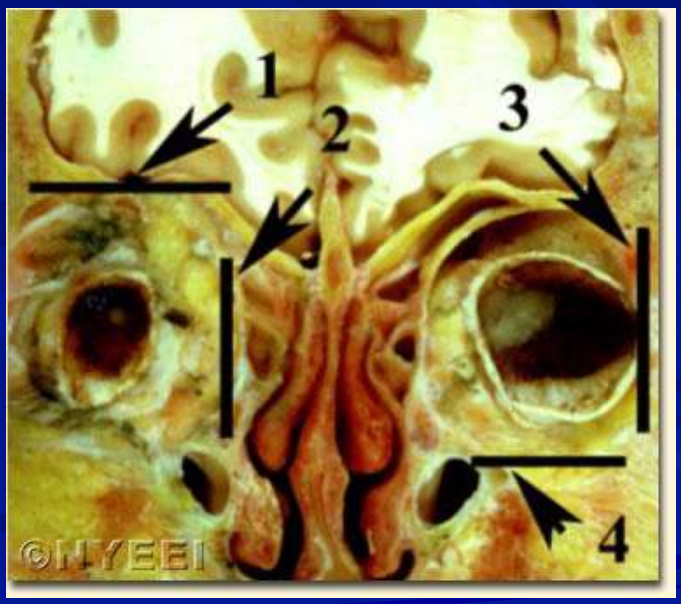
# Optic Neuropathy

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

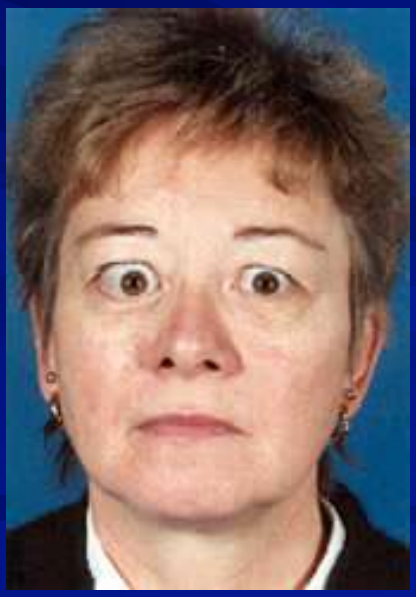


# Orbital Decompression

- 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

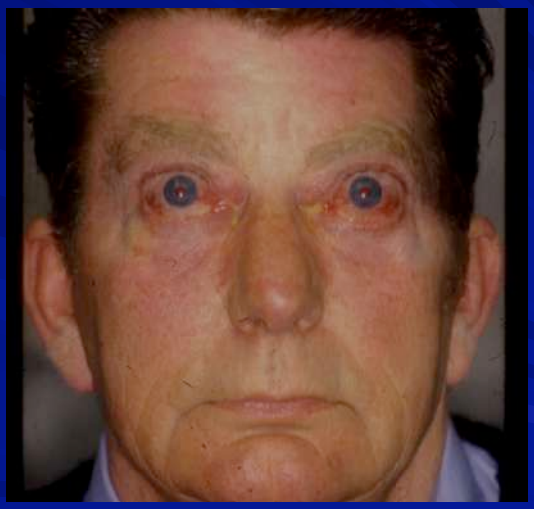


# Orbital Decompression
## (Surgical/Cosmetic)

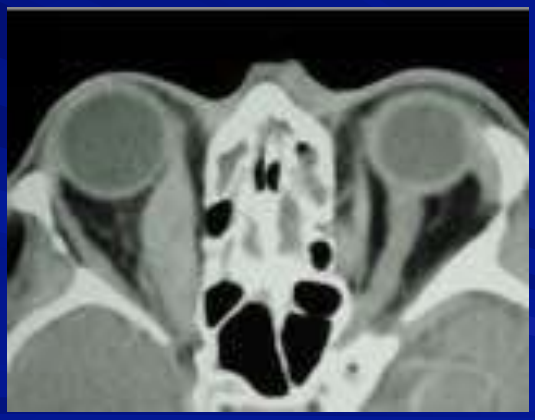


# Thyroid Eye Disease and Depression

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



# Orbital Decompression
## (Medical/Vision Threatened)



# IOP in Thyroid Eye Disease

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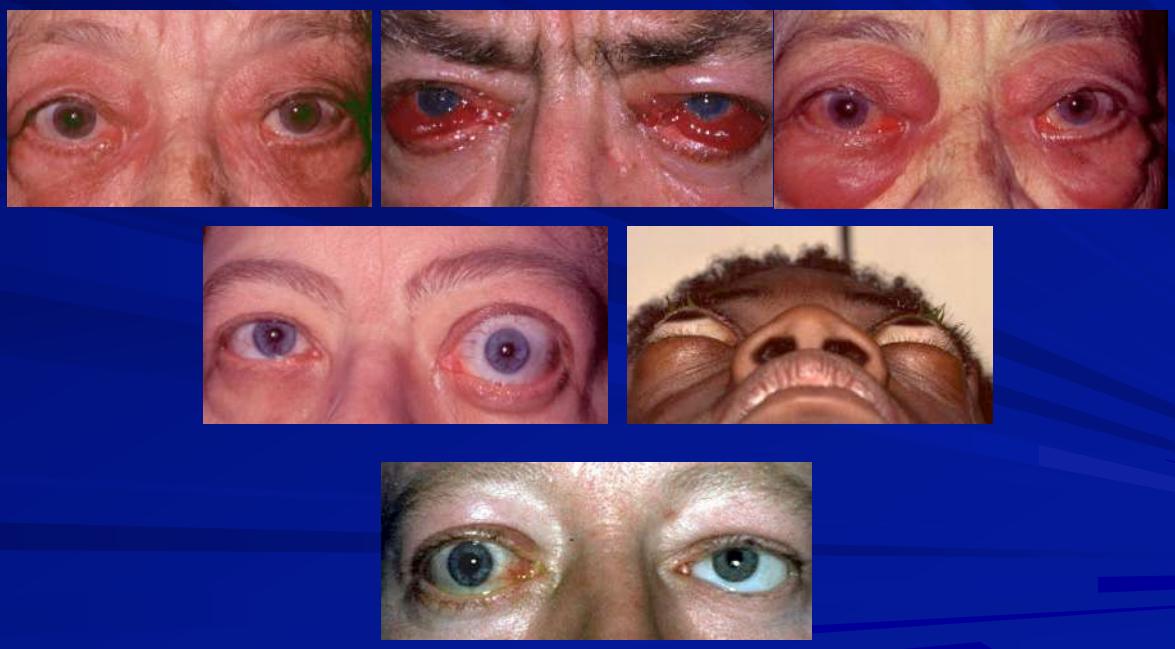
  - Restrictive myopathy
- Some literature reports IOP in up gaze to be part of the diagnoses of thyroid dysfunction….let' s discuss

# IOP in Thyroid Eye Disease



# 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

# 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

# February 25, 2019

## "Nothing Else Can Be Done"

# Clinical Activity Score (CAS)

CAS

**Table 2** | Clinical Activity Score

| | Clinical Activity Score |
|---|---|
| 1 | Painful feeling behind globe |
| 2 | Pain on attempted gaze |
| 3 | Redness of eyelids |
| 4 | Redness of conjunctiva |
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For initial CAS, items 1–7 are tallied at one point each for a final CAS based on a 7-point scale. On follow-up visits, the final three items are added for a CAS out of 10 points

# February 25, 2019

## "Nothing Else Can Be Done"

# February 25, 2019

"Nothing Else Can Be Done"

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

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

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

# March 25, 2019

# Methylprednisolone

☆ FEATURED

Published in Eye Care

Journal Scan / Research · September 02, 2023

## Early Response to Intravenous Methylprednisolone Therapy for Restrictive Myopathy in Patients With Thyroid Eye Disease

Graefe's Archive for Clinical and Experimental Ophthalmology

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TAKE-HOME MESSAGE

- In this study, the authors evaluated the therapeutic effects of intravenous methylprednisolone (IVMP) in patients with restrictive myopathy secondary to thyroid eye disease (TED). Treatment with IVMP decreased the mean TED clinical activity score at all time points; however, the mean deviation angle in prism diopters and extraocular muscle movement limitation both significantly increased at 1, 3, and 6 months compared with baseline. Specifically, the deviation angle increased in 39% of the patients and stayed the same in 25% of the patients. No specific factors were identified that resulted in an increased risk of worsening strabismus.
- Although IVMP may be helpful in mitigating the inflammatory phase in TED, there may be associated worsening of the strabismus and diplopia with restrictive myopathy.

– Zachary Bergman, MD, MPH


PURPOSE

To report the therapeutic efficacy of intravenous methylprednisolone (IVMP) in patients with restrictive myopathy caused by thyroid eye disease (TED).

METHODS

The present prospective uncontrolled study comprised 28 patients with TED and restrictive myopathy who presented with diplopia that had developed within 6 months before their visit. All patients were treated with IVMP for 12 weeks. Deviation angle, limitation of extraocular muscle (EOM) movement, binocular single vision score, Hess score, clinical activity score (CAS), modified NOSPECS score, exophthalmometric value, and the size of EOMs on computed tomography were evaluated. The patients were divided into two groups: those whose deviation angle had decreased or remained unchanged 6 months after treatment (group 1; n = 17) and those whose deviation angle had increased in that time (group 2; n = 11).

RESULTS

The mean CAS of the whole cohort significantly decreased from baseline to 1 month and 3 months after treatment ($P = 0.03$ and $P = 0.02$, respectively). The mean deviation angle significantly increased from baseline to 1, 3, and 6 months ($P = 0.01$, $P < 0.01$, and $P < 0.01$, respectively). The deviation angle decreased in 10 (36%), remained constant in seven (25%), and increased in 11 (39%) of the 28 patients. When groups 1 and 2 were compared, no single variable was identified as a cause of deviation angle deterioration ($P > 0.05$).

CONCLUSIONS

When treating patients with TED who have restrictive myopathy, physicians should be aware that some patients show worsening of the strabismus angle despite inflammation control with IVMP therapy. Uncontrolled fibrosis can result in motility deterioration.




# March 25, 2019

# April 22, 2019

April 22, 2019

MEETING NEWS


# Thyroid eye disease therapy shows promise

Primary Care Optometry News, December 2018



CHICAGO — Teprotumumab, an IGF-1 receptor antagonist antibody, demonstrated improvement of double vision in patients with thyroid eye disease, according to a study presented here.

If approved by the FDA, teprotumumab (Horizon Pharma) would be the first drug with an indication for thyroid eye disease, **Raymond S. Douglas, MD, PhD,** said at the American Academy of Ophthalmology annual meeting.

COMMENT

If approved by the FDA, teprotumumab (Horizon Pharma) would be the first drug with an indication for thyroid eye disease, **Raymond S. Douglas, MD, PhD,** said at the American Academy of Ophthalmology annual meeting.

In the phase 2 trial, 42 patients were treated with the study drug and 45 patients made up the placebo control arm. At week 24, which marked the end of the controlled trial, statistically significantly more patients taking the study drug achieved the primary endpoint of improvement in clinical activity score and reduction of proptosis ($P < .001$). Diplopia improvement was "impressive" at week 24, and of the patients with diplopia at baseline who did improve, 70% continued to have that improvement 48 weeks later, Douglas said.

The most reported adverse event was hyperglycemia, which returned to normal after discontinuation of the drug, he said.

"Teprotumumab ... appears to have stable improvement and durability of improving the double vision, proptosis and clinical activity in these patients and appears to reverse the effects of thyroid eye disease," Douglas said. "The phase 3 trial will also have the added benefit of having a crossover group who will receive open-label therapy if [patients are] nonresponders at week 24, which ... may make this even more universally applicable to patients with long-standing disease." – *by Patricia Nale, ELS*

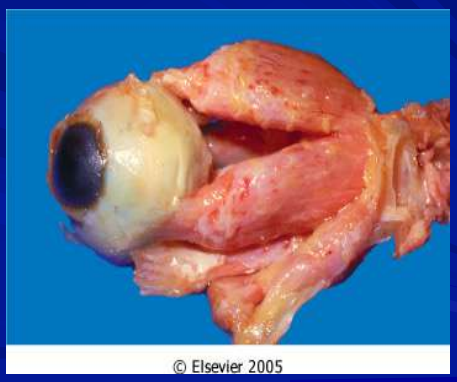
**Reference:**

Douglas RS. Diplopia response in a controlled trial with teprotumumab, an IGF-1 receptor antagonist antibody for thyroid eye disease. Presented at: American Academy of Ophthalmology annual meeting; Oct. 27-30, 2018; Chicago.

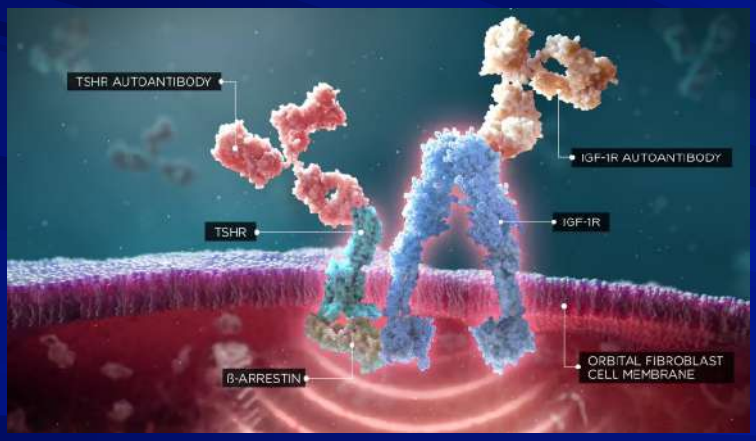
**Disclosure:** Douglas reports no relevant financial disclosures.

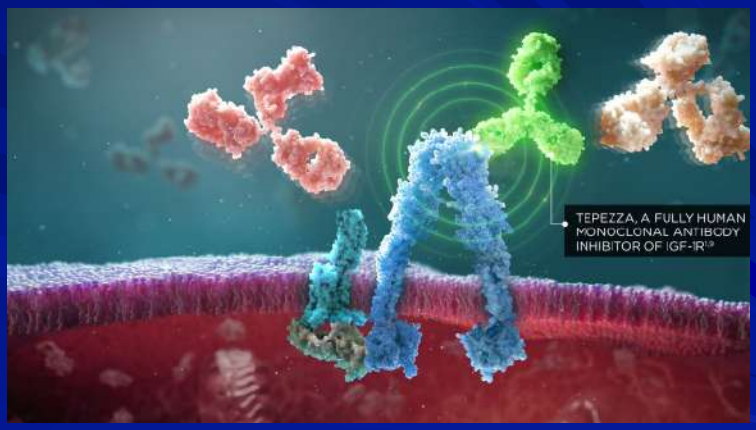
# Teprotumumab-trbw (Tepezza)

- Horizon Therapeutics – HQ Dublin, Ireland and US based Chicago
- Biologic pharmaceutical
  - Chinese Hamster Ovary
  - Infusion, 8 total, every 3 weeks
- Thyroid eye disease
  - IGR-1 (Insulin like growth factor 1) and TSH receptors are over expressed
- 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
  - Published - New England Journal of Medicine
- PDUFA- March 2020, was approved early in 2020



# Teprotumumab-trbw (Tepezza)

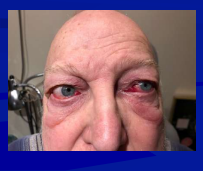



https://www.tepezza.com/hcp/tepezza-moa/

# Immunosuppression?

- Biologics
  - Immunosuppression biologics – suppress the immune system to get the effe3ct
    - Remicade – "1st generation"
      - Chimeric molecule – mouse and human protein, a lot of sensitivity
    - Humira
      - Anti-TNF (RA and Crohn's Disease
      - Fully human protein, less sensitivity
    - Rituxan
      - CD 20 suppressor (B cell suppression)
    - Actively suppress the immune system
  - Immunomodulary
    - Tepezza
      - IGF-1R inhibitor
      - Full humanized monoclonal antibody
        - All the proteins are human – less to no sensitivity – more focused effect
      - Obital fibroblasts to myofibroblast or adipocytes
      - Hyaluronic acid, glycosaminoglycan



# Teprotumumab-trbw (Tepezza)

- Optics and Optic-X Studies
  - 8 infusions, every 3 weeks, 24 weeks
  - Optics – acute, less than 9 months of disease
  - Optics X – chronic, 12-16 months disease
- Clinical Activity Score
  - Spontaneous pain, gaze evoked pain, eyelid erythema, chemosis, inflammation
  - Scale of 7, needed 4 to be in the study
- Proptosis
  - Improvement of 2 mm or better
- Diplopia
  - Scale of 0, 1, 2, or 3
- Grave's Ophthalmopathy -Quality of Life Score
  - Scale 0-100

# Teprotumumab-trbw (Tepezza)

- Clinical Activity Score (CAS)
  - Spontaneous pain, gaze evoked pain, eyelid erythema, chemosis, inflammation
  - Scale of 7, needed 4 to be in the study
    - 78% improved to 0 or 1, 7% improved 0 or 1 with placebo
- Proptosis
  - Improvement of 2 mm or better
    - 83% had 2 mm or better, 10% with placebo
    - Average was 3.2 mm at week 24
- Diplopia
  - Scale of 0, 1, 2, or 3
    - 68% improved 1 point, 29% with placebo
- Grave's Ophthalmopathy -Quality of Life Score
  - Scale 0-100
    - 17.28 point improved, 1,80 with placebo

# Teprotumumab-trbw (Tepezza)

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

# Teprotumumab-trbw (Tepezza)

- **Infusion Reactions (mild/moderate):** approximately 4% of patients
  - transient increases in blood pressure, feeling hot, tachycardia, dyspnea, headache, and muscular pain
  - consideration should be given to premedicating with an antihistamine, antipyretic, or corticosteroid and/or administering at a slower infusion rate.

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

# Teprotumumab-trbw (Tepezza)

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

# Biologics Used Off Label for TED

**Table 1 | Biologic therapies for TED**

| Small Molecule Therapies | Target | Dosing | Findings | Side Effects |
|---|---|---|---|---|
| Rituximab | CD20 | 2 infusions of 1000 mg each 2 weeks apart | Mixed results in improvement of CAS, proptosis, and motility | Exacerbation of inflammatory bowel disease, arthralgias, hypotension |
| Adalimumab | TNF-α | Subcutaneous injections of initial 80 mg dose, then biweekly 40 mg doses for a total of 10 weeks | 6/10 showed decrease in inflammation, no changes in proptosis or extraocular motility | Sepsis (1/10) |
| Infliximab | TNF-α | Infusions at 5 mg/kg each dose over 2 hours | Case reports showed improvement in visual acuity and CAS after 1 dose and complete resolution in 3 cases after 3 doses | Infections, malignancies (especially lymphoma), drug-induced lupus |
| Tocilizumab | IL-6 | 3 infusions at 8 mg/kg given every 4 weeks | 93% with ≥2-point improvement in CAS, mean proptosis reduction of 1.5 mm, no change in diplopia | High recurrence rate, transaminitis, pyelonephritis |
| Teprotumumab | IGF-1R | Initial infusion at 10 mg/kg, followed by 7 infusions at 20 mg/kg given every 3 weeks | Reduced proptosis in 79–83% of patients, improved CAS in 69%, reduced diplopia in 68% | Most common: muscle spasms fatigue, nausea, diarrhea, hyperglycemia, hearing impairment, and alopecia. Between 5% and 12% with serious adverse events requiring early withdrawal |

**CAS**, Clinical Activity Score; **CD**, cluster of differentiation; **FcRn**, neonatal Fc receptor for immunoglobulin G; **IL**, interleukin; **TNF**, tumor necrosis factor.

Additionally, multiple case reports published since

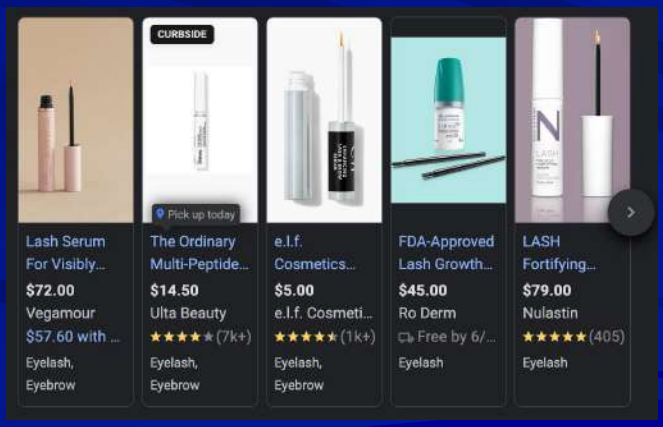
# Optometry's Opportunity

# Eyelash and Brow Loss

- Hypothyroidism or hyperthyroidism, hair loss can be an unfortunate side effect
- Dry, brittle hair, thinning on the scalp, and even loss of lashes and brows
- Some drugs used to treat thyroid conditions can also contribute to the loss of hair
- Left untreated, the hormonal changes associated with hypothyroidism or hyperthyroidism can completely stop new hair strands from developing

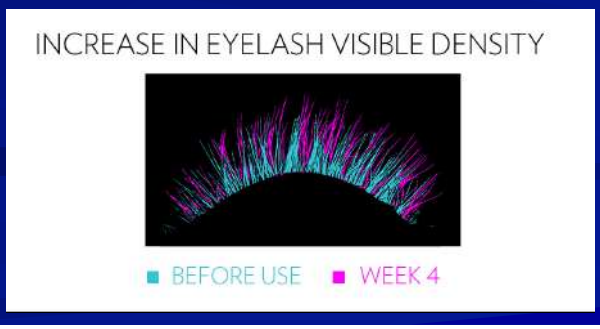
# Current Treatments

- Latisse – bimatoprost 0.03%
- Lash Boost – Rodan Fields - contain isopropyl cloprostenate
  - Synthetic analog of the medication found in Latisse.
  - Highly potent prostaglandin F2-alpha receptor agonist



# New and All Natural

- Lash and Brow Serum – Nu Colour – Nu Skin
  - June 22, 2023 – Available in USA
  - Formulation of natural extracts and peptides
  - Prostaglandin free
  - BAK free
  - No Rx needed – sold in the office
  - Clinical studies preformed




# Lash and Brow Serum

- No Prostaglandin analogs
  - 3 peptides and 5 extracts
- No iris or skin color changes
- No BAK
  - No impact to dry eye
- Not a prescription
- Safe for contact lens wears
- Works within 4 weeks
- 1 bottle (5 ml) lasts 2-3 months
- 3-year self life
- Favorable pricing and profitability
- Able to offer a safer solution to the patient
- Able to capture a part of this $1.7 billion USD market
- Resources for your office – posters and banners

# New and All Natural

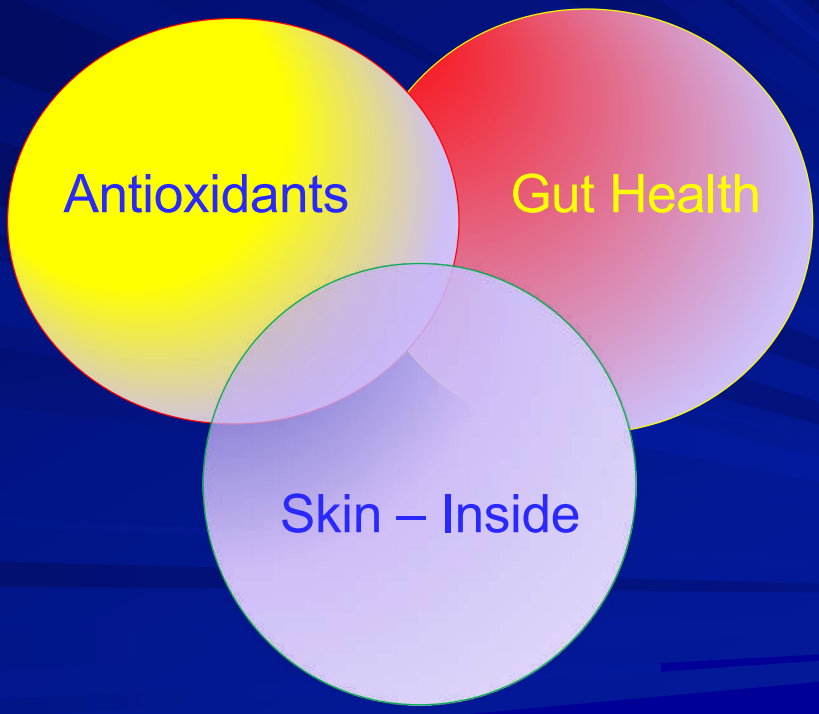
# Functional Interventions

Immune System Support

Gut Microbiome Support


Credit to: James LaValle, RPh, CCN

# Optometry's Opportunity
# Optom-Portunity

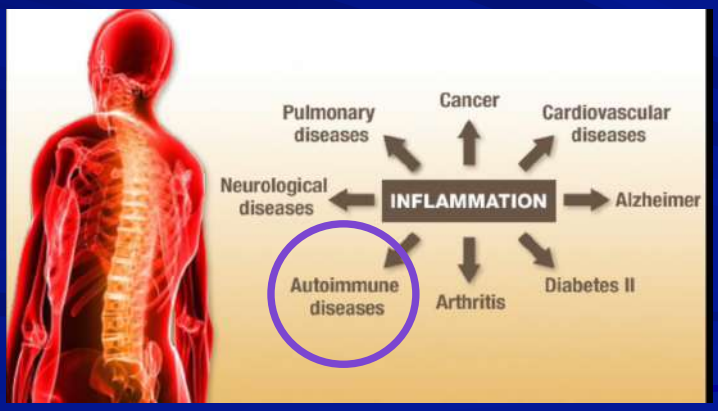


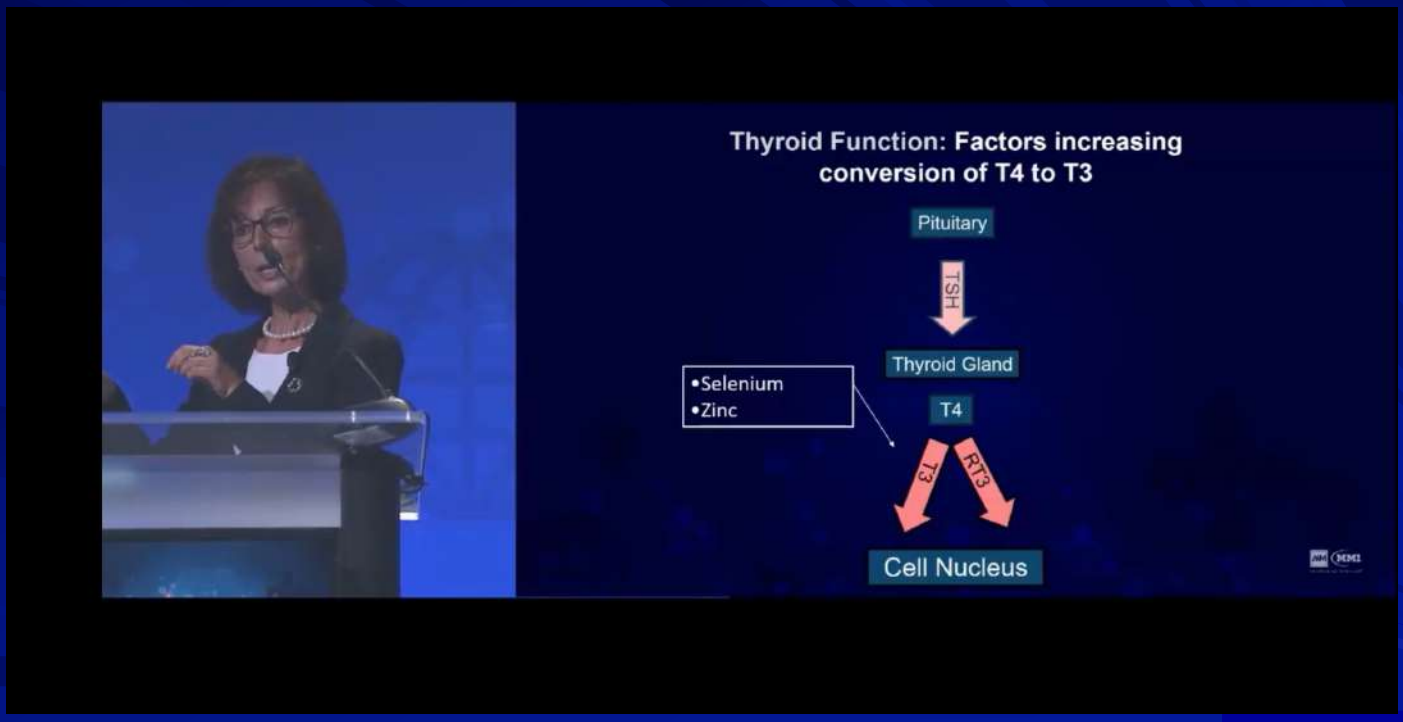
# Chronic and Low-Grade Inflammation

Science has proven that chronic, low-grade inflammation can turn into a silent killer that contributes to cardiovascular disease, cancer, type 2 diabetes, diabetic retinopathy, cataracts, macular degeneration, and many other conditions

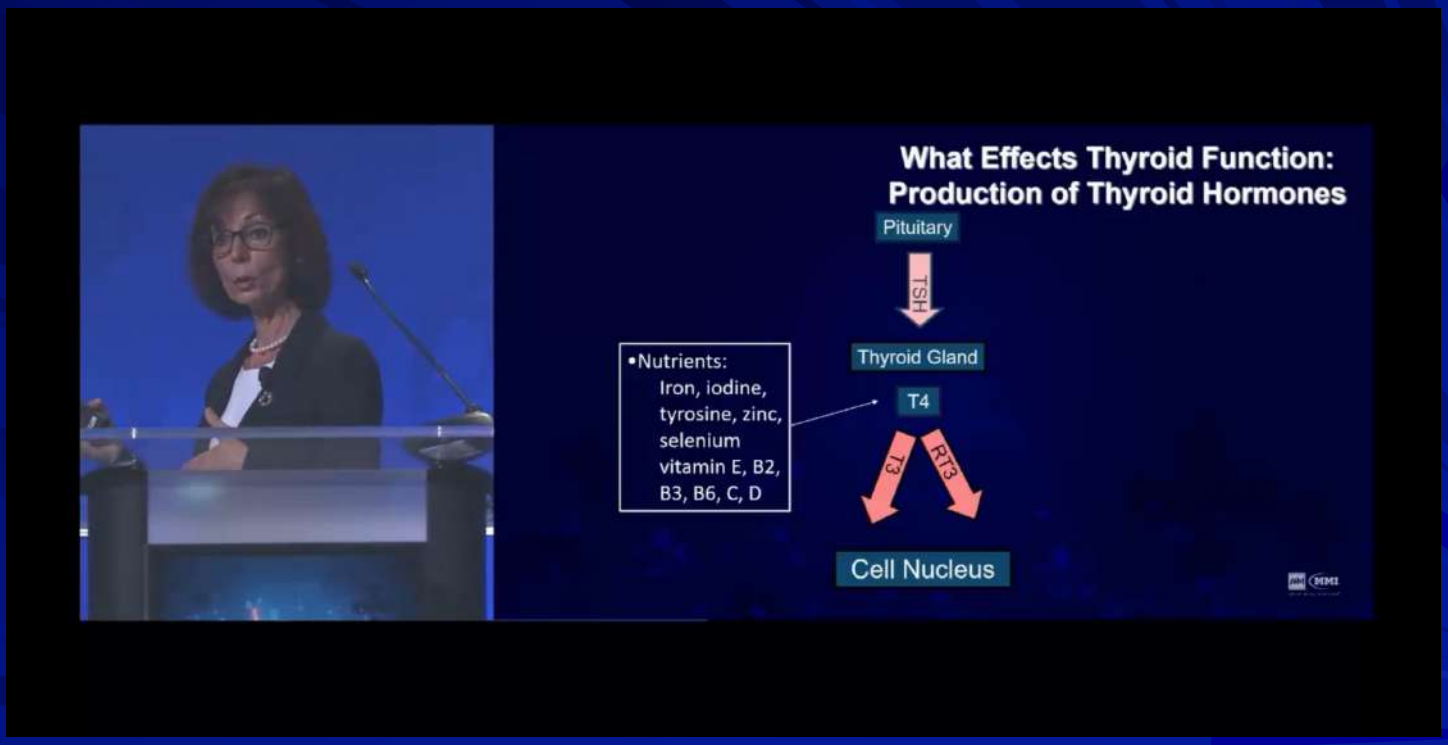
# Chronic and Low-Grade Inflammation

Like cancers and other slow-burn diseases, identifying these conditions early can make the difference between full recovery or a dramatically reduced quality of life or even death  (vision loss or blindness)

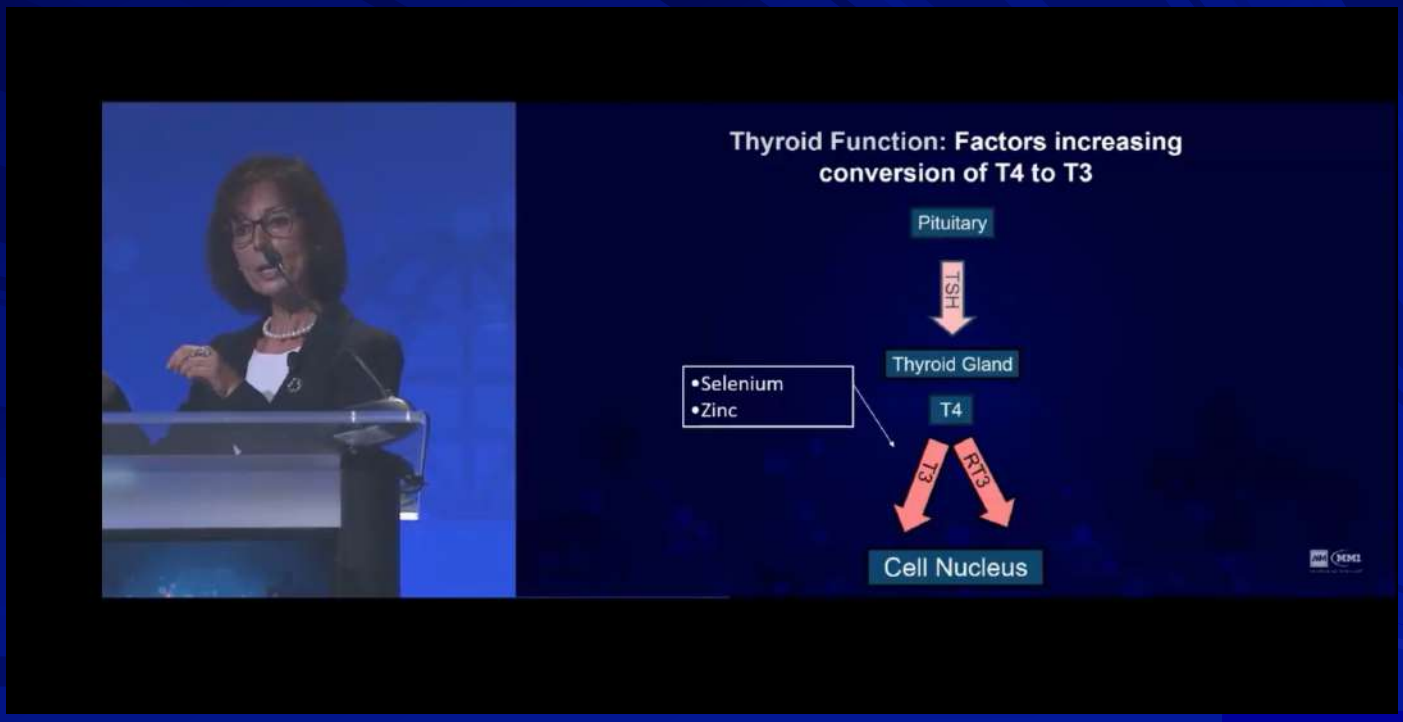




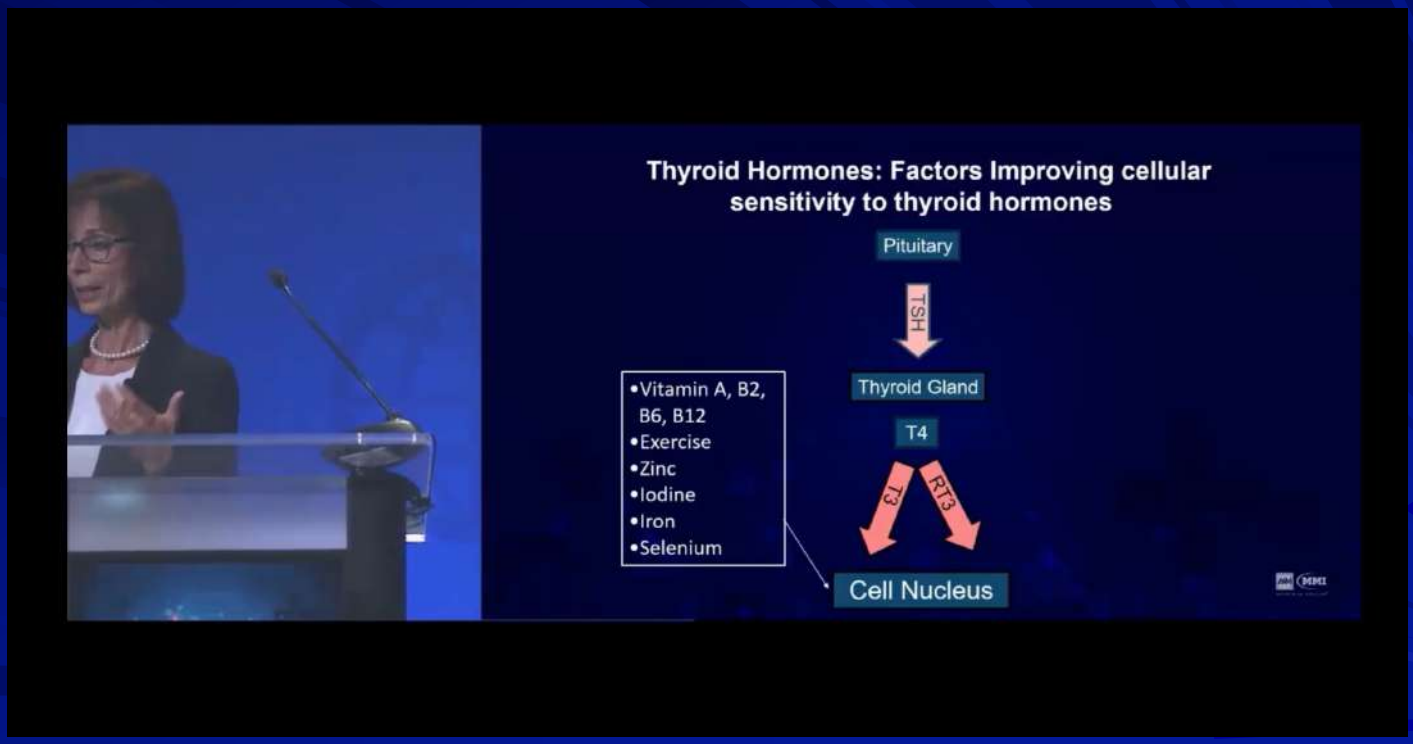

Credit to: Filomena Trindade, MD



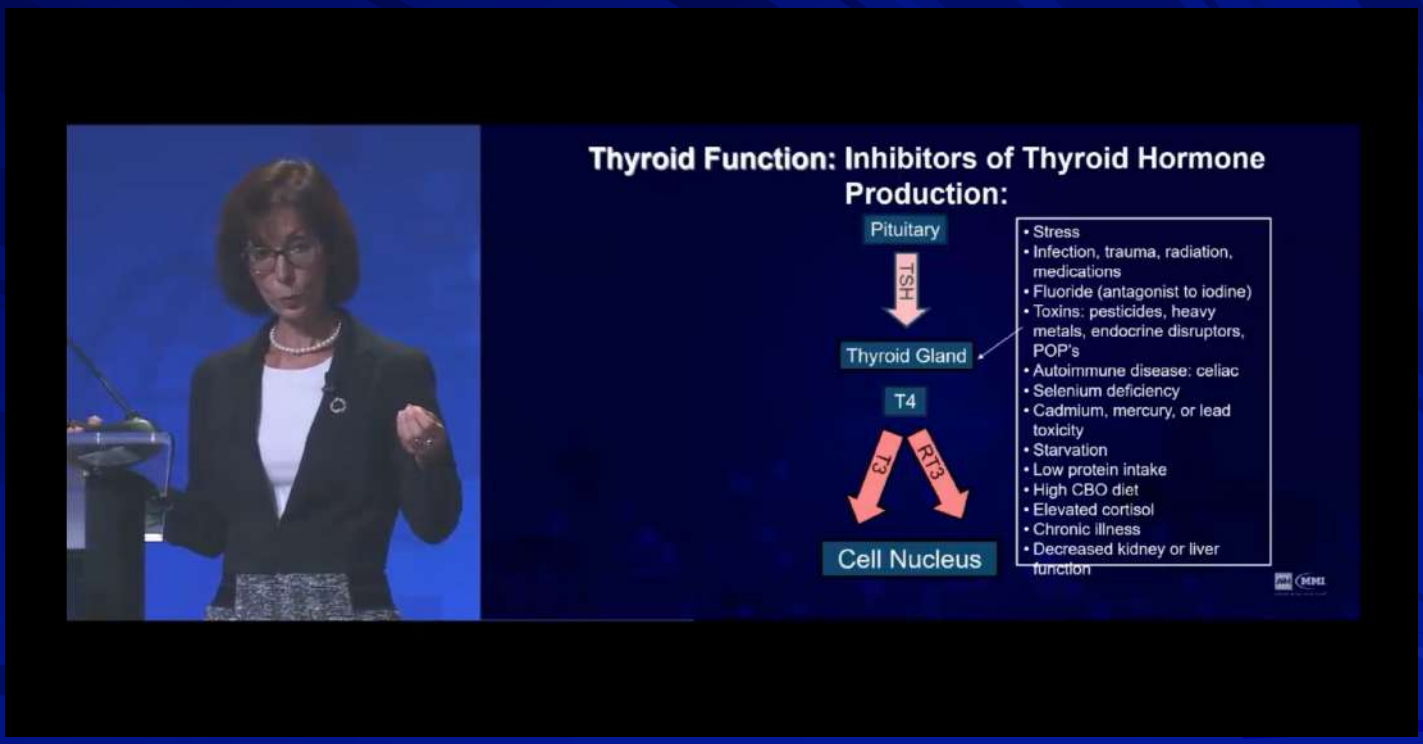

Credit to: Filomena Trindade, MD




Credit to: Filomena Trindade, MD




Credit to: Filomena Trindade, MD

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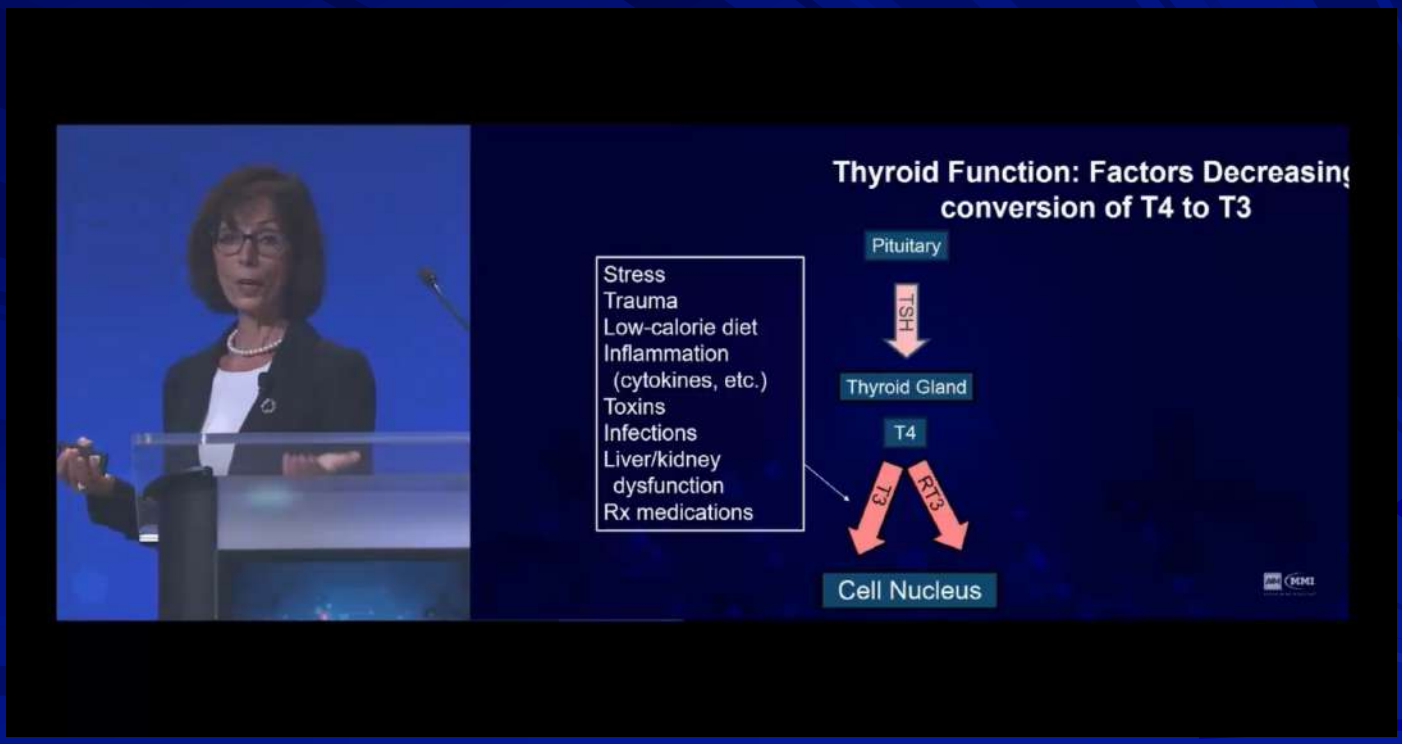


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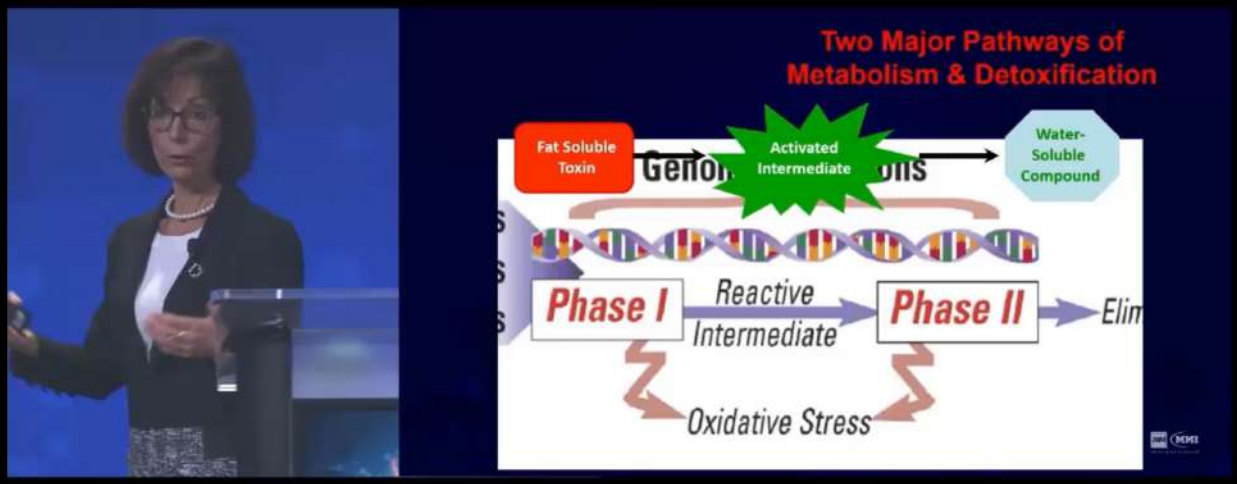


Credit to: Filomena Trindade, MD

## Skin Carotenoid Levels
## Oxidative Stress/Inflammation/Anti-Oxidant Deficient

NIH National Institutes of Health
*Turning Discovery Into Health*

- **Quick Test (approx. 30 sec)**
- **Portable**
- **Cost Effective**
- **Remeasure in 60 days**
- **Reassurance to you and patient**

## Ingredients

| Ingredients | Amount | % Daily Value |
|---|---|---|
| **Serving Size: 1 Packet** | | |
| Vitamin A (83% as Beta Carotene (1875 mcg RAE) from *Blakeslea trispora*, and Vitamin A palmitate) (375 mcg RAE) | 2250 mcg RAE | 250% |
| Vitamin C (as Calcium Ascorbate) | 200 mg | 222% |
| Vitamin D (as Cholecalciferol) | 5 mcg (200 IU) | 25% |
| Vitamin E (as D-Alpha-Tocopheryl Acetate, D-Alpha Tocopherol, Tocotrienols) | 50.3 mg | 335% |
| Vitamin K (as Phytonadione) | 20 mcg | 17% |
| Thiamin (as Thiamine Mononitrate) | 3.75 mg | 313% |
| Riboflavin (as Riboflavin) | 4.25 mg | 327% |
| Niacin (as Niacinamide) | 17.5 mg NE | 109% |
| Vitamin B6 (as Pyridoxine Hydrochloride) | 5 mg | 294% |
| Folate | 500 mcg DFE (300 mcg folic acid) | 125% |
| Vitamin B12 (as Cyanocobalamin) | 15 mcg | 625% |
| Biotin (as Biotin) | 75 mcg | 250% |
| Pantothenic Acid (as D-Calcium Pantothenate) | 15 mg | 300% |
| Calcium (as Calcium Carbonate, Di-Calcium Malate, Calcium Ascorbate) | 250 mg | 19% |
| Iodine (as Potassium Iodide) | 50 mcg | 33% |
| Magnesium (as Magnesium Glycinate, Magnesium Oxide) | 125 mg | 30% |
| Zinc (as Zinc Bisglycinate) | 7.5 mg | 68% |
| Selenium (as L-Selenomethionine, Sodium Selenite) | 70 mcg | 127% |
| Copper (as Copper Bisglycinate) | 0.5 mg | 56% |
| Manganese (as Manganese Bisglycinate) | 1 mg | 43% |
| Chromium (as Chromium Nicotinate Glycinate) | 100mcg | 286% |
| Molybdenum (as Molybdenum Bisglycinate) | 37.5 mcg | 83% |
| Polyphenol and Flavonoid Blend | 97.5 mg | * |
| Catechins (from *Camellia sinensis* Leaf Extract) | (45 mg) | * |
| Quercetin | (25 mg) | * |
| Grape Seed Extract (min. 95% Polyphenols) | (12.5 mg) | * |
| Citrus Bioflavonoids (from Citrus Fruits) | 12.5 mg) | * |
| Resveratrol (from *Polygonum cuspidatum* root extract) | (2.5 mg) | * |
| Mixed Tovopherols (Gamma, Delta & Beta Tocopherols) | 53 mg | * |
| Alpha-Lipoic Acid | 15 mg | * |
| Inositol (as Inositol) | 5 mg | * |
| Carotenoid Blend | 3.5 mg | * |
| Lycopene (as Lycopene) | (2.5 mg) | * |
| Lutein (from Marigold Flower Extract) | (1 mg) | * |
| Boron (as Boron Citrate) | 1.5 mg | * |
| Vanadium (as Vanadyl Sulfate) | 10 mcg | * |

OTHER INGREDIENTS: Gelatin, Microcrystalline Cellulose, Crosmarmellose Sodium, Stearic Acid, Magnesium Stearate, Silicon Dioxide, Titanium Dioxide.

CONTAINS: Fish (Cod, Pollack, Haddock, Hake, Cusk, Redfish, Sole, Flounder).

SUPPLEMENT FACTS

## Supplement Facts

| Serving Size 2 Softgels | Servings Per Container 60 | |
|---|---|---|
| **Amount Per Serving** | | **% DV** |
| Total Calories | 15 | |
| Total Fat | 1 g | 1%* |
| Saturated Fat | 0 g | 0%* |
| *Trans* Fat | 0 g | |
| Vitamin $D_3$ (as cholecalciferol) | 12.5 mcg (500 IU) | 63% |
| Vitamin $K_2$ (as menaquinone-7) | 20 mcg | 17% |
| Ultra-pure fish oil concentrate: | 1055 mg | ** |
| EPA (Eicosapentaenoic acid) | 300 mg | ** |
| DHA (Docosahexaenoic acid) | 200 mg | ** |
| Citrus Bioflavonoids (including hesperidin and naringin) | 100 mg | ** |
| Purple corn (*Zea mays L.*) cob extract including anthocyanins | 66.67 mg | ** |
| Alpha Lipoic Acid | 50 mg | ** |
| Quercetin (from *Dimorphandra mollis* fruit extract) | 37.5 mg | ** |
| D-Limonene (from *Citrus sinensis* peel) | 25 mg | ** |
| Rosemary (*Rosmarinus officinalis L.*) leaf extract including carnosic acid | 18.75 mg | ** |
| Resveratrol (from *Polygonum cuspidatum* root) | 15 mg | ** |
| Coenzyme $Q_{10}$ | 15 mg | ** |
| Lycopene | 2.5 mg | ** |
| Lutein (from marigold flower (*Targetes erecta*)) | 2 mg | ** |
| Astaxanthin (from *Haematococcus pluvialis* algae) | 0.5 mg | ** |

* Percent Daily Values are based on a 2,000 Calorie Diet.
** Daily Value (DV) not established.

**OTHER INGREDIENTS:** Gelatin, Glycerin, Beeswax, Sunflower Lecithin, Vanillin.

**CONTAINS:** Fish (anchovies, sardines, mackerel).


Credit to: James LaValle, RPh, CCN

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# The Relationship between Gastrointestinal Health, Micronutrient Concentrations, and Autoimmunity: A Focus on the Thyroid

by Michael Ruscio [1], Gavin Guard [1,*], Gabriela Piedrahita [2] and Christopher R. D'Adamo [2,3]

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(This article belongs to the Special Issue Thyroid in the Periphery: Diet Supplementation in Health and Disease)

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**Abstract**

Currently, there is a lack of understanding of why many patients with thyroid dysfunction remain symptomatic despite being biochemically euthyroid. Gastrointestinal (GI) health is imperative for absorption of thyroid-specific nutrients as well as thyroid function directly. This comprehensive narrative review describes the impact of what the authors have conceptualized as the "nutrient–GI–thyroid axis". Compelling evidence reveals how gastrointestinal health could be seen as the epicenter of thyroid-related care given that: (1) GI conditions can lower thyroid-specific nutrients; (2) GI care can improve status of thyroid-specific nutrients; (3) GI conditions are at least 45 times more common than hypothyroidism; (4) GI care can resolve symptoms thought to be from thyroid dysfunction; and (5) GI health can affect thyroid autoimmunity. A new appreciation for GI health could be the missing link to better nutrient status, thyroid status, and clinical care for those with thyroid dysfunction.

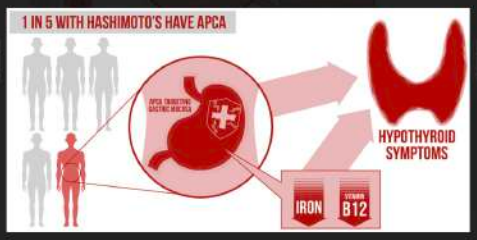
*Keywords:* **gastrointestinal health; hypothyroid; nutrients; IBS; nutrient–GI–thyroid axis**

## 1. Introduction

The primary etiology of hypothyroidism is autoimmunity in Western populations where frank iodine insufficiency is not endemic. While many of these patients will require lifelong

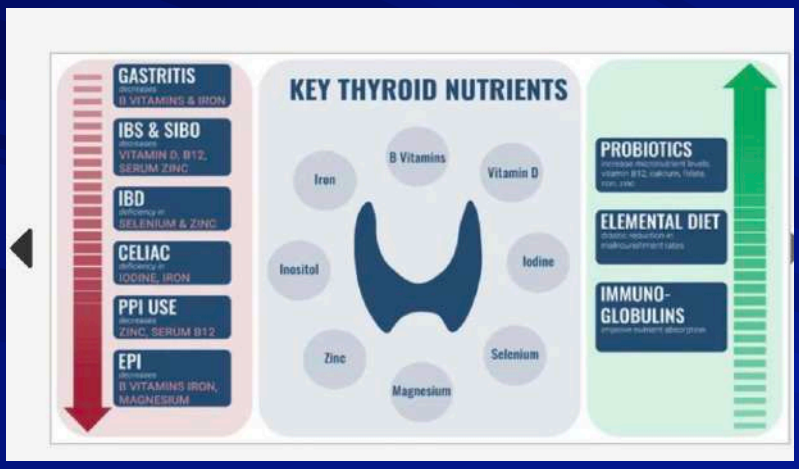
Top

**Figure 1**
Relationship between Hashimoto's, parietal cell antibodies, nutrient deficiencies, and apparent thyroid symptoms.






1 of 3


GASTRITIS
B VITAMINS & IRON
IBS & SIBO
VITAMIN D, B12, SERUM ZINC
IBD
SELENIUM & ZINC
CELIAC
IODINE, IRON
PPI USE
ZINC, SERUM B12
EPI
B VITAMINS IRON, MAGNESIUM
KEY THYROID NUTRIENTS
B Vitamins
Vitamin D
Iron
Inositol
Iodine
Zinc
Selenium
Magnesium
PROBIOTICS
ELEMENTAL DIET
IMMUNO-GLOBULINS

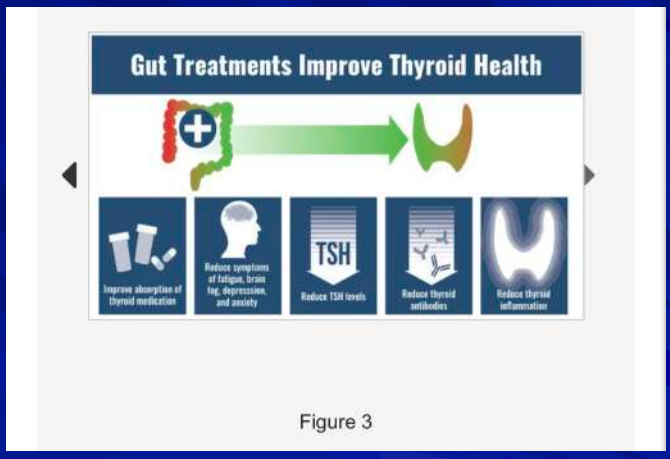

Gut Treatments Improve Thyroid Health
Improve absorption of thyroid medication
Reduce symptoms of fatigue, brain fog, depression, and anxiety
TSH
Reduce TSH levels
Reduce thyroid antibodies
Reduce thyroid inflammation

Figure 3

# Gut Microbiome

## What about Probiotics?

**Prebiotics** – fibrous compounds that the good bacteria in your intestines can feed on.

**Probiotics** – living bacteria that help to increase good bacteria numbers in your gut

**Postbiotics** – the beneficial by-products of when prebiotics eat probiotics

## PREBIOTICS

- Not digested within the small intestine
- Reach the large intestine
- Become fuel for gut bacteria
- Increases growth of good gut bacteria

Abundance and diversity of good gut bacteria

1. Aid digestion
2. Promote immune function
3. Protect against inflammation

## PROBIOTICS

- Living micro-organisms (good bacteria) that have he benefits in adequate quantities

Low FODMAP Probiotic Foods

## POSTBIOTICS

- "Waste products" produced when prebiotic fibre feeds probiotics
- Responsible for the majority of benefits provided by pre- and probiotics
- Eating more pre and probiotics will produce more postbiotics
- However more research in this area is needed

https://fodmapfriendly.com/what-are-fodmaps/

# Signs in Thyroid Eye Disease

- Dalrymple's sign: Lid retraction
- von Graefe's sign: Upper lid lag on downward gaze
- Griffith's sign: Lower lid lag on downward gaze
- Boston's sign: Jerky irregular movement of the upper lid on downward gaze
- Jellinek's sign: Increased 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

Optometric Education Consultants


# Questions and Thank You!

## Thyroid Eye Disease
### What Every Clinician Needs to Know

Greg Caldwell, OD, FAAO

Music City Fall Classic
Optometric Education Consultants
Saturday, October 21, 2023