



Optometric
Education
Consultants



Thyroid and Thyroid Eye Disease Clinical Pearls and Innovations for 2023

Greg Caldwell, OD, FAAO
Pittsburgh Primary Eye Care Conference
Saturday, February 18, 2023



Disclosures- Greg Caldwell, OD, FAAO

All relevant relationships have been mitigated

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- Envolve: PA Medical Director, Credential Committee
- Healthcare Registries – Chairman of Advisory Council for Diabetes and AMD
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Financial Obligations



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

Key Tenants of Aging, Performance and Vitality



Oxidative Stress / Inflammation



Hormonal Balance



Stress Hormones



Glucose / Insulin Regulation



GUT integrity and microbiome diversity



Immune Balance

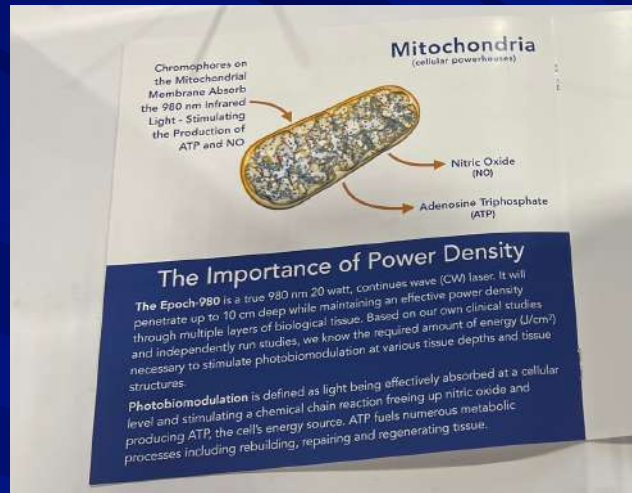


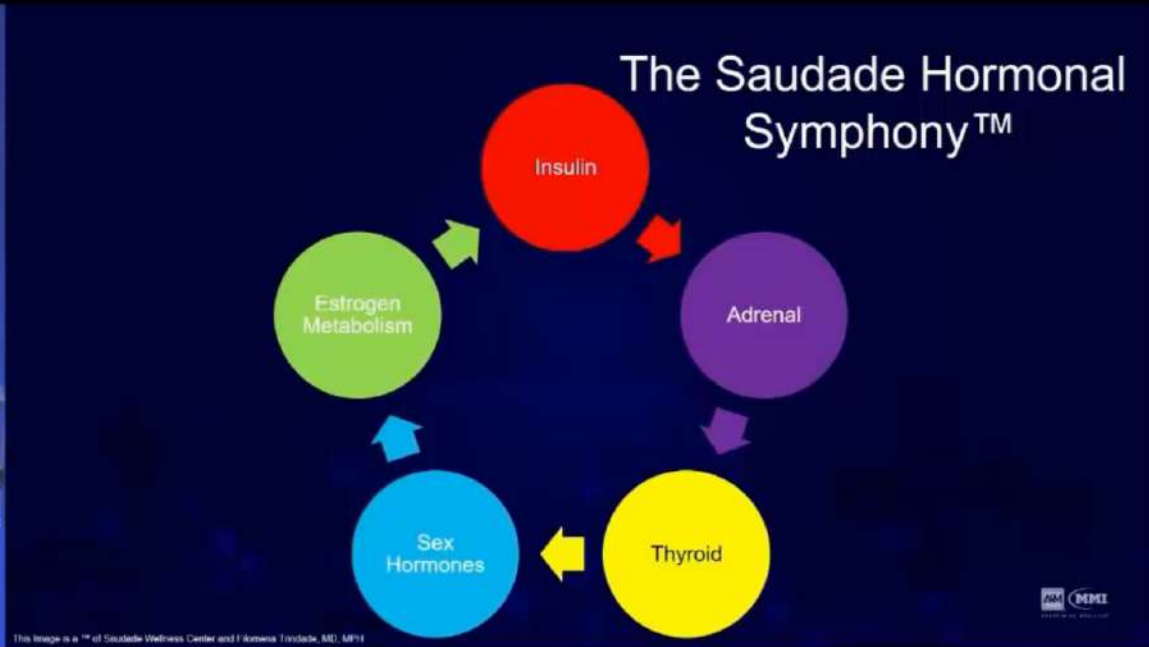
Environmental Exposure/Burden



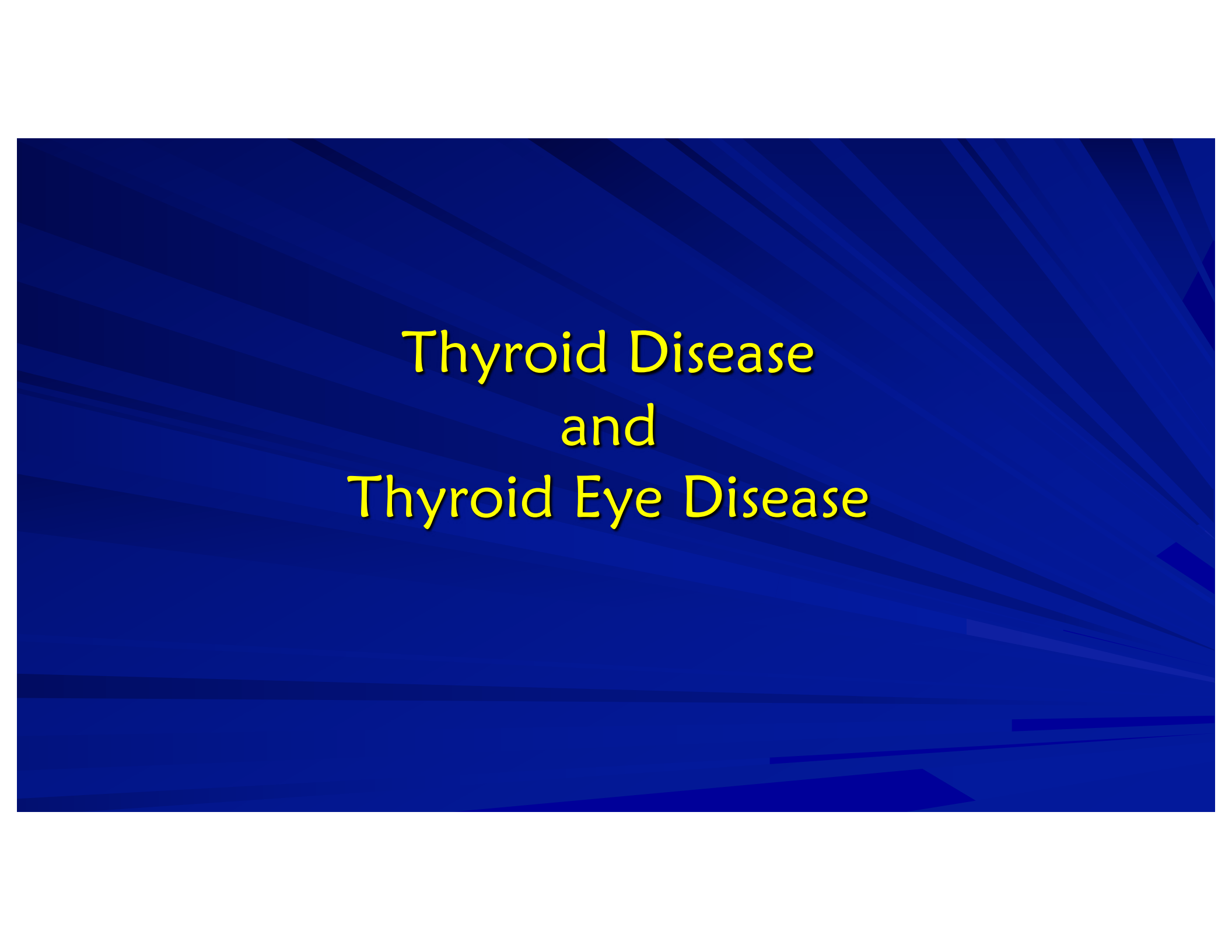
Individuality

Credit to: James LaValle, RPh, CCN





Credit to: Filomena Trindade, MD

The background is a solid dark blue color with a pattern of lighter blue diagonal lines radiating from the top right corner towards the bottom left, creating a sense of depth and movement.

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

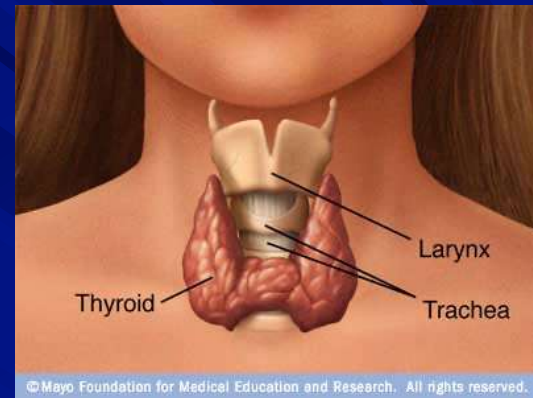
- ★ Digestive glands have ducts for releasing the digestive enzymes
- ★ Salivary glands, sweat glands and glands within the gastrointestinal tract

👓 Pancreas is both endocrine and exocrine

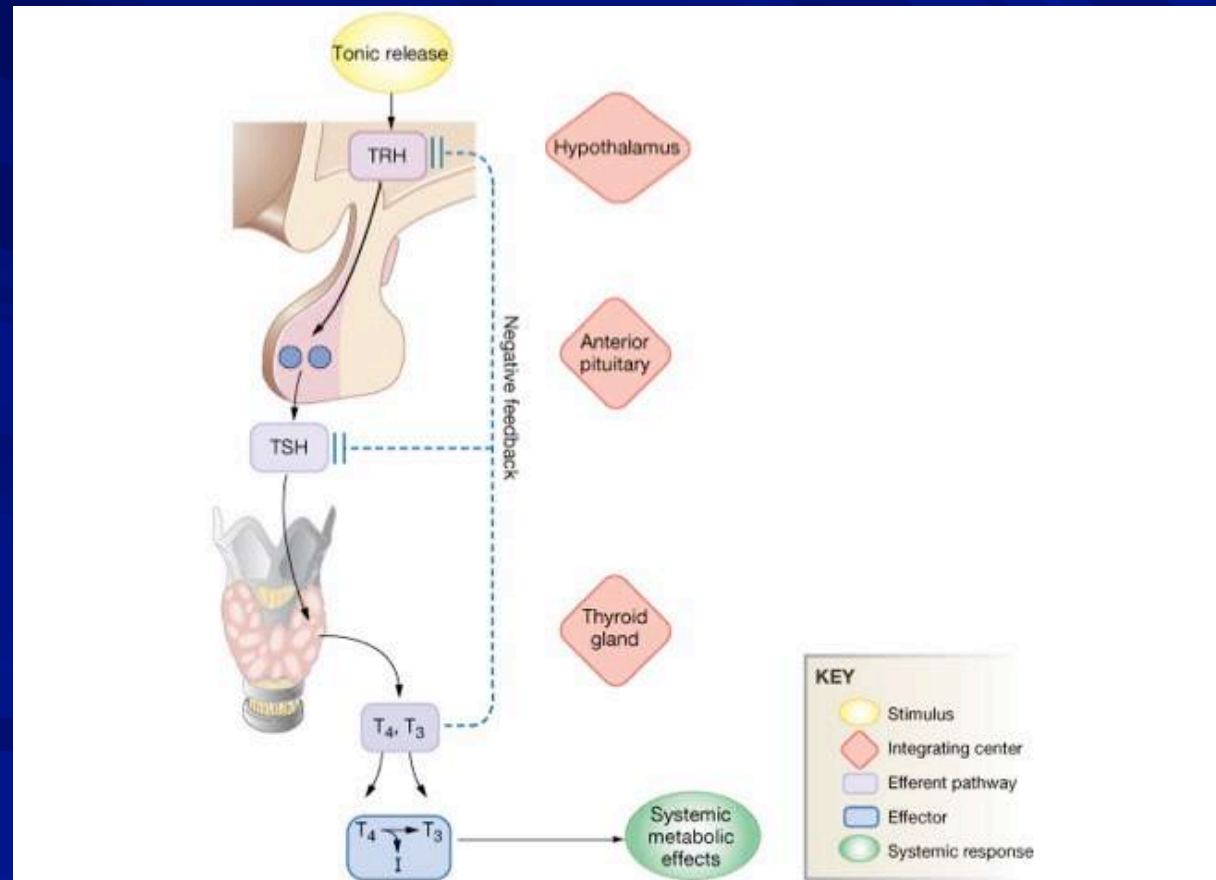
- ★ Exocrine (ducted gland) secreting digestive enzymes into the small intestine.
- ★ Endocrine (ductless gland) in that the islets of Langerhans secrete insulin and glucagon to regulate the blood sugar level.

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?

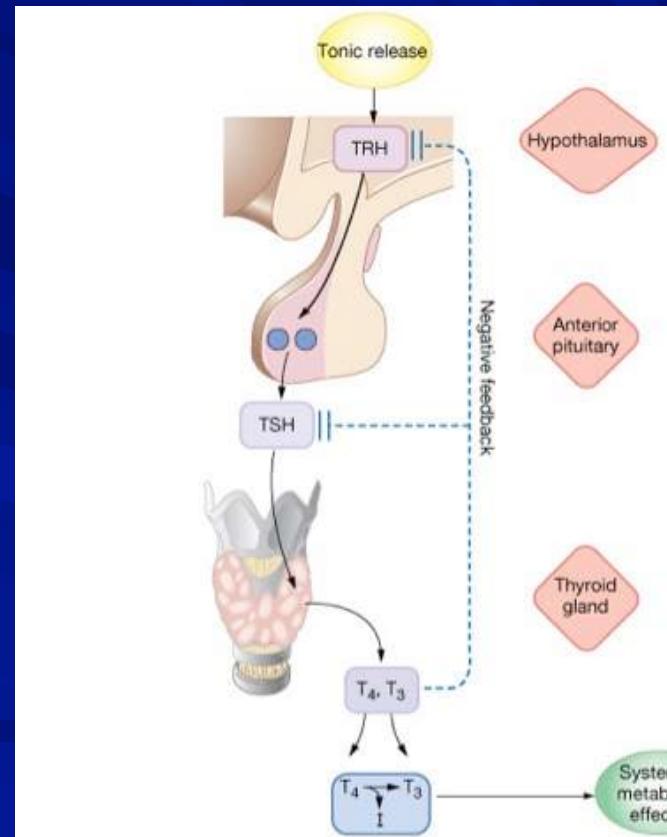
- A. Cancer
- B. Surgically induced
- C. Medication toxicity or side effect
- D. Pregnancy
- E. Autoimmune disease

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

- ★ Antibodies, immunoglobulins

Thyroid Dysfunction

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



Antibodies of Thyroid Dysfunction

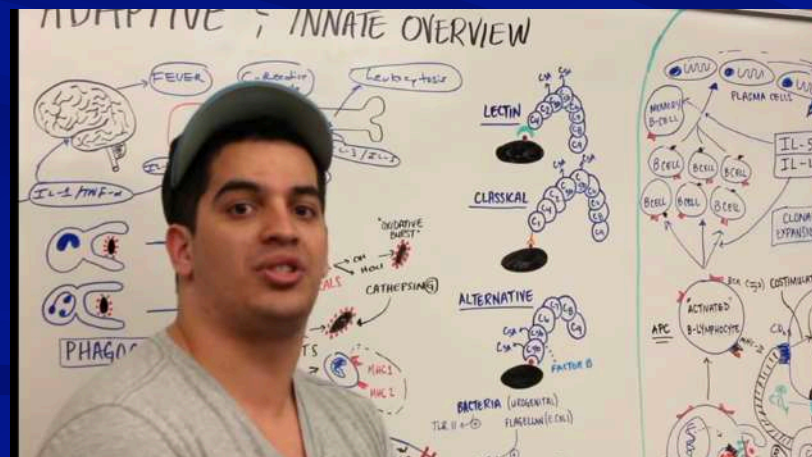
🔗 TSH Receptor Antibodies

- ★ Stimulating TSH receptor antibody
 - 📋 Thyroid Stimulating Immunoglobulin (TSI)
- ★ Thyroid blocking antibody (TBAAb)

🔗 Thyroid Peroxidase Antibodies (TPOAb)

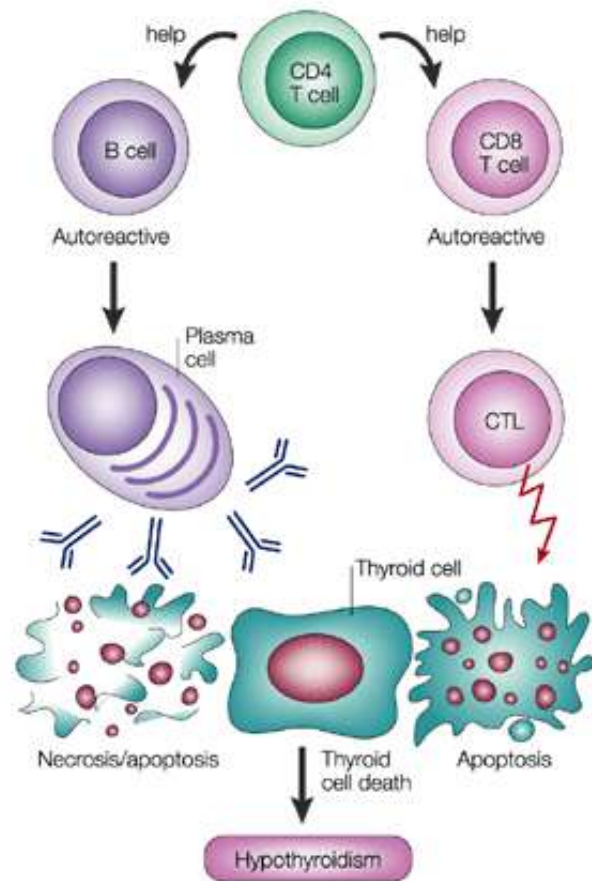
- ★ TPO is found in thyroid follicle cells where it converts the thyroid hormone T4 to T3
- ★ TPOAb contributes to thyroid cellular destruction

🔗 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

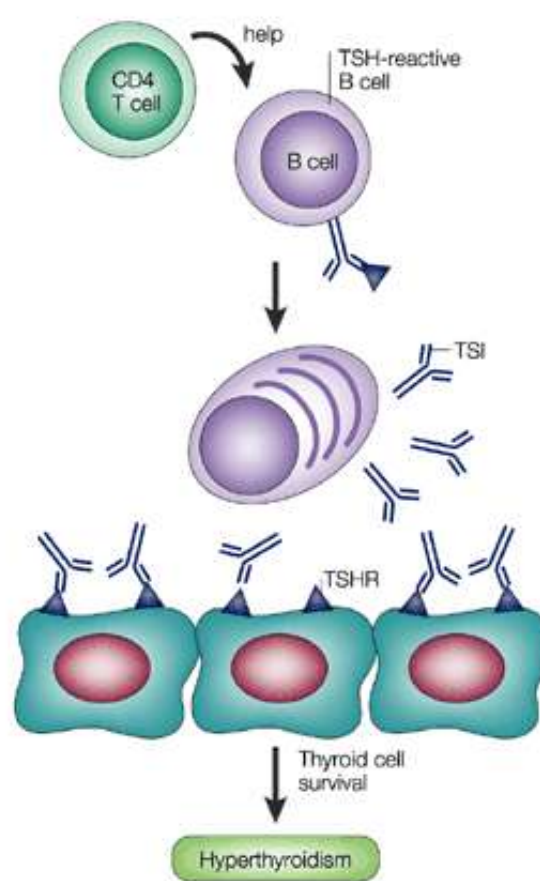


Ninja Nerd Science
YouTube

a Hashimoto's thyroiditis



b Graves' disease



Nature Reviews | Immunology

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nature > nature reviews immunology > review articles > article

Published: 01 March 2002

Autoimmune thyroid disease: new models of cell death in autoimmunity

Giorgio Stassi & Ruggero De Maria

Nature Reviews Immunology 2, 195–204 (2002) | [Cite this article](#)

5162 Accesses | 199 Citations | 7 Altmetric | [Metrics](#)

Key Points

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PATIENT'S RISK OF ED AMD

LOW

CONTRIBUTION TO RISK RESULTS
The AMD Lifetime Risk is calculated based upon the patient's genetics, ocular findings, demographic and behavior status. The table below lists the patient's individual factors contributing to their individual risk.

RISK FACTORS

PATIENT FACTOR MEASURED	LOWER RISK	MODERATE RISK	HIGHER RISK	PATIENT RESULTS
AMD Grading	0-2 Factors	3 Factors	4 Factors	LOWER
Genetic Markers	Low	Moderate	High	LOWER
Race	Non-White	-	White	HIGHER
Smoking Status	Never	Past	Current	LOWER
BMI Score	<25	25-29	≥30	HIGHER
Gender	Male	-	Female	LOWER
Age (years)	55-64	65-74	≥75	LOWER

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AMD LIFETIME RISK REPORT
age related macular degeneration

RISK FACTORS

GENE	SNPS	ALLELE	RISK	PATIENT RESULTS
ARMS2/HTRA1 (HTRA Serine Peptidase 1)	rs10490924	GG	Lower Risk (Reference)	X
		GT	Moderate Risk	
		TT	Higher Risk	
CFH (Complement Factor H)	rs1061170	TT	Highly Protective	X
		CT	Moderately Protective	
		CC	Higher Risk (Reference)	
		CC	Lower Risk (Reference)	
CFH (Complement Factor H)	rs121913059	CT	Moderate Risk	X
		TT	Higher Risk	
		AA	Highly Protective	
C3 (Complement Component 3)	rs1410996	GA	Moderately Protective	X
		GG	Higher Risk (Reference)	
		GG	Lower Risk (Reference)	
C3 (Complement Component 3)	rs2230199	GC	Moderate Risk	X
		CC	Higher Risk	
		CC	Higher Risk	

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CURRENT AGE: 80 RISK OF ADVANCED AMD

PATIENT'S PROBABILITY OF ADVANCED AMD

HIGH

2 YEARS 18%
5 YEARS 49%
10 YEARS 90%
20 YEARS 100%
30 YEARS 100%

PROBABILITY OF ADVANCED AMD (%)

YEARS

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AMD PROGRESSION REPORT
age related macular degeneration

RISK FACTORS

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2 of 3

PATIENT'S RISK OF ED AMD

MODERATE

CONTRIBUTION TO RISK RESULTS
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AMD LIFETIME RISK REPORT
age related macular degeneration

RISK FACTORS

GENE	SNPS	ALLELE	RISK	PATIENT RESULTS
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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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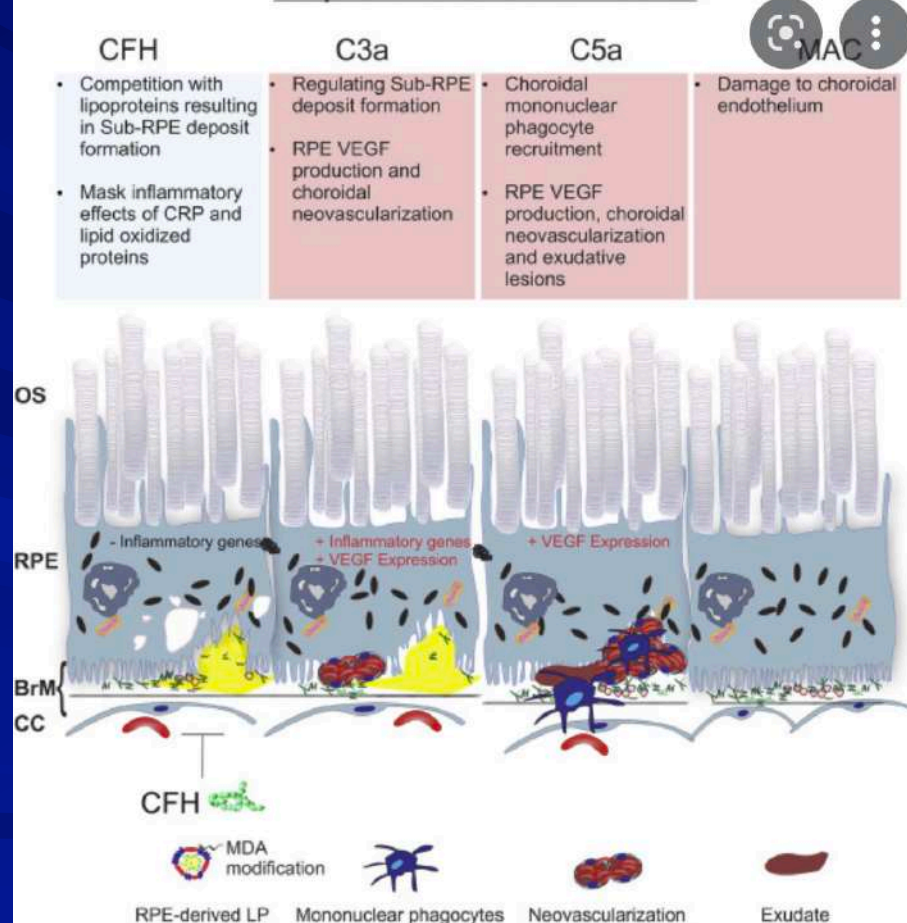
Abstract

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 this

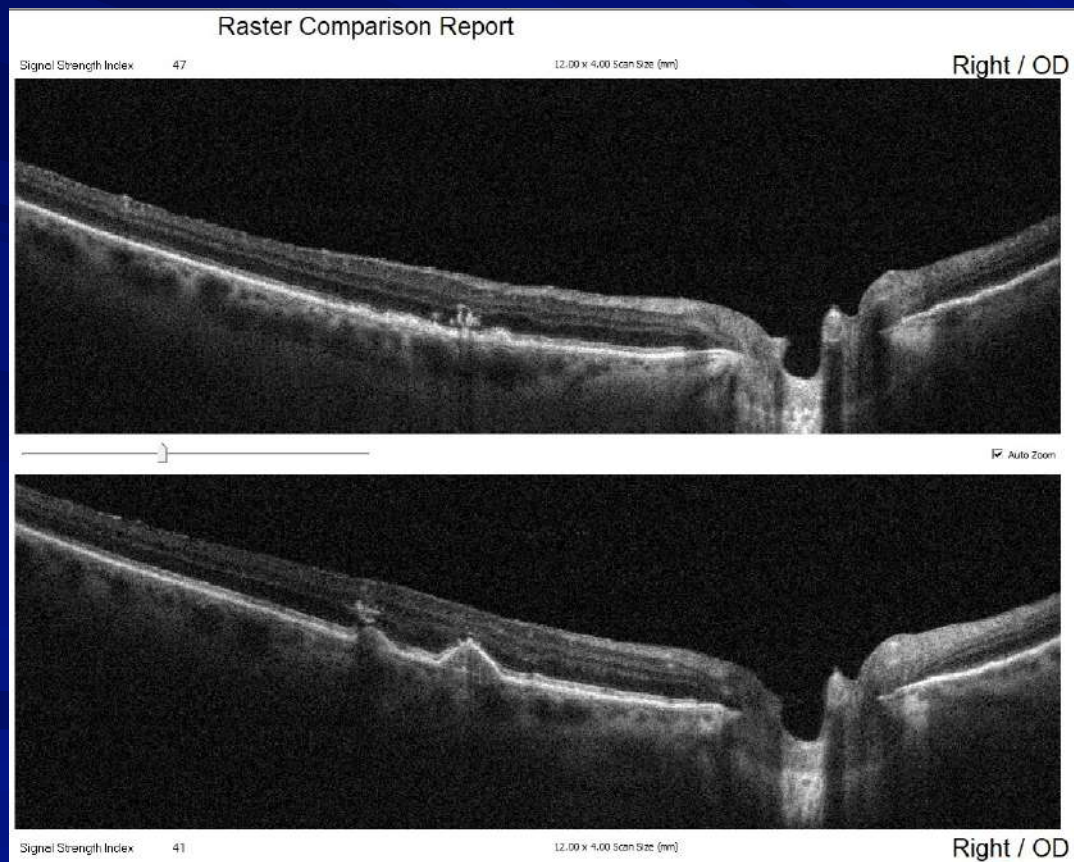
FEEDBACK 

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Complement Cascade Effectors in AMD

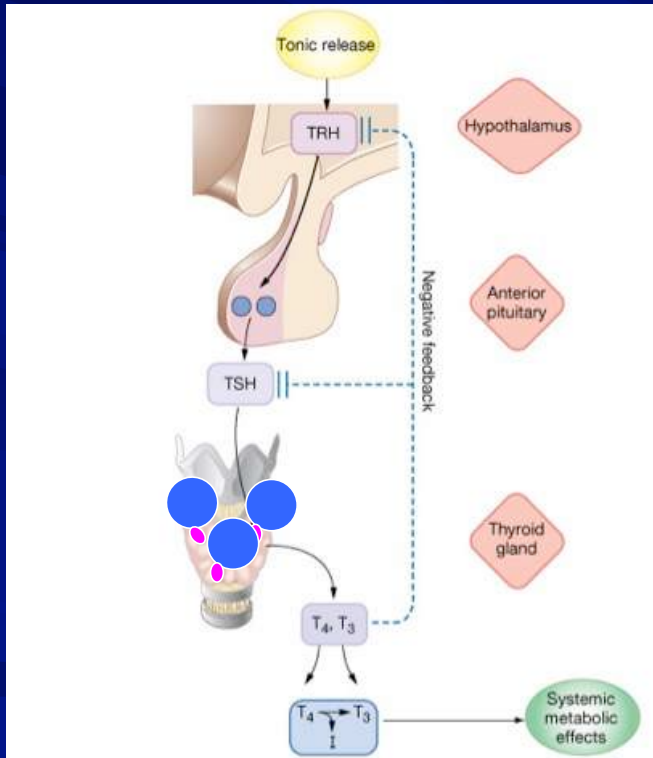


April 27, 2021 – January 26, 2022 (9 months)



Melanie Clemmons, OD
May 20, 2022 AACO Nashville

Hyperthyroid

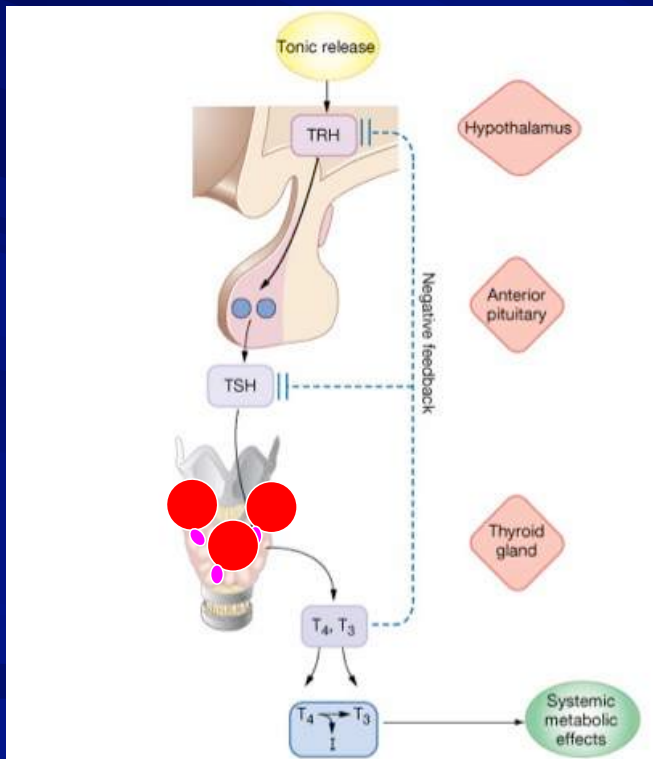


☞ TSI attacks the thyroid

☞ 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

(Hyperthyroidism)

👉 A multisystem disorder consisting of a triad

- ★ Hyperthyroidism with diffuse hyperplasia of the thyroid gland
- ★ Infiltrative dermopathy
- ★ Infiltrative ophthalmopathy

👉 Prevalence:

- ★ 20-40 year old female (F:M = 7:1)
- ★ Genetic link

👉 Etiology:

- ★ Autoimmune disease: hypersensitivity reaction with thyroid stimulation by the circulation of abnormal thyroid-stimulating immunoglobulins (TSI)

Hashimoto's Thyroiditis

(Hypothyroidism)

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

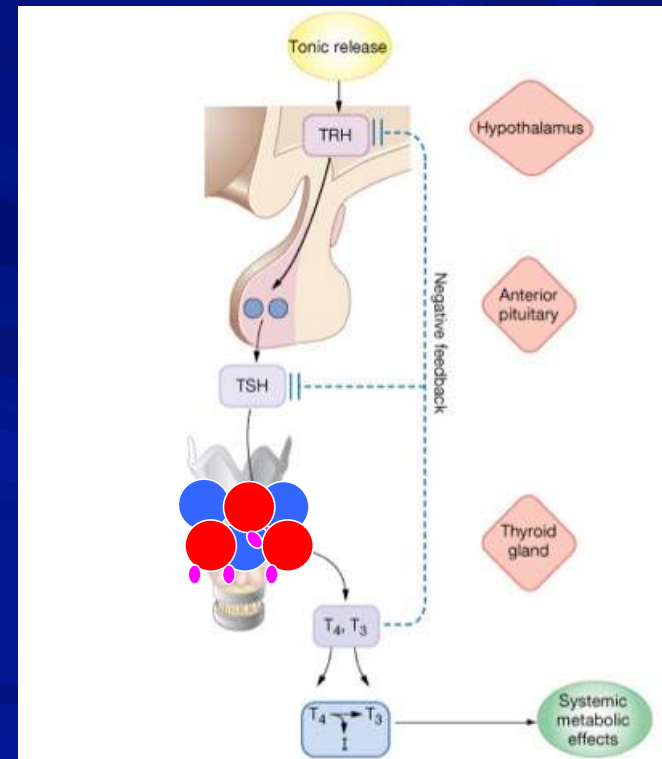
- ✎ This form of TED resolves within a few weeks after thyroid hormone levels (FT_4 and FT_3) are corrected and brought back into the normal range
- ✎ The pituitary hormone TSH can stay low or suppressed for many months during the course of treatment for hyperthyroidism and doesn't mean that the patient 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



[Redacted]		
12-27-14	TSH 6.123	50mcg Synthroid
2-3-15	2.922	
6-16-15	2.579	
10-16-15	3.932	
1-26-16	2.670	
6-4-16	1.210	
10/11/16	40.010	25 mcg Synthroid
My symptoms began in Nov		
12/14/16	0.856	TSI for T4
Dr. Haerian 2-10-17	1.048	
* Stopped Synthroid 2-10-17	Thyroglobulin Antibodies	<1.0
2-10-17	Thyroid Peroxidase AB	11
2-10-17	Thyroid Stim Immunoglobulin	344
6-21-17		(≤13)
3-21-17	TSH 2.268	
	Free T4 0.83	Free T4 0.94
5-31-17	TSH 2.147	Free T4 0.92
7-19-17	TSH 3.079	

You're in the Know

Normal Values

Thyroglobulin 20 IU/ml

Peroxidase <35 IU/ml

TSI 1.75 IU/ml

It does work!

General Ocular Symptoms

- 👁️ Prominent eyes, stare
- 👁️ Pain
- 👁️ 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 ≥ 3 mm between eyes, or if progression of ≥ 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 $\geq 8^\circ$ 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

- Immunity 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)

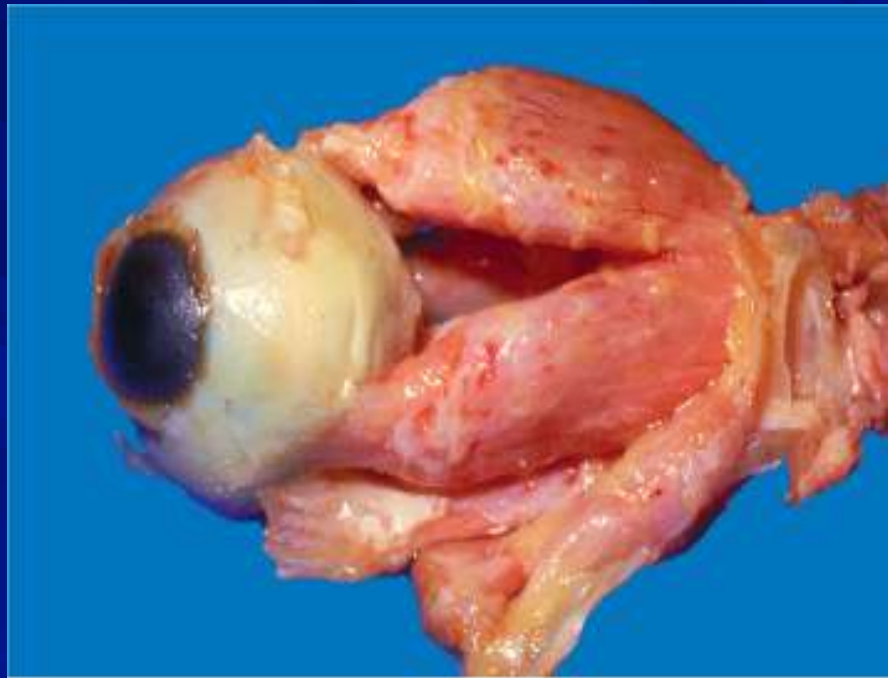
- 👁️ Thyroid Eye Disease is most common cause of unilateral and bilateral exophthalmos
- 👁️ The term exophthalmos is reserved for prominence of the eye secondary to thyroid disease
- 👁️ May need MRI to determine or obvious exophthalmos may be present
- 👁️ It is permanent in 70% of cases
- 👁️ Caused by 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)





© Elsevier 2005

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

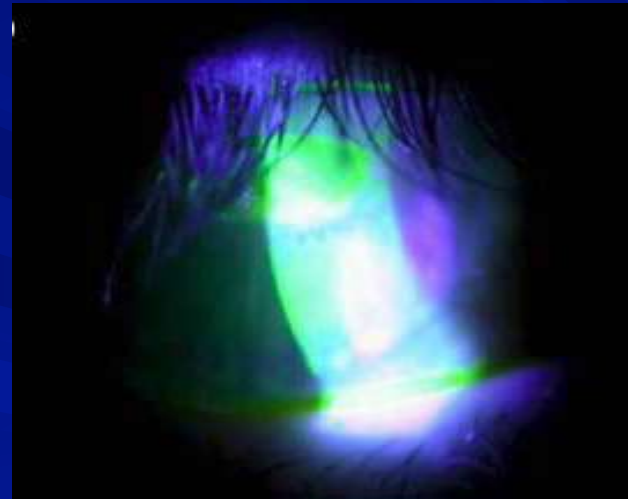
Restrictive Myopathy



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

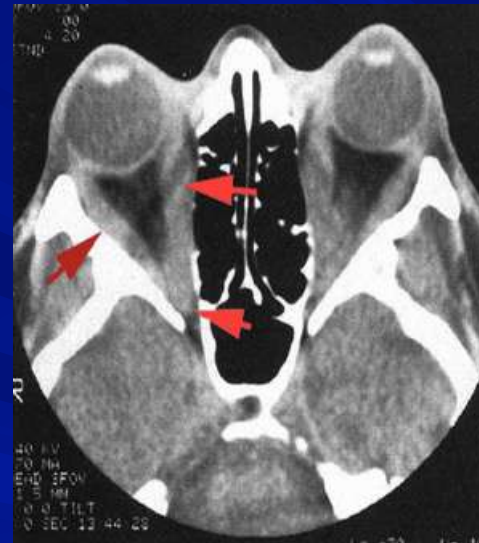
Corneal Exposure

- ⌘ 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

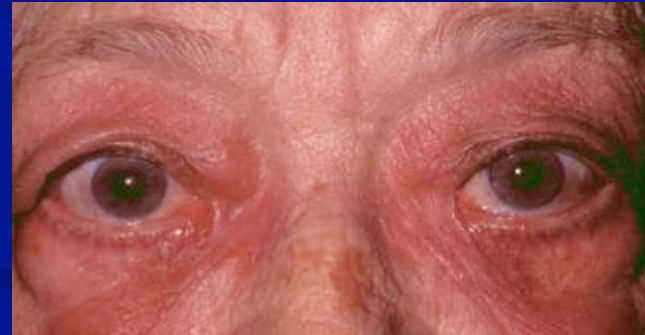
👁️ Oral steroids

- ★ 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



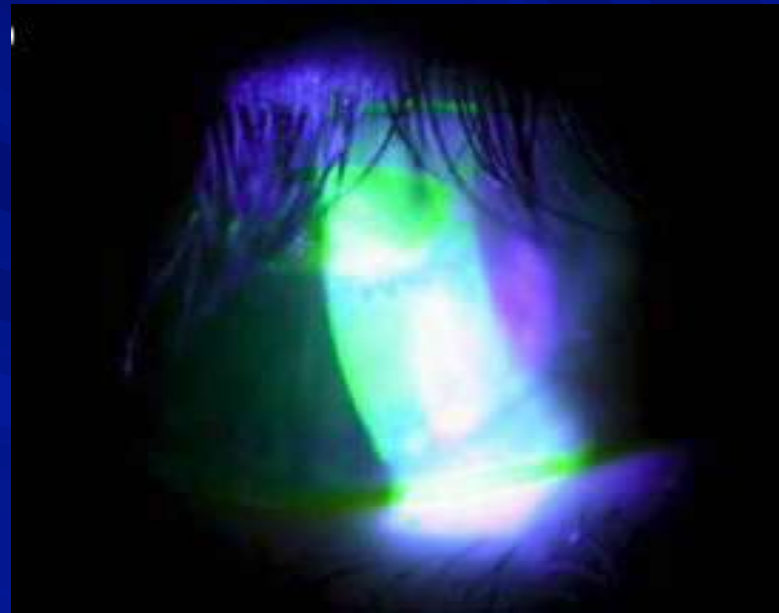
Corneal Exposure

🔗 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

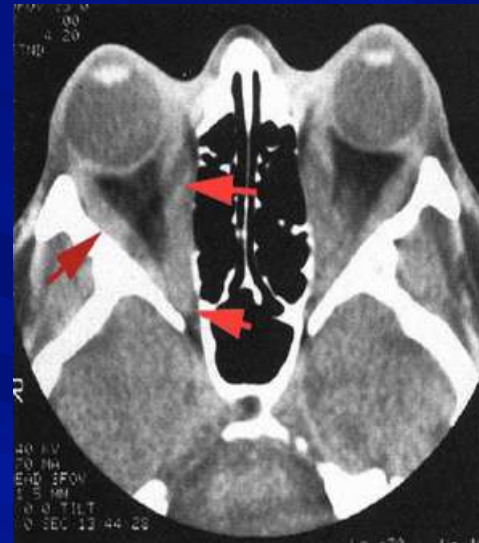
Systemic Steroids

- ★ 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

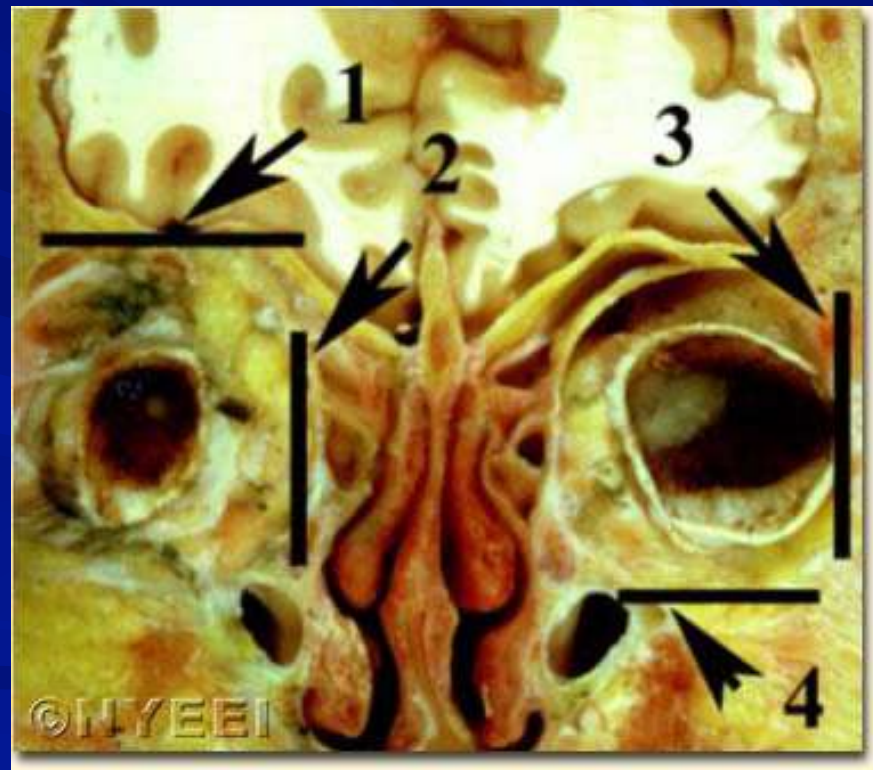
Orbital decompression



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

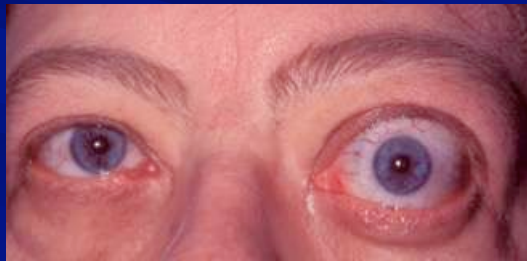
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👁️ I would have higher suspicion when you see

- ★ Periorbital edema
- ★ Exophthalmos, proptosis
- ★ Restrictive myopathy

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

IOP in Thyroid Eye Disease



Laboratory Testing

☞ Thyroid Hormone Levels

- ★ Serum TSH concentration
- ★ Serum total T4 (Thyroxine)
- ★ Serum total T3 (Triiodothyronine)
- ★ 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
5	Chemosis
6	Inflammatory eyelid swelling
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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



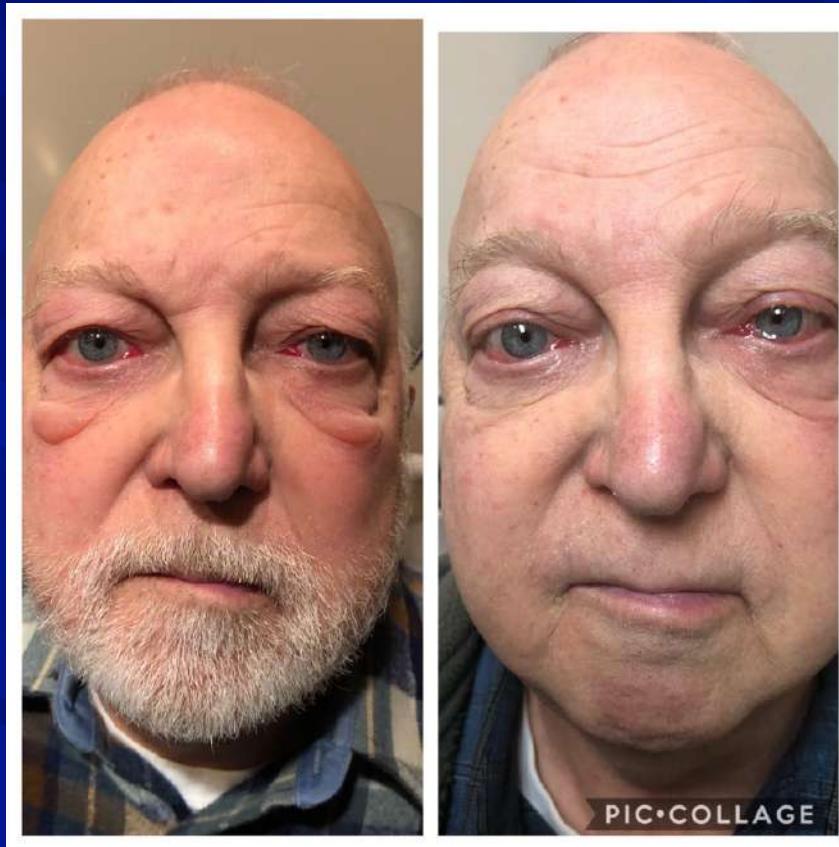
March 1, 2019 (4 days later)
Oral and Topical Steroids



March 25, 2019



March 25, 2019



April 22, 2019





April 22, 2019



Healio > Optometry > Primary Care Optometry

MEETING NEWS



Thyroid eye disease therapy shows promise

Primary Care Optometry News, December 2018



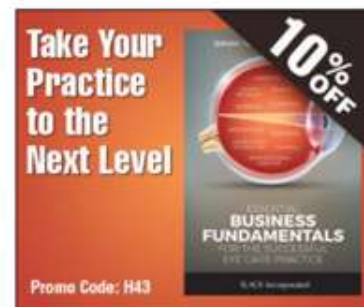
COMMENT



+ ADD TOPIC TO EMAIL ALERTS

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.





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.

beyond their
clinical needs



CLICK TO EXPAND



Healio  **Jobs.com**

Pediatric Ophthalmologist
Dallas, TX
UT Southwestern Medical-Ophthalmology

Communications & Marketing Manager
Baltimore, MD
Johns Hopkins University

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

- ★ IGF-1 (Insulin like growth factor 1) and TSH receptors are over expressed

🔗 IGF-1 receptor inhibitor monoclonal antibody

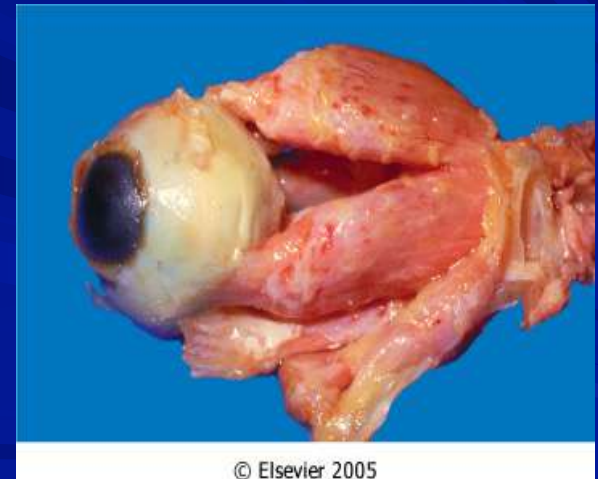
- ★ On the orbital fibroblasts
 - 📋 Inhibiting downstream inflammatory cascade
 - Cytokines, hyaluran, leukotriene
 - Differentiation into adipocytes and myofibroblasts

🔗 Phase 2 and published in New England Journal of Medicine

🔗 Phase 3 completed

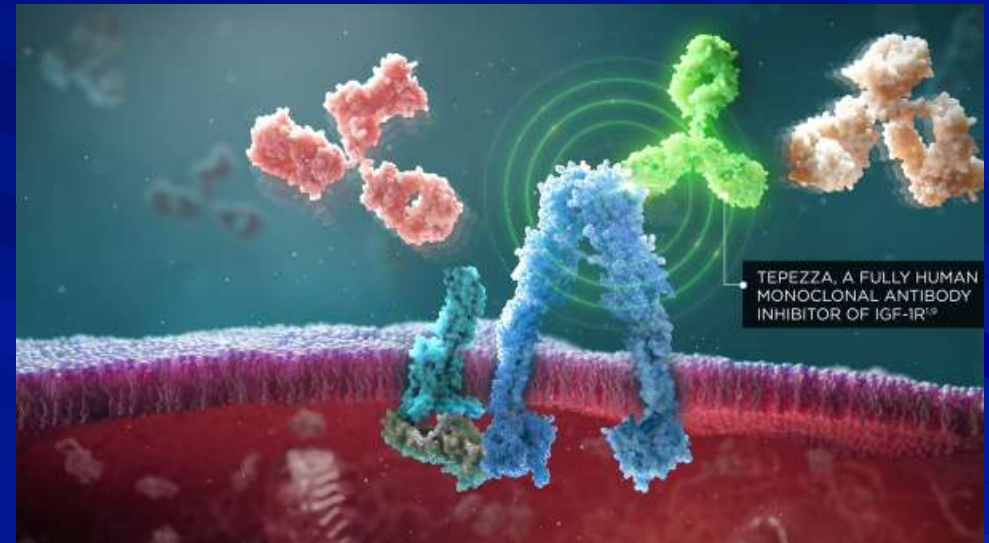
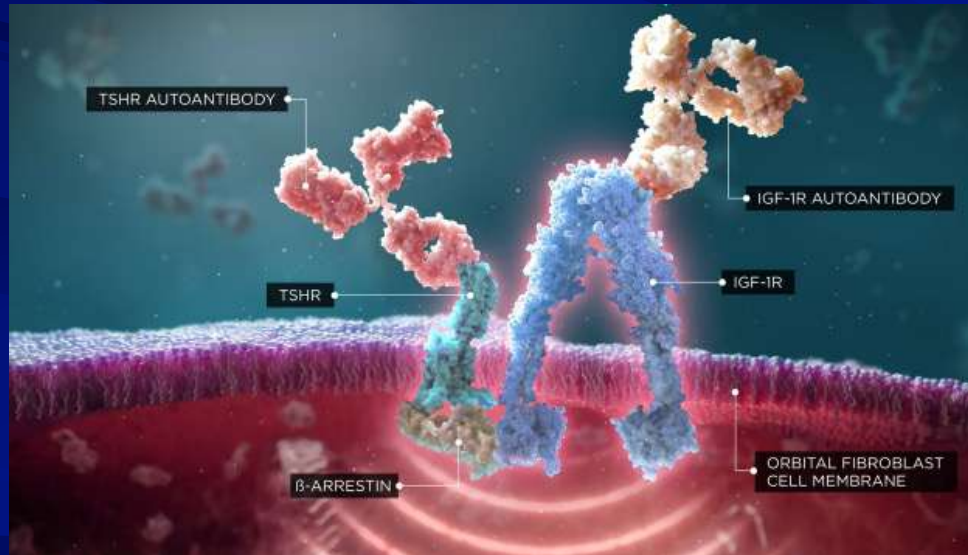
- ★ Published - New England Journal of Medicine

🔗 PDUFA- March 2020, was approved early in 2020





Teprotumumab-trbw (Tepezza)



Immunosuppression?

🔗 Biologics

★ Immunosuppression biologics – suppress the immune system to get the effect

- 📋 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

★ Immunomodulatory

- 📋 Tepezza
 - IGF-1R inhibitor
 - Full humanized monoclonal antibody
 - All the proteins are human – less to no sensitivity – more focused effect
 - Orbital 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 $\geq 5\%$ 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

Key Tenants of Aging, Performance and Vitality



Oxidative Stress / Inflammation



Hormonal Balance



Stress Hormones



Glucose / Insulin Regulation



GUT integrity and microbiome diversity



Immune Balance



Environmental Exposure/Burden

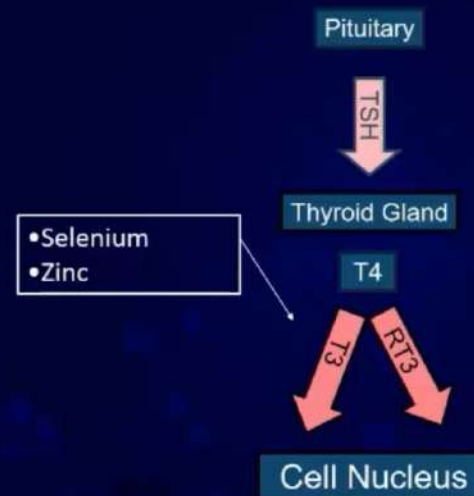


Individuality

Credit to: James LaValle, RPh, CCN



Thyroid Function: Factors increasing conversion of T4 to T3

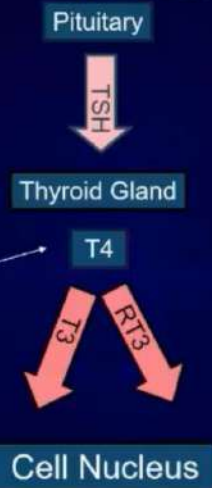


Credit to: Filomena Trindade, MD



What Effects Thyroid Function: Production of Thyroid Hormones

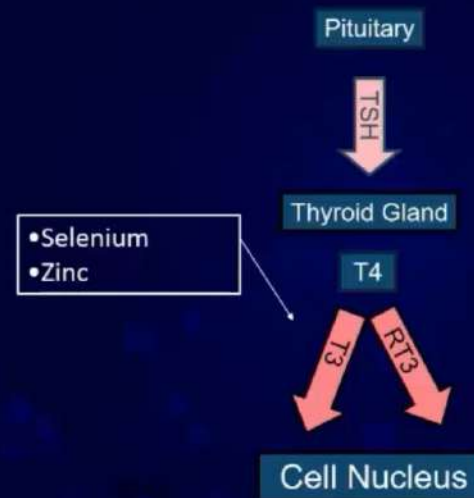
- Nutrients:
Iron, iodine,
tyrosine, zinc,
selenium
vitamin E, B2,
B3, B6, C, D



Credit to: Filomena Trindade, MD



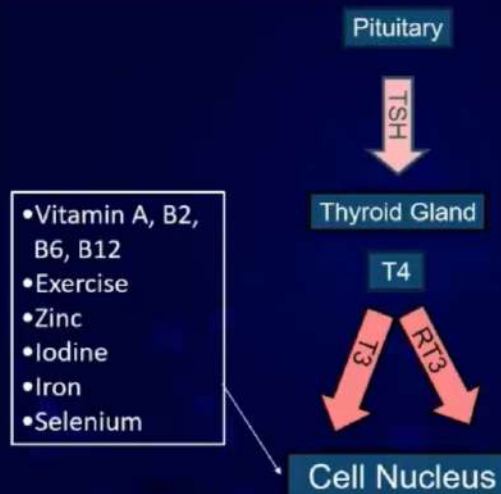
Thyroid Function: Factors increasing conversion of T4 to T3



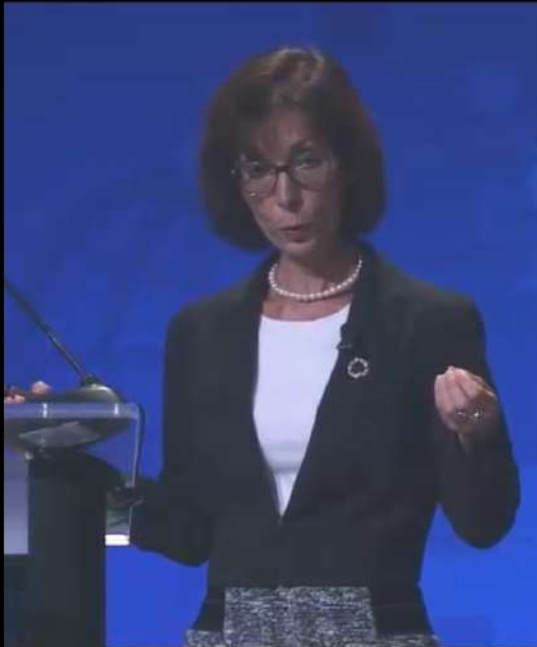
Credit to: Filomena Trindade, MD



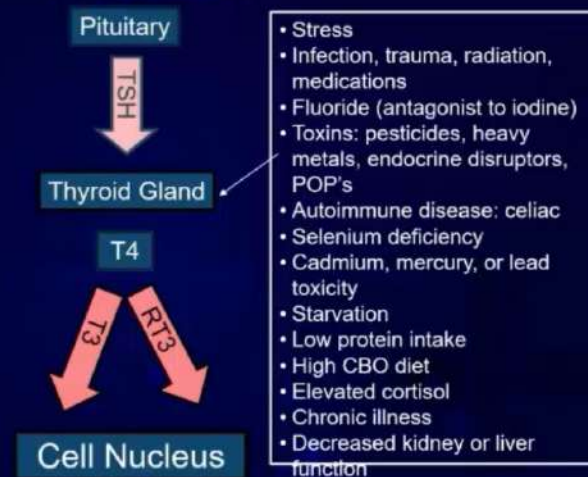
Thyroid Hormones: Factors Improving cellular sensitivity to thyroid hormones



Credit to: Filomena Trindade, MD



Thyroid Function: Inhibitors of Thyroid Hormone Production:

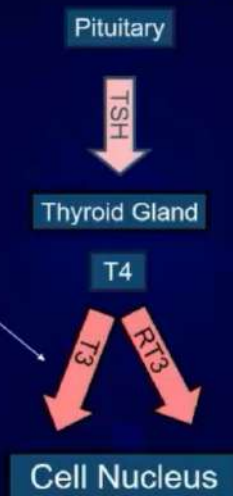


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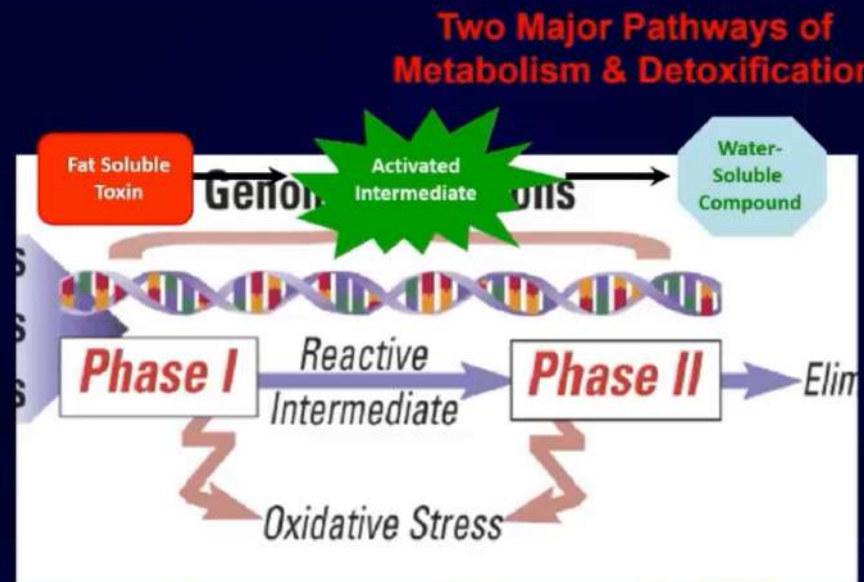


Thyroid Function: Factors Decreasing conversion of T4 to T3

Stress
Trauma
Low-calorie diet
Inflammation
(cytokines, etc.)
Toxins
Infections
Liver/kidney
dysfunction
Rx medications



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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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Abstract

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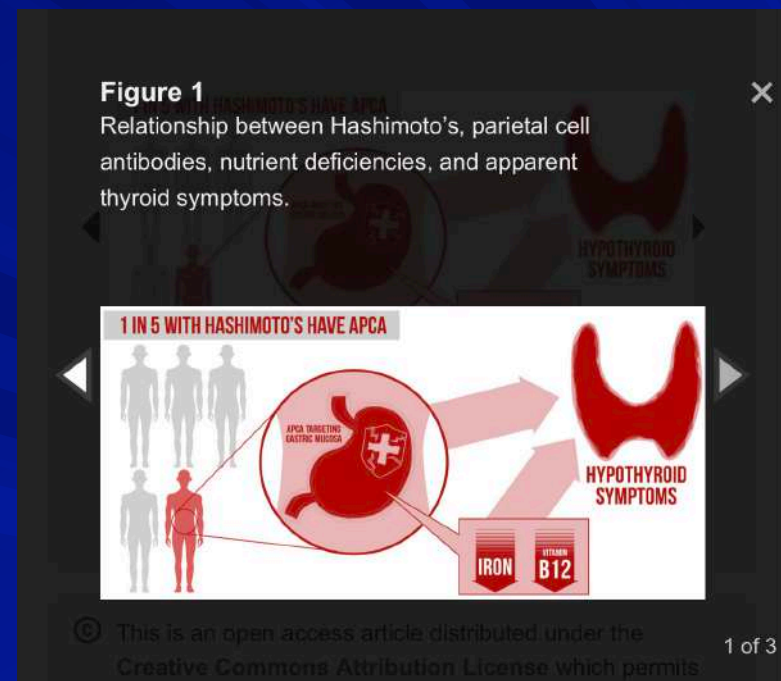
Abstract

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



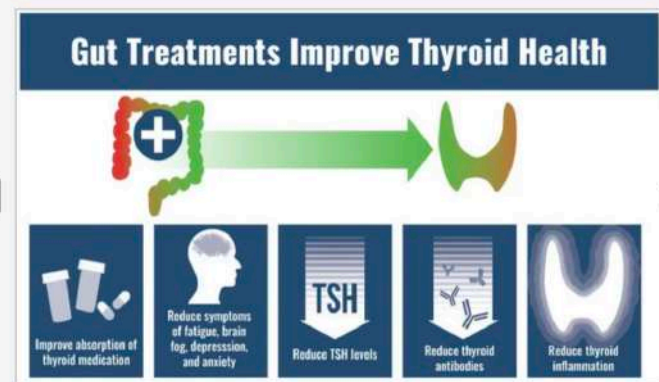
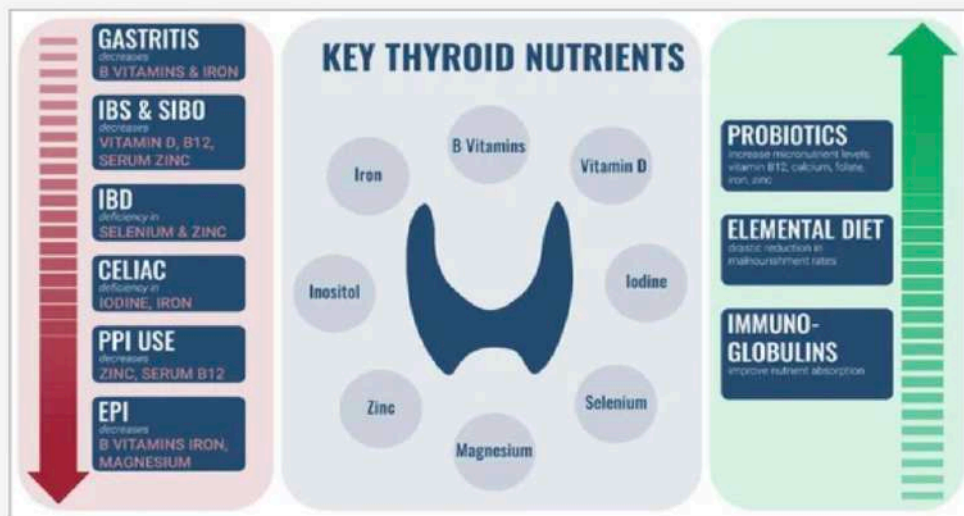


Figure 3

Skin Carotenoid Levels

Oxidative Stress/Inflammation/Anti-Oxidant Deficient



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 <i>Blakeslea trispora</i> , 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%

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 <i>Camellia sinensis</i> 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 <i>Polygonum cuspidatum</i> root extract)	(2.5 mg)	*
Mixed Tocopherols (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, Croscarmellose 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	100 mg	**
(including hesperidin and naringin)		
Purple corn (<i>Zea mays</i> L.) cob extract	66.67 mg	**
including anthocyanins		
Alpha Lipoic Acid	50 mg	**
Quercetin (from <i>Dimorphandra mollis</i> fruit extract)	37.5 mg	**
D-Limonene (from <i>Citrus sinensis</i> peel)	25 mg	**
Rosemary (<i>Rosmarinus officinalis</i> L.) leaf extract	18.75 mg	**
including carnosic acid		
Resveratrol (from <i>Polygonum cuspidatum</i> root)	15 mg	**
Coenzyme Q10	15 mg	**
Lycopene	2.5 mg	**
Lutein (from marigold flower (<i>Tagetes erecta</i>))	2 mg	**
Astaxanthin (from <i>Haematococcus pluvialis</i> 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).

Key Tenants of Aging, Performance and Vitality



Oxidative Stress / Inflammation



Hormonal Balance



Stress Hormones



Glucose / Insulin Regulation



GUT integrity and microbiome diversity



Immune Balance



Environmental Exposure/Burden



Individuality

Credit to: James LaValle, RPh, CCN

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 and Thyroid Eye Disease Clinical Pearls and Innovations for 2023

Greg Caldwell, OD, FAAO
Pittsburgh Primary Eye Care Conference
Saturday, February 18, 2023

