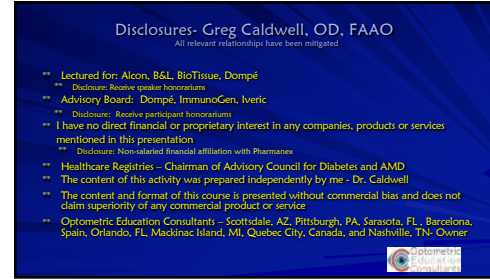


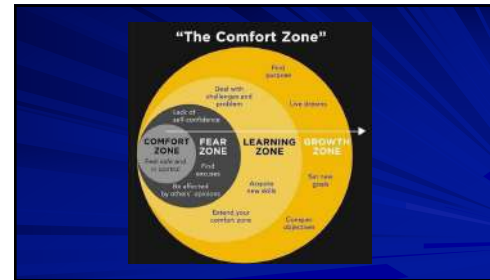
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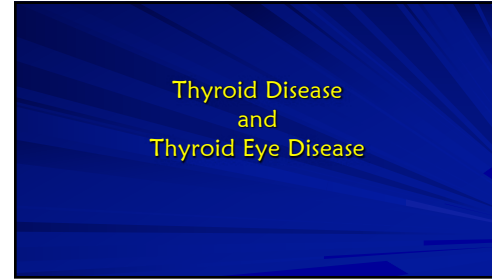
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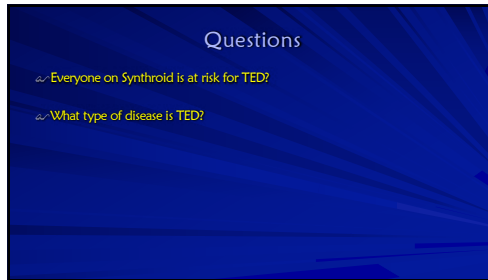
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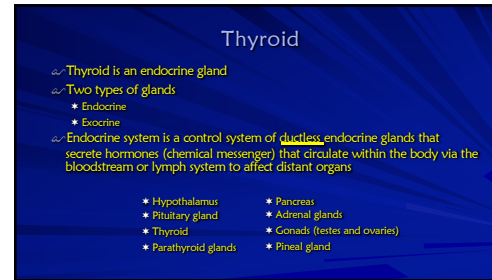
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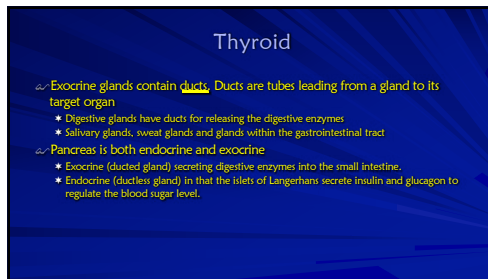
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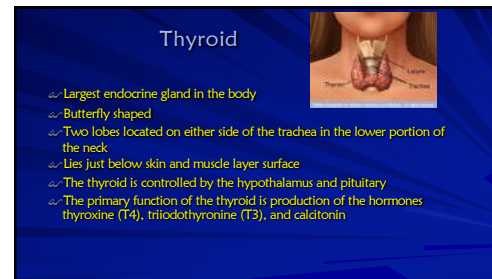
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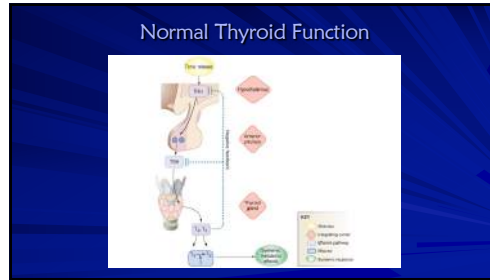
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15



16

### Thyroid Dysfunction

~ What is the most common cause of thyroid dysfunction?

- Cancer
- Surgically induced
- Medication toxicity or side effect
- Pregnancy
- Autoimmune disease

~ In autoimmune disease the body typically produces \_\_\_\_\_ that attacks itself, this can be systemic or organ specific

- Antibodies, immunoglobulins

17

### Why Autoimmune Disease is on the Rise?

18

### Why Autoimmune Disease is on the Rise?

"Hundreds of autoimmune cases began to be observed at the age of 10 in the 1980s." - Jon Hall for "Chronic" - "However, we are now seeing some strange occurrences that never had such close before."

"The example, the biggest recent increase in autoimmune disease cases has been in a Middle East and Asia, before that they had mostly seen the disease."

"Autoimmune disease range from type 2 diabetes, rheumatoid arthritis, autoimmune thyroid disease and multiple sclerosis. In each case, the immune system goes to the wrong and attacks healthy tissue instead of infecting agents."

"These food dyes lack safety in people with sensitivities, such as those, and evidence suggests the alteration affects a person's microbiome - the collection of microorganisms that we have in our gut and which play a key role in controlling our body functions." - Science said.

"These changes in our environment with the ongoing autoimmune diseases, of which more than 200 types have now been discovered."

Such as insulin resistance that is related to obesity. Diabetes were treated by controlling such diseases, whereas that also included other, chronic as well as acute, which happens to be more an acute condition, and can cause damage to various organs, including the heart."

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### Thyroid Dysfunction

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

20

### Antibodies of Thyroid Dysfunction

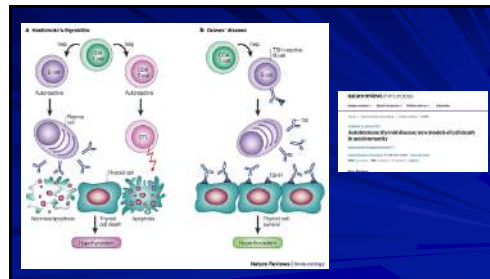
- ↳ **TSH Receptor Antibodies**
  - Stimulating TSH receptor antibody
    - Thyroid Stimulating Immunoglobulin (TSI)
  - Thyroid blocking antibody (TBAb)
- ↳ **Thyroid Peroxidase Antibodies (TPOAb)**
  - TPO is found in thyroid follicle cells where it converts the thyroid hormone T4 to T3
  - TPOAb contributes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

21

Ninja Nerd Science  
 YouTube

22



23



24

25

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

Melanie Clemmons, OD  
 May 20, 2022 AACO Nashville

26

### Hyperthyroid

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

27

### Hypothyroid

- ⌚ TBAB attacks the thyroid
- ⌚ T3 and T4 decrease
- ⌚ TSH increases

28

### Thyroid Dysfunction

<p><b>Hyperthyroidism</b> (Thyrotoxicosis)</p> <ul style="list-style-type: none"> <li>⌚ <b>Primary-autoimmune</b> <ul style="list-style-type: none"> <li>• Graves</li> <li>◻ Graves-Basedow or von Basedow's</li> </ul> </li> <li>⌚ <b>Secondary/Tertiary</b> <ul style="list-style-type: none"> <li>• Excess thyroid medication for treatment of hypo or goiter</li> <li>• Toxic multinodular goiter</li> <li>• Toxic adenoma</li> <li>• Excess iodine</li> <li>• Thyroiditis (inflammatory induced)</li> <li>• Excess hormone production ectopic sites</li> <li>• Thyroid carcinoma</li> </ul> </li> </ul>	<p><b>Hypothyroidism</b> (most common organ-specific autoimmune disorder)</p> <ul style="list-style-type: none"> <li>⌚ <b>Primary-autoimmune</b> <ul style="list-style-type: none"> <li>• Chronic autoimmune thyroiditis</li> <li>◻ Hashimoto's thyroiditis</li> <li>• Autoimmune atrophic thyroiditis</li> </ul> </li> <li>◻ <b>Primary myxedema</b> <ul style="list-style-type: none"> <li>◻ Opposite of Graves disease</li> </ul> </li> <li>• <b>Postpartum thyroiditis</b></li> <li>⌚ <b>Secondary/Tertiary</b> <ul style="list-style-type: none"> <li>• Lithium medication</li> <li>• Pregnancy</li> <li>• Surgically induced</li> <li>• Disorders of the pituitary gland or hypothalamus</li> </ul> </li> </ul>
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29

### 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 immunoglobulin (TSI)

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### Hashimoto's Thyroiditis (Hypothyroidism)

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

31

### Autoimmune atrophic thyroiditis (Hypothyroidism)

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

32

### Postpartum Thyroiditis (Hypothyroidism)

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

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

<p><b>Symptoms</b></p> <ul style="list-style-type: none"> <li>Nervousness</li> <li>Heat intolerance</li> <li>Sweating</li> <li>Fatigue</li> <li>Palpitation</li> <li>Insomnia</li> <li>Early waking</li> <li>Alopecia</li> <li>Vitiligo</li> <li>Brittle nails</li> </ul>	<p><b>Signs</b></p> <ul style="list-style-type: none"> <li>Sweating</li> <li>Muscle Weakness</li> <li>Emotionally labile</li> <li>Tremor</li> <li>Tachycardia</li> <li>Arrhythmia</li> <li>Hypertension</li> <li>Brisk tendon reflex</li> <li>Diabetes</li> <li>T<sub>3</sub>Toxicosis &amp; Ca<sup>2+</sup> CHO</li> <li>Microcytic anemia</li> <li>Possible goiter</li> <li>Myxedema</li> </ul>
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### Systemic Manifestations of Hypothyroid (Primary or Secondary)

<p><b>Symptoms</b></p> <ul style="list-style-type: none"> <li>Cold intolerance</li> <li>Weakness</li> <li>Reduced energy</li> <li>Lethargy</li> <li>Muscle cramps</li> <li>Constipation</li> <li>Increased sleeping</li> <li>Weight gain</li> <li>Reduced appetite</li> <li>Joint stiffness</li> </ul>	<p><b>Signs</b></p> <ul style="list-style-type: none"> <li>Cool, scaling skin</li> <li>Puffy hands and face</li> <li>Deep voice</li> <li>Myotonia</li> <li>Delirium</li> <li>Bradycardia</li> <li>Slow reflexes</li> <li>Obesity</li> <li>Hypothermia</li> <li>Myxedema</li> </ul>
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35

### Thyroid Eye Disease (TED)

**Other names used**

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

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### Why is this so confusing?

**Thyroid Eye Disease**

- Is often seen in conjunction with Graves' Disease (hyperthyroid)
- Is seen in people with no other evidence of thyroid dysfunction
- Is seen in patients who have Hashimoto's Disease (Hypothyroid)

Most thyroid patients, however, will not develop thyroid eye disease

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### Why is this so confusing?

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

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### Why is this so confusing?

- While eye disease may be brought on by thyroid dysfunction
  - Successful treatment of the thyroid gland does not guarantee that the eye disease will improve
  - No particular thyroid treatment can guarantee that the eyes will not continue to deteriorate
  - Once inflamed, the eye disease may remain active from several months to as long as three years
  - There may be a gradual or, in some cases, a complete improvement

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### Thyroid Eye Disease

- Commonly known as Graves' ophthalmopathy
- About 80% of all patients with TED have the autoimmune hyperthyroid disorder known as Graves' disease
- Another 10% of all cases are seen in patients with autoimmune hypothyroidism, either Hashimoto's thyroiditis, atrophic thyroiditis or Hashitoxicosis
- Another 10% of all cases are seen in people with normal thyroid function
  - When thyroid function is normal, the eye condition is referred to as euthyroid Graves' disease
  - Euthyroid is a term meaning that thyroid function tests are normal. Most people with euthyroid Graves' disease develop a thyroid disorder within eighteen months of the emergence of the eye disorder
  - But some people with euthyroid Graves' disease never develop thyroid dysfunction

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### Thyroid Eye Disease

- What causes the Thyroid Eye Disease signs and symptoms?
- The high and low levels of T3 and T4
- The antibodies that are attacking the thyroid gland

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### Thyroid Eye Disease

- Thyroid Eye Disease has 2 phases
  - A phase secondary to abnormal thyroid hormone levels
    - Increased or decreased FT3 and FT4 levels
    - Once these levels are normalized, ocular symptoms will resolve
  - Congestive Autoimmune form of Thyroid Eye Disease
    - Active phase-stimulating or blocking TRAb are causing ocular activity
    - Plateau phase-reduced activity
    - Resolution phase-symptoms regress and eyes return to normal

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### Phase secondary to abnormal thyroid hormone levels (T<sub>3</sub>/T<sub>4</sub>) (Thyroid Eye Disease)

<ul style="list-style-type: none"><li><b>Hyperthyroidism eye symptoms</b><ul style="list-style-type: none"><li>Excess hormone acting on the nerves that supply the eye</li><li>Usually spastic and include staring</li><li>Dryness</li><li>Eyelid retraction</li></ul></li></ul>	<ul style="list-style-type: none"><li><b>Hypothyroidism eye symptoms</b><ul style="list-style-type: none"><li>Deficient hormone causing venous congestion, impaired circulation and fluid reabsorption</li><li>Periorbital edema</li></ul></li></ul>
--	--

- 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
- Keeping on the TSH level can be misleading and in treating TED

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

- Caused by both stimulating and blocking TSH receptor antibodies (TRAb) and also immune system chemicals known as cytokines
- Secondary targets appear to be TSH receptor antigens (epitopes) located on orbital fibroblasts as well as dermal fibroblasts
- Active "inflammatory" phase of TED varies
  - Symptoms resolve quickly although on average the active phase lasts about 12-18 months
  - TRAb levels are high, patients are smokers, nutrient deficiencies are present, or the patient continues to be exposed to environmental triggers such as excess dietary iodine, the active phase can last as long as 5 years
  - Avoid any lid, muscle or orbital surgery
- Plateau phase and Resolution "Passive" phase
  - An individual may be left with structural changes, such as eye protrusion, eyelid retraction, and in some cases, double vision
  - There are corrective procedures that can be performed to address these problems

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### Euthyroid Graves' disease

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

45

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

46

You're in the Know

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

It does work!

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### General Ocular Symptoms

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

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### NOSPECS: Grading System

~ 1969 by S.C. Werner

- Class 0: No signs or symptoms
- Class 1: Only signs, upper lid retraction
- Class 2: Soft Tissue Involvement with symptoms
- Class 3: Proptosis
- Class 4: BOM involvement
- Class 5: Corneal involvement
- Class 6: Sight Loss

~ Class 2 & 6 document severity

- 0: absent
- A: minimal
- B: moderate
- C: marked

~ Within classes 2 to 6 the investigator has to differentiate the severity grades 0, A, B, C

~ NOSPECS, classifies severity but not the activity or stage (active/inflammatory or passive/congestive)

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### NOSPECS: Grading System

- ~ 0: No symptoms or signs
- ~ 1: Only signs (upper lid retraction without lid lag or proptosis)
- ~ 2: Soft tissue involvement with symptoms (excess) lacrimation, sandy sensation, retrobulbar discomfort
  - Grade 0: absent
  - Grade A: minimal (edema of lids, injection, sandy feeling)
  - Grade B: moderate (edema of lids, injection, chemosis, FBSS, 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 mm between eyes, or if progression of mm under observation

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### NOSPECS: Grading System

- 4: EOM involvement (usually with diplopia)
  - 0: absent
  - A: minimal (limitation of motion, patient reports diplopia but no obvious restriction)
  - B: moderate (evident restriction of motion)
  - C: marked (position of globe is fixed)
- 5: Corneal involvement (due to proptosis, incomplete closure, lagophthalmos)
  - 0: absent
  - a: minimal (staining)
  - b: moderate (ulceration)
  - c: marked (clouding, necrosis, perforation)
- 6: Sight loss (due to optic nerve involvement)
  - 0: absent
  - A: minimal (disc pallor or edema, or VF defect, vision 20/20-20/60)
  - B: moderate (same as A but VA 20/70-20/200)
  - C: marked (blindness, VA < 20/200)

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### LEMO Classification

- 1991-Boergen and Pickardt
- Complements NOSPECS
- 4 finding-categories
  - Lid
  - Exophthalmos
  - Muscular
  - Optic nerve
- Grade between 0 and 4 depending on severity
- LEMO, classifies severity but not the activity or stage (active/inflammatory or passive/congestive)

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### LEMO Classification

<p><b>Lid (L)</b></p> <ul style="list-style-type: none"> <li>0: missing</li> <li>1: lid edema only</li> <li>2: retraction (impaired lid closing)</li> <li>3: retraction and upper lid edema</li> <li>4: retraction and global lid edema</li> </ul>	<p><b>Exophthalmos (E)</b></p> <ul style="list-style-type: none"> <li>0: missing</li> <li>1: eyes closing not impaired</li> <li>2: conjunctival injection in the morning</li> <li>3: persistent conjunctival injection</li> <li>4: corneal complications</li> </ul>
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### LEMO Classification


<p><b>Muscular (M)</b></p> <ul style="list-style-type: none"> <li>0: missing</li> <li>1: detectable in imaging only</li> <li>2: Pseudoparesis</li> <li>3: Pseudoparalysis</li> </ul>	<p><b>Optic Nerve (O)</b></p> <ul style="list-style-type: none"> <li>0: missing</li> <li>1: regarding color vision only or detected via VEP</li> <li>2: peripheral scotoma</li> <li>3: central scotoma</li> </ul>
--	---

**LEMO200**  
 Endocrine ophthalmopathy with lid edema, exophthalmos, pseudoparesis of external eye muscles, and no optic nerve involvement

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### 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



55

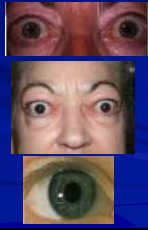
### Lid Involvement

- Lid Retraction
- Lid Lag
- Lagophthalmos

56

### Lid Retraction

- ~ Sclera show in primary gaze
- ~ Most commonly seen complication
  - 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
    - 12 mm above the limbus
  - Lower lid coincident or 1-2mm below the limbus



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### Eyelid Lag: von Graefe's Sign

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



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### Lagophthalmos

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

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### Soft Tissue Involvement

- ~ Conjunctiva
- ~ Chemosis
- ~ Periorbital edema

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### Conjunctiva

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



61

### "If it is Red think TED"


Dr. Andy Morgenstern 12.7.2013, OMS Contemporary Resort



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### Periorbital Edema

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



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### Infiltrative Orbitopathy (Exophthalmos/Proptosis)

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

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### Infiltrative Orbitopathy (Exophthalmos/Proptosis)



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### Infiltrative Orbitopathy (Exophthalmos/Proptosis)



66



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### Exophthalmometry


- ~ Is race dependent? (Asian vs Black men is statistically significant)
- ~ Hertel or Ludde results
- ~ Adults
  - \* Average reading 17 mm
  - \* 95% of population have readings between 13-21mm
- ~ General concerns
  - \* A difference of 2 mm or more between the eyes
  - \* A measurement of more than 24 mm

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

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### Restrictive Myopathy

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




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### IOP in Thyroid Eye Disease

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

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### Restrictive Myopathy

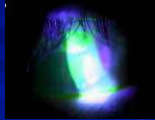


Obvious restrictive myopathy but also note the periorbital edema, and conjunctival hyperemia

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### Corneal Exposure

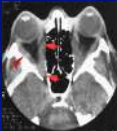

- Exposure keratopathy secondary to exophthalmos and lagophthalmos
- Significant threat to visual function



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### Optic Neuropathy

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

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### Treatment of Thyroid Eye Disease

- Depends on what phase of the disease we are in:
  - Phase secondary to abnormal thyroid hormone levels
  - Active "Inflammatory" phase
  - Plateau phase and Resolution "Passive" phase
- Depends on what orbital tissue or structures are involved
- Depends on the risk of vision loss
- Depends if primary, secondary or tertiary thyroid dysfunction
- Management consists of:
  - Control of inflammation
  - Prevention of ocular and visual damage
  - Addressing ocular motor abnormalities
  - Improving cosmetic disfigurement
- Patient education is essential
- Communication with an endocrinologist or internist will ensure proper patient care

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### Treatment of Thyroid Eye Disease

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



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

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### Treatment of Thyroid Eye Disease

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

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### Lid Retraction, Eyelid Lag, Lagophthalmos

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



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### Lid Retractor Surgery



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### Conjunctiva, Periorbital edema


- ~ Topical lubricants
  - Artificial tears
  - Ointments at night
  - Topical steroids
  - Restasis
- ~ Tape eyelids closed at night or use mask
- ~ Blevate head at night to decrease lid edema
- ~ Oral diuretic: Acetazolamide
- ~ Oral steroids
  - 60 mg/day for 3 months
- ~ IV steroids
- ~ Periocular steroids
  - Kenalog last 1 month



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### Infiltrative Orbitopathy (Exophthalmos/Proptosis)


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



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### Restrictive Myopathy

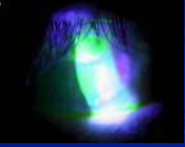
- Non-surgical (while waiting for stability)
  - Teach proper head position to alleviate diplopia
  - Prism in spectacle correction (Fresnel or ground in)
  - Oral steroids
  - Botulinum toxin injection
- Surgical Consult
  - Recession of the rectus muscle(s) involved
  - Diplopia in primary gaze, reading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



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### Corneal Exposure

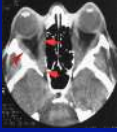

- Manage the corneal defect as first line
  - Lubricating and antibiotic
  - Lid taping
  - Moisture barrier
- Orbital Disease Consult
  - High dose oral steroids
    - 120-140mg/day x 7 days
  - Orbital decompression



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### Optic Neuropathy

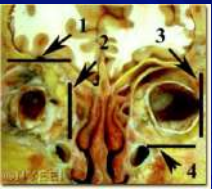
- Systemic Steroids
  - If rapidly progressive and painful in the early stage of the disease
  - Only if no contraindications
  - Prednisolone 80-100mg, expect results within 48hrs. Taper dose and d/c within 3 mo
- IV Methylprednisolone
- Radiotherapy: if contraindication to steroid
- Orbital decompression

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### Orbital Decompression

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



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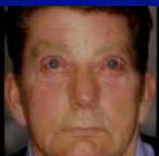
### Orbital Decompression (Surgical/Cosmetic)



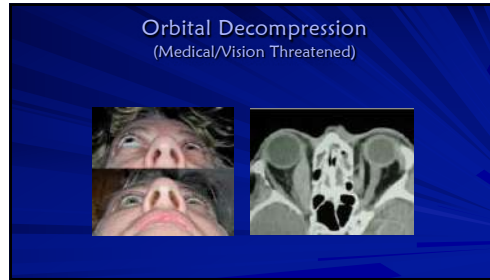
85

### Thyroid Eye Disease and Depression

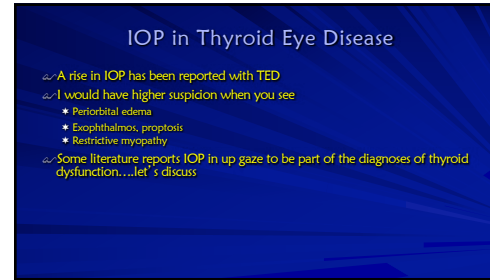
- When facial disfigurement occurs, thyroid eye disease is equivalent to the diagnosis of cancer and AIDS



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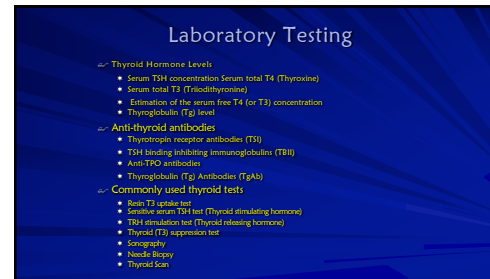
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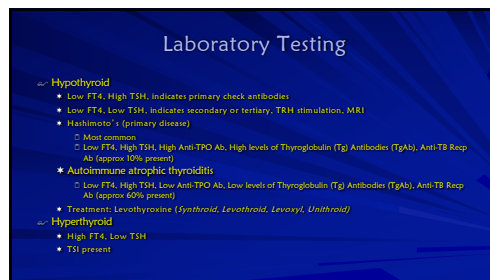
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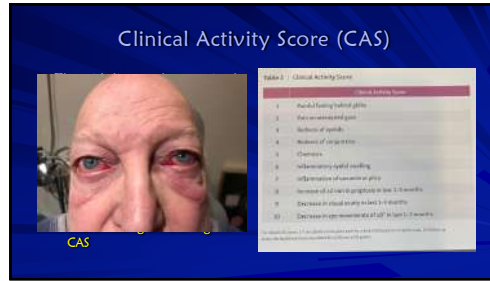


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Clinical Activity Score (CAS)



Clinical Activity Score	
1	Mild to moderate eyelid edema
2	Mild to moderate conjunctival injection
3	Mild to moderate chemosis
4	Mild to moderate eyelid erythema
5	Chemosis
6	Mild to moderate eyelid swelling
7	Mild to moderate eyelid erythema
8	Mild to moderate eyelid edema
9	Mild to moderate eyelid erythema
10	Mild to moderate eyelid edema
11	Mild to moderate eyelid erythema
12	Mild to moderate eyelid edema
13	Mild to moderate eyelid erythema
14	Mild to moderate eyelid edema
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45	Mild to moderate eyelid erythema
46	Mild to moderate eyelid edema
47	Mild to moderate eyelid erythema
48	Mild to moderate eyelid edema
49	Mild to moderate eyelid erythema
50	Mild to moderate eyelid edema

CAS

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February 25, 2019  
 "Nothing Else Can Be Done"



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February 25, 2019  
 "Nothing Else Can Be Done"



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



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



97

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

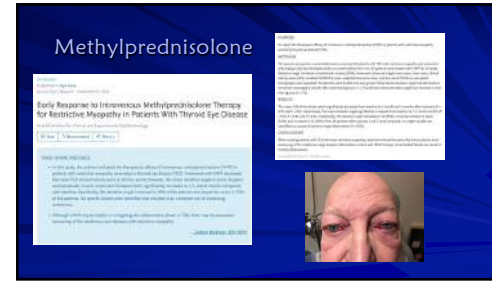


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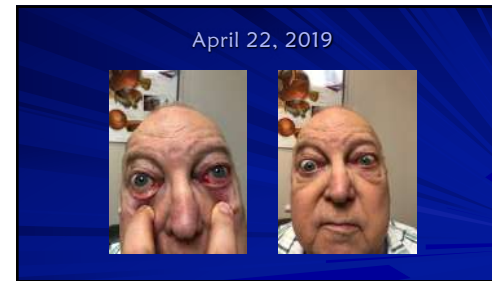
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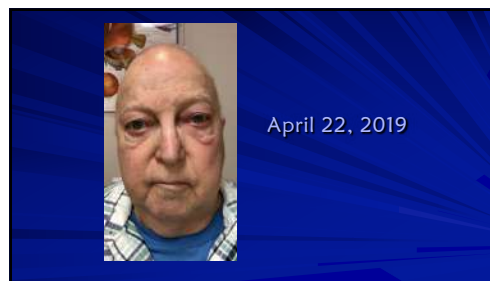
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### Teprotumumab-trbw (Tepezza)

- Horizon Therapeutics – HQ Dublin, Ireland and US based Chicago
- Biologic pharmaceutical
  - Chimeric Molecule
  - Infusion, 8 total, every 3 weeks
- Thyroid eye disease
  - IGF1 (Insulin like growth factor 1) and TSH receptors are over expressed
  - IGF1 receptor inhibitor monoclonal antibody
    - On the orbital fibroblasts
      - Inhibiting downstream inflammatory cascade
        - Chemokine production
        - 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




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### Teprotumumab-trbw (Tepezza)

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### Immunosuppression?

- Biologics
  - Immunosuppression biologics – suppress the immune system to get the effect
    - Remicade – “1<sup>st</sup> 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
        - Orbit fibroblasts to myofibroblasts or adipocytes
        - Hyaluronic acid, glycosaminoglycan



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### Teprotumumab-trbw (Tepezza)

- Optics and Optic-X Studies
  - 8 infusions, every 3 weeks, 24 weeks
  - Optics – acute, less than 9 months of disease
  - Optic-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

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### 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
    - 63% had 2 mm or better, 10% with placebo
    - Average was 3.2 mm at week 24
- Diplopia
  - Scale of 0, 1, 2, or 3
    - 66% improved 1 point, 29% with placebo
- Grave’s Ophthalmopathy -Quality of Life Score
  - Scale 0-100
    - 17.20 point improved, 1.80 with placebo

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### 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.

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### 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

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### Teprotumumab-trbw (Tepezza)

~ **Infusion center**

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


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### Biologics Used Off Label for TED

Drug Name	Indication	Off-label Use	Notes
Humira	100 mg	Induction of TED	Approved for rheumatoid arthritis, psoriasis, Crohn's disease, and ulcerative colitis.
Enbrel	50 mg	Induction of TED	Approved for rheumatoid arthritis, psoriasis, Crohn's disease, and ulcerative colitis.
Humira	100 mg	Maintenance of TED	Approved for rheumatoid arthritis, psoriasis, Crohn's disease, and ulcerative colitis.
Enbrel	50 mg	Maintenance of TED	Approved for rheumatoid arthritis, psoriasis, Crohn's disease, and ulcerative colitis.
Humira	100 mg	Prevention of TED	Approved for rheumatoid arthritis, psoriasis, Crohn's disease, and ulcerative colitis.
Enbrel	50 mg	Prevention of TED	Approved for rheumatoid arthritis, psoriasis, Crohn's disease, and ulcerative colitis.

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### Optometry's Opportunity



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### 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



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### 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



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### 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 performed



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### 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



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### New and All Natural



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### Functional Interventions

- Immune System Support
- Gut Microbiome Support

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### Key Tenants of Aging, Performance and Vitality

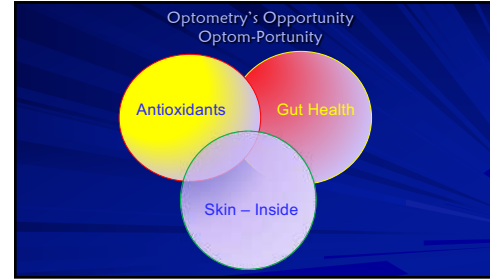
- Oxidative Stress / Inflammation
- Hormonal Balance
- Stress Hormones
- Glucose / Insulin Regulation
- GUT integrity and microbiome diversity
- Immune Balance
- Environmental Exposure/Burden
- Individuality

Credit to: James LaVella, BPh, DCN

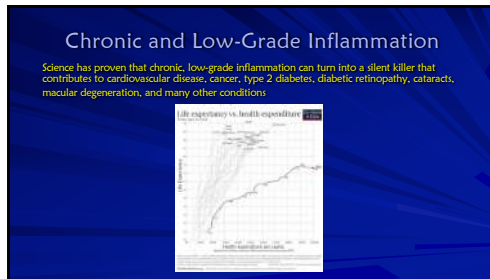
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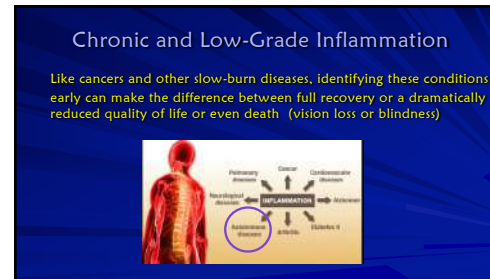
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Thyroid Function: Factors increasing conversion of T4 to T3

Factors:

- Vitamin A, B12
- Iron
- Zinc
- Selenium
- Iodine

Credit to: Filomena Trindade, MD

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Thyroid Hormones: Factors Improving cellular sensitivity to thyroid hormones

Factors:

- Vitamin A, B12
- Iron
- Zinc
- Selenium
- Iodine

Credit to: Filomena Trindade, MD

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Thyroid Function: Inhibitors of Thyroid Hormone Production:

Inhibitors:

- Stress
- Trauma
- Low-calorie diet
- Inflammation (gout, etc.)
- Sarcoid
- Malnutrition
- Medications

Credit to: Filomena Trindade, MD

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Thyroid Function: Factors Decreasing conversion of T4 to T3

Factors:

- Stress
- Trauma
- Low-calorie diet
- Inflammation (gout, etc.)
- Sarcoid
- Malnutrition
- Medications

Credit to: Filomena Trindade, MD

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Two Major Pathways of Metabolism & Oxidation

Phase I: Reactive Intermediate

Phase II: Reactive Intermediate

Oxidative Stress

Credit to: Filomena Trindade, MD

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Skin Carotenoid Levels

Oxidative Stress/Inflammation/Anti-Oxidant Deficient

NIH National Institutes of Health

Quick Test (approx. 30 sec)

Portable

Cost Effective

Remeasure in 60 days

Reassurance to you and patient

Credit to: Filomena Trindade, MD

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**Ingredients:**

Ingredient	Amount	Other
Ascorbic Acid (Vitamin C)	1000 mg	
Calcium	1000 mg	
Cholecalciferol (Vitamin D3)	2000 IU	
Cyanocobalamin (Vitamin B12)	1000 mcg	
Iron	100 mg	
Magnesium	100 mg	
Methylcobalamin (Vitamin B12)	1000 mcg	
Niacin (Vitamin B3)	1000 mg	
Panthenol (Vitamin B5)	100 mg	
Pyridoxine Hydrochloride (Vitamin B6)	100 mg	
Riboflavin (Vitamin B2)	100 mg	
Selenium	100 mcg	
Thiamine Mononitrate (Vitamin B1)	100 mg	
Zinc	100 mg	

**Supplement Facts**

Amount Per Serving	% Daily Value
Ascorbic Acid (Vitamin C)	200%
Calcium	20%
Cholecalciferol (Vitamin D3)	400%
Cyanocobalamin (Vitamin B12)	200%
Iron	20%
Magnesium	20%
Methylcobalamin (Vitamin B12)	200%
Niacin (Vitamin B3)	200%
Panthenol (Vitamin B5)	20%
Pyridoxine Hydrochloride (Vitamin B6)	20%
Riboflavin (Vitamin B2)	20%
Selenium	20%
Thiamine Mononitrate (Vitamin B1)	20%
Zinc	20%

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**SUPPLEMENT FACTS**

**Supplement Facts**

Amount Per Serving	% Daily Value
Ascorbic Acid (Vitamin C)	200%
Calcium	20%
Cholecalciferol (Vitamin D3)	400%
Cyanocobalamin (Vitamin B12)	200%
Iron	20%
Magnesium	20%
Methylcobalamin (Vitamin B12)	200%
Niacin (Vitamin B3)	200%
Panthenol (Vitamin B5)	20%
Pyridoxine Hydrochloride (Vitamin B6)	20%
Riboflavin (Vitamin B2)	20%
Selenium	20%
Thiamine Mononitrate (Vitamin B1)	20%
Zinc	20%

**OTHER INGREDIENTS:** Cellulose, Croscarmellose, Dicalcium Phosphate, Hydroxypropyl Methylcellulose, Polyethylene Glycol, Stearic Acid, Talc, Titanium Dioxide, Triethyl Citrate, Xanthan Gum.

**CONTAINS 14 (14) Tablets.**

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**The Relationship between Gut Microbiome Health, Microbiome Concentrations, and Autoimmunity & Folate in the Thyroid**

**Figure 1: Relationship between Gut Microbiome Health, Microbiome Concentrations, and Autoimmunity & Folate in the Thyroid**

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**What about Probiotics?**

**Probiotics** - Live bacteria that help to restore good bacteria numbers in your gut.

**Postbiotics** - The by-products of when probiotics eat bacteria.

**PREBIOTICS**

- Non-digestible food ingredients that feed the good bacteria in your gut.
- Helps to improve gut health.
- Helps to improve gut health.

**PROBIOTICS**

- Live bacteria that help to restore good bacteria numbers in your gut.
- Helps to improve gut health.
- Helps to improve gut health.

**POSTBIOTICS**

- By-products of when probiotics eat bacteria.
- Helps to improve gut health.
- Helps to improve gut health.

<https://doctorsforthyroid.com/what-are-probiotics/>

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### 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 lid
- ↳ Stellwag's sign: Infrequent blinking
- ↳ Kocher's sign: Increased lid retraction with visual fixation
- ↳ Enroth's sign: Puffy swelling of the lid
- ↳ Rosenbach's sign: Tremor of closed lid
- ↳ Mobius' sign: Weakness of convergence
- ↳ Baile's sign: Palsy of one or more extraocular muscles
- ↳ Saker's sign: Weakness of fixation on lateral gaze
- ↳ Cowen's sign: Jerky papillary contraction to consensual light
- ↳ Knies' sign: Unequal dilatation of the pupils
- ↳ Jeffrey's sign: Absence of forehead wrinkling on upward gaze

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Optometric  
Education  
Consultants

**Questions/Thank You!**

**Thyroid Eye Disease  
What Every Clinician Needs to Know in 2024**

Greg Caldwell, OD, FAAO  
Mid-Winter Getaway  
Optometric Education Consultants  
Saturday, January 27, 2024



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