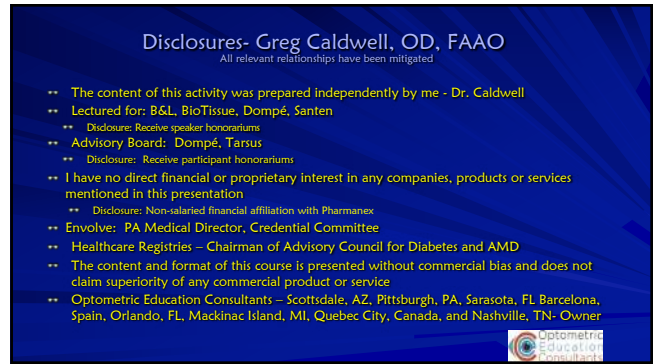




1



2



4



5



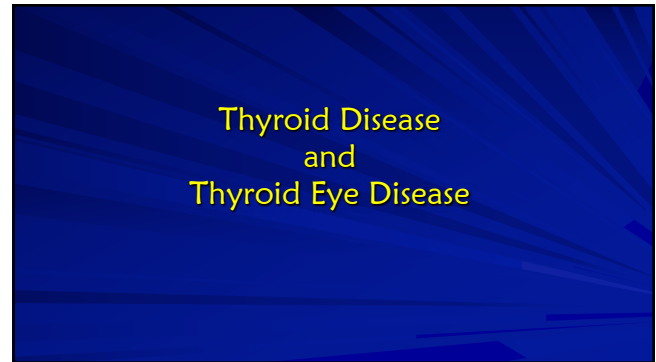
6



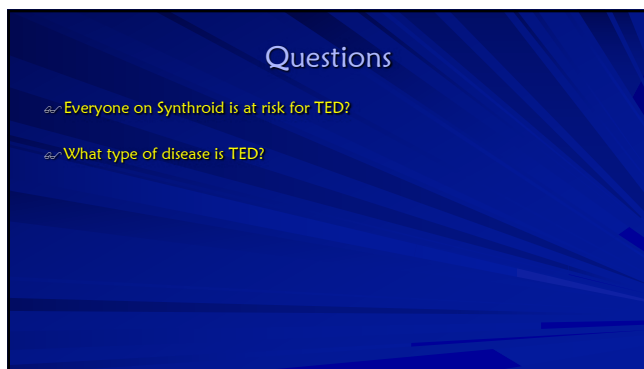
7



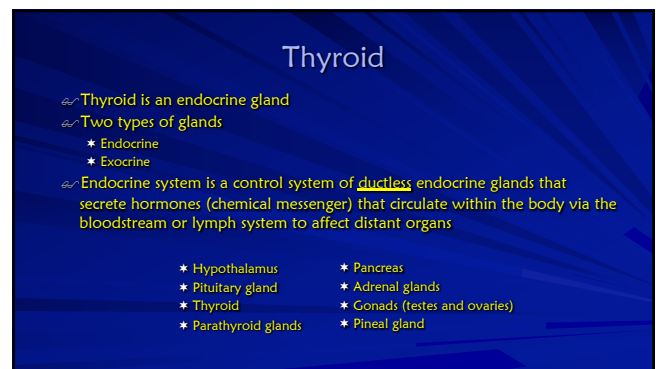
8



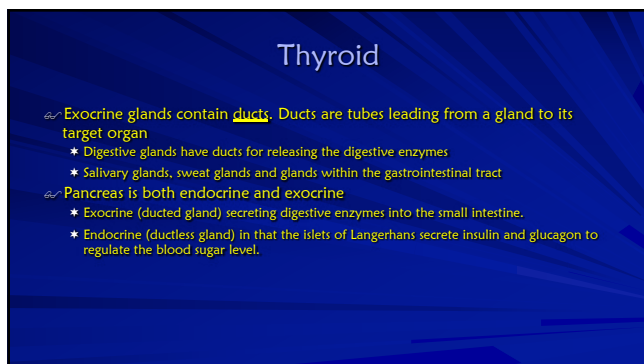
9



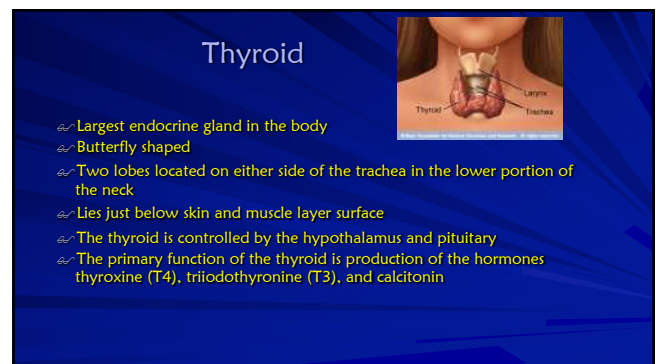
10



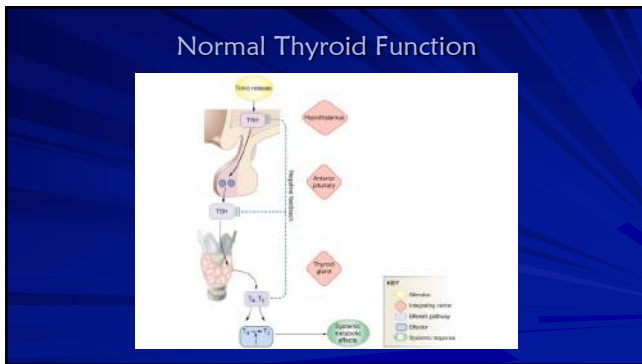
11



12



13



14



15

### 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

16

### Thyroid Dysfunction

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

17

### 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

18

Ninja Nerd Science  
YouTube

19



### Thyroid Dysfunction

<p><b>Hyperthyroidism</b> (Thyrotoxicosis)</p> <ul style="list-style-type: none"> <li>~ Primary-autoimmune                     <ul style="list-style-type: none"> <li>* Graves                             <ul style="list-style-type: none"> <li>□ Graves-Basedow or von Basedow's</li> </ul> </li> </ul> </li> <li>~ Secondary/Tertiary                     <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 tissue</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>~ Primary-autoimmune                     <ul style="list-style-type: none"> <li>* Chronic autoimmune thyroiditis                             <ul style="list-style-type: none"> <li>□ Hashimoto's thyroiditis</li> </ul> </li> <li>* Autoimmune atrophic thyroiditis                             <ul style="list-style-type: none"> <li>□ Primary myxedema</li> <li>□ Opposite of Graves disease</li> </ul> </li> <li>* Postpartum thyroiditis</li> </ul> </li> <li>~ Secondary/Tertiary                     <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>
---	---

26

### GRAVE'S (Hyperthyroidism)

- ~ A multisystem disorder consisting of a triad
  - \* Hyperthyroidism with diffuse hyperplasia of the thyroid gland
  - \* Infiltrative demopathy
  - \* 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)

27

### 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

28

### Autoimmune atrophic thyroiditis (Hypothyroidism)

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

29

### Postpartum Thyroiditis (Hypothyroidism)

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

30

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

<p>~ Symptoms</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>~ Signs</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>* Britk tendon reflex</li> <li>* Diabetes</li> <li>* ↑Triglycerides &amp; Ca, ↓CHO</li> <li>* Microcytic anemia</li> <li>* Possible goiter</li> <li>* Myxedema</li> </ul>
--	---

31

### 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

32

### 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

33

### 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

34

### 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

35

### 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

36

### 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

37

### 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

38

### 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

39

### 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>~ Hyperthyroidism eye symptoms                             <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>~ Hypothyroidism eye symptoms                             <ul style="list-style-type: none"> <li>* Deficient hormone causing venous congestion, impaired circulation and fluid stagnation</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
- ~ Relying on the TSH level can be misleading and in treating TED

40

### 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

41

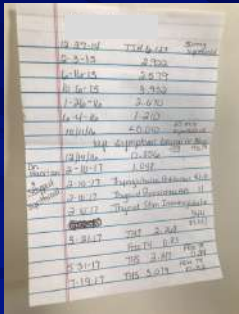
### Euthyroid Graves' disease

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

42

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

43



You're in the Know

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

It does work!

44

### General Ocular Symptoms

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

45

### 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)

46

### NOSPECS: Grading System

- ~ 0: No symptoms or signs
- ~ 1: Only signs (upper lid retraction without lid lag or proptosis)
- ~ 2: Soft tissue involvement with symptoms (excess lacrimation, sandy sensation, retrobulbar discomfort)
  - \* Grade 0: absent
  - \* Grade A: minimal (edema of lids, injection, sandy feeling)
  - \* Grade B: moderate (edema of lids, injection, chemosis, FBS, pain behind eyes)
  - \* Grade C: marked
- ~ 3: Proptosis associated with classes 2-6 only
  - \* Grade 0: absent
  - \* Grade A: minimal: 21mm -23mm
  - \* Grade B: moderate: 24mm -27mm
  - \* Grade C: marked: 28mm or more
  - \* Specify if inequality of  $\geq 3$  mm between eyes, or if progression of  $\geq 3$  mm under observation

47

### 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)

48

### 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)

49



### 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

50

### 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

L1E1M200  
Endocrine ophthalmopathy with lid edema, exophthalmos, pseudoparesis of external eye muscles, and no optic nerve involvement

51

### Clinical Activity Score (CAS)

Thyroid disease characterized by:

- \* Severity
- \* Activity – want 3 or above
- CAS (1-7)

Studies by Tepezza

Payers using CAS for approval

- \* Due to wide open label
- \* Those infusing are charting the CAS

Table 3 Clinical Activity Score	
	Clinical Activity Score
1	Proptosis behind globe
2	Pain on retrobulbar globe
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 2-3 months
9	Decrease in visual acuity in last 3-7 months
10	Decrease in eye movements of 30° in last 1-3 months

52

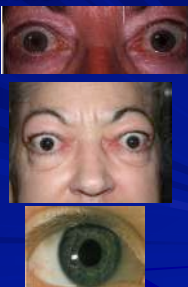
### Lid Involvement

- ~ Lid Retraction
- ~ Lid Lag
- ~ Lagophthalmus

53

### 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



54

### 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



55

### Lagophthalmos

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

56

### Soft Tissue Involvement

- ~ Conjunctiva
- ~ Chemosis
- ~ Periorbital edema

57

### 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



58

"If it is Red think TED"

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



59

### Periorbital Edema

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



60

### 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

61



62



63



64

### 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

65

### 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

66

### 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

67

### Restrictive Myopathy

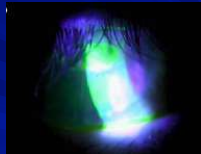


Obvious restrictive myopathy but also note the periorbital edema, and conjunctival hyperemia

68

### Corneal Exposure

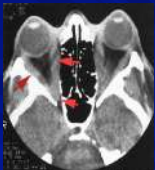

Exposure keratopathy secondary to exophthalmos and lagophthalmos  
Significant threat to visual function



69

### 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

70


### 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

71

### 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

72


### 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

73

### 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



74


### Lid Retractor Surgery



75

### 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



76

### Infiltrative Orbitopathy (Exophthalmos/Proptosis)


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



77

### Restrictive Myopathy

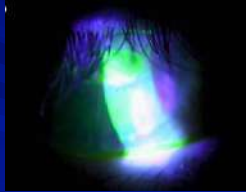
- ~ Non-surgical (while waiting for stability)
  - \* Teach proper head position to alleviate diplopia
  - \* Prism in spectacle correction (Fresnel or ground in)
  - \* Oral steroids
  - \* Botulinum toxin injection
- ~ Surgical Consult
  - \* Recession of the rectus muscle/s involved
  - \* Diplopia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



78

### 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



79

### Optic Neuropathy

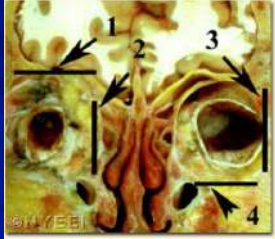
- ~ Systemic Steroids
  - \* If rapidly progressive and painful in the early stage of the disease
  - \* Only if no contraindications
  - \* Prednisolone 80-100mg, expect results within 48hrs. Taper dose and d/c within 3 mo
- ~ IV Methylprednisolone
- ~ Radiotherapy; if contraindication to steroid
-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

80

### 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



81

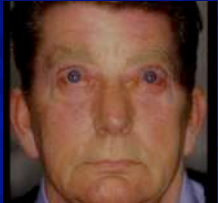
### Orbital Decompression (Surgical/Cosmetic)



82

### Thyroid Eye Disease and Depression

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



83

### Orbital Decompression (Medical/Vision Threatened)

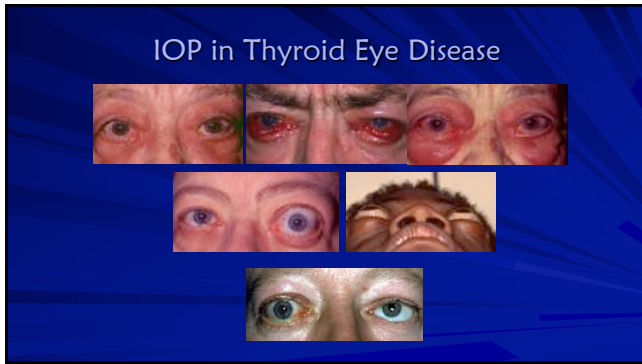


84

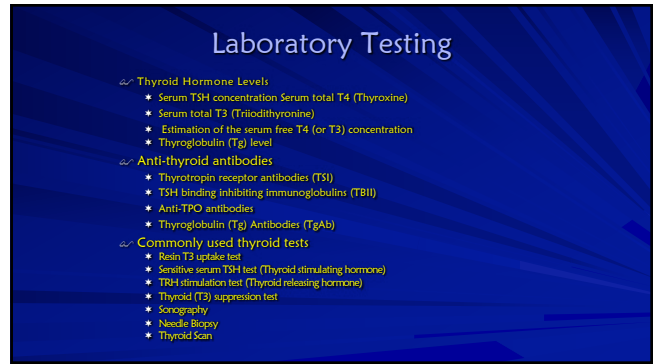
### IOP in Thyroid Eye Disease

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

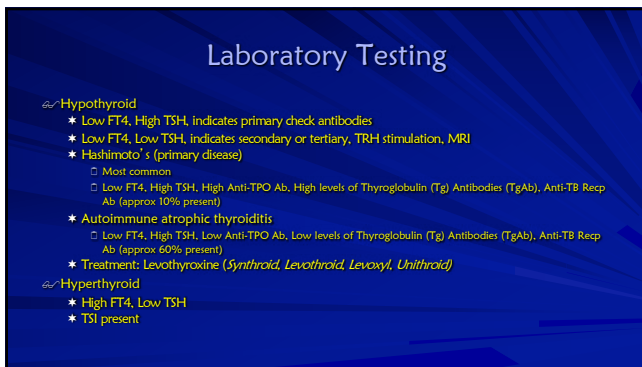
85



86



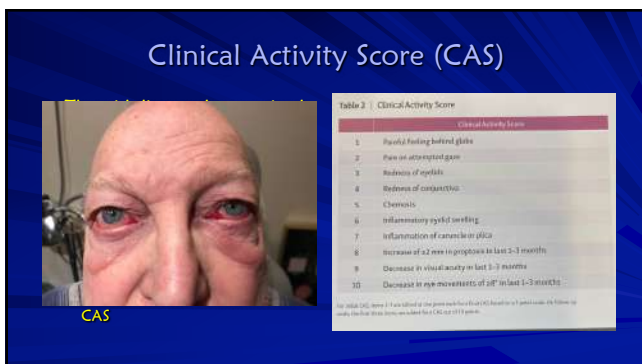
87



88



89



90



91



92



93



94



95



96

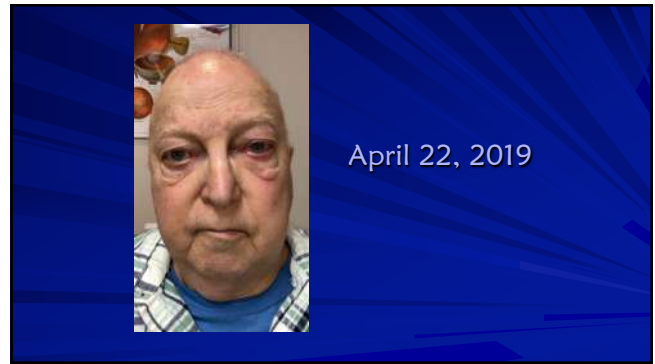


97





98



99



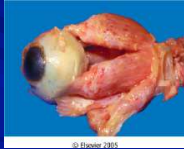
100



101

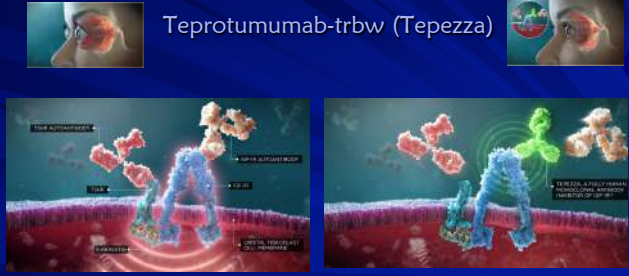
### Teprotumumab-trbw (Tepezza)

- Horizon Therapeutics – HQ Dublin, Ireland and US based Chicago
- Biologic pharmaceutical
  - Chinese Hamster Ovary
  - Infusion, 8 total, every 3 weeks
- Thyroid eye disease
  - IGF1 (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, hyaluron, 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



102

### Teprotumumab-trbw (Tepezza)



<https://www.tepezza.com/hcp/tepezza-mia/>

103

## 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
      - Orbital fibroblasts to myofibroblast or adipocytes
      - Hyaluronic acid, glycosaminoglycan

104

## 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

105

## 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

106

## Teprotumumab-trbw (Tepezza)

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

107

## 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

108

## Teprotumumab-trbw (Tepezza)

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

109


### Biologics Used Off Label for TED

Small Molecule Therapy	Target	Timing	Goal/Effect	Side Effects
Humira®	CD20	2 infusions of 400 mg each, 2 weeks apart	Modest results in improvement of CAS, ptosis, and orbitopathy	Liver failure, inflammation, blood issues, infections, lymphoma
Abatacept®	TNF-α	Subcutaneous injection of 800 mg every 2 weeks for 16 weeks	Modest decrease in inflammation or change in ptosis or orbitopathy	Upper respiratory tract infections, sinusitis, pneumonia, tuberculosis
Infliximab	TNF-α	Infusions at 5 mg/kg each dose over 2 years	Less reports of improvement in visual symptoms, CAS, or ptosis compared to Humira	Infections, malignancies, hepatitis, tuberculosis
Tecovian®	IL-6	3 infusions of 8 mg/kg given every 4 weeks	20% with all signs improved in CAS, most patients with 25% or more change in ptosis	High incidence of infections, pneumonia
Teprotumumab	IGF-1R	Initial infusion of 10 mg/kg, followed by 2 infusions of 20 mg/kg given every 2 weeks	Modest improvement in CAS, ptosis, and orbitopathy	Diabetes, thyroiditis, hypoparathyroidism, and other endocrine disorders, severe allergic reactions

110

### 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



111

### 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



112

### 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



113


### 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 wear
- ~ Works within 4 weeks
- ~ 1 bottle (5 ml) lasts 2-3 months
- ~ 3-year shelf 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



114

### New and All Natural



115





SUPPLEMENT FACTS		Servings Per Container (120)	
Amount Per Serving			% Daily Value*
Vitamin A	10,000 IU	200%	
Vitamin B1	100 mg	2000%	
Vitamin B2	100 mg	2000%	
Vitamin B6	100 mg	2000%	
Vitamin B12	1000 mcg	20000%	
Vitamin C	1000 mg	2000%	
Vitamin D3	10,000 IU	2000%	
Vitamin E	1000 IU	2000%	
Vitamin K	100 mcg	200%	
Magnesium	1000 mg	200%	
Zinc	100 mg	2000%	
Selenium	100 mcg	200%	
Copper	100 mcg	200%	
Manganese	100 mg	2000%	
Chromium	100 mcg	200%	
Molybdenum	100 mcg	200%	
Calcium	1000 mg	200%	
Iron	100 mg	2000%	
Potassium	1000 mg	200%	
Sodium	100 mg	200%	
Iodine	100 mcg	200%	
Biotin	100 mcg	200%	
Niacin	100 mg	2000%	
Panthenol	100 mg	2000%	
Inositol	100 mg	2000%	
Choline	100 mg	2000%	
Phosphorus	100 mg	2000%	
Sulfur	100 mg	2000%	
Vanillin	100 mg	2000%	

**OTHER INGREDIENTS:** Gelatin, Glycerin, Beeswax, Sunflower Lecithin, Vanillin.  
**CONTAINS:** Fish (anchovies, sardines, mackerel).

128

**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 LaVelle, RPh, CCN*

129

- ### 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
  - Stellweg'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

130

### Questions and Thank You!

**Thyroid and Thyroid Eye Disease  
Clinical Pearls and Innovations for 2023**

**Greg Caldwell, OD, FAAO**  
Woo University  
Monday, September 25, 2023

131