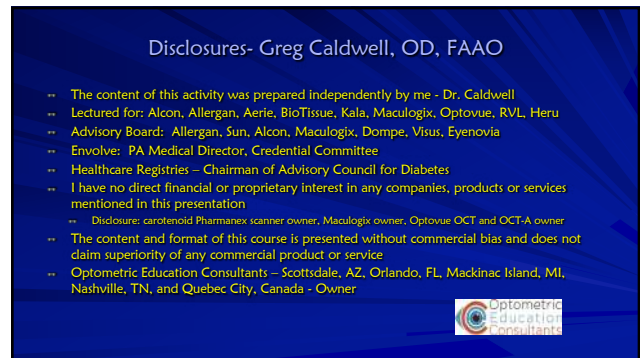
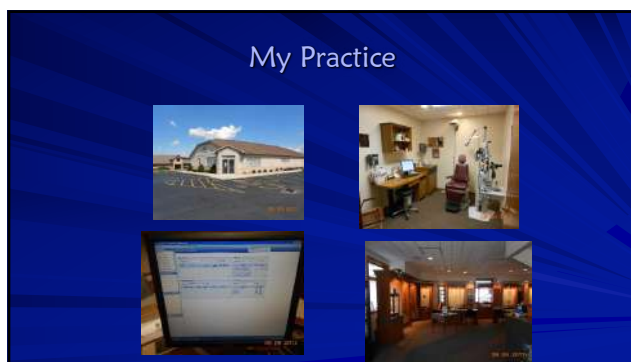


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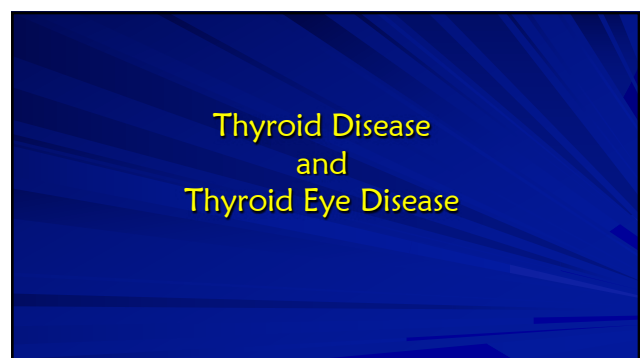
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6



7

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

8

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.

9

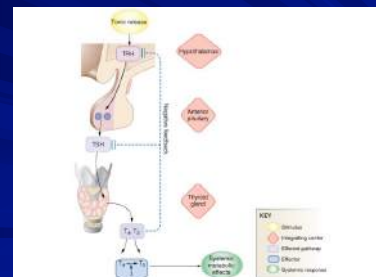
Thyroid



- 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

10

Normal Thyroid Function



11

Discussion



12

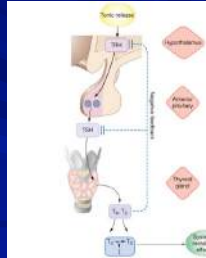
Thyroid Dysfunction

- 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

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Thyroid Dysfunction

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



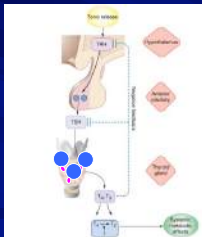
14

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

15

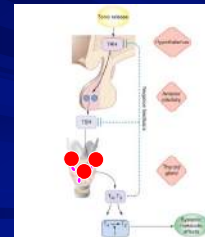
Hyperthyroid



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

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Hypothyroid



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

17

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

18

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)

19

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

20

Autoimmune atrophic thyroiditis (Hypothyroidism)

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

21

Postpartum Thyroiditis (Hypothyroidism)

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

22

Systemic Manifestations of Hyperthyroid (Primary or Secondary)

- | | |
|--|---|
| <ul style="list-style-type: none"> • Symptoms <ul style="list-style-type: none"> * Nervousness * Heat intolerance * Sweating * Fatigue * Palpitation * Insomnia * Early waking * Alopecia * Vitiligo * Brittle nails | <ul style="list-style-type: none"> • Signs <ul style="list-style-type: none"> * Sweating * Muscle Weakness * Emotionally labile * Tremor * Tachycardia * Arrhythmia * Hypertension * Brisk tendon reflex * Diabetes * ↑Triglycerides & Ca, ↓CHO * Microcytic anemia * Possible goiter * Myxedema |
|--|---|

23

Systemic Manifestations of Hypothyroid (Primary or Secondary)

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

24

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

25

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

26

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

27

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

28

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

29

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

30

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

31

Phase secondary to abnormal thyroid hormone levels (T₃/T₄) (Thyroid Eye Disease)

- Hyperthyroidism eye symptoms
 - Excess hormone acting on the nerves that supply the eye
 - Usually spastic and include staring
 - Dryness
 - Eyelid retraction
- Hypothyroidism eye symptoms
 - Deficient hormone causing venous congestion, impaired circulation and fluid stagnation
 - Periorbital edema

This form of TED resolves within a few weeks after thyroid hormone levels (FT₄ and FT₃) are corrected and brought back into the normal range

The pituitary hormone TSH can stay low or suppressed for many months during the course of treatment for hyperthyroidism and doesn't mean that the patient is still hyperthyroid

TSH also lags at least 6 weeks behind thyroid hormone levels and often remains elevated longer in people who have been hypothyroid

Relying on the TSH level can be misleading and in treating TED

32

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

33

Euthyroid Graves' disease

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

34

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

35

You're in the Know

Normal Values

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

It does work!

36

General Ocular Symptoms

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

37

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)

38

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 mm between eyes, or if progression of mm under observation

39

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)

40

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)

41

LEMO Classification

Lid (L) <ul style="list-style-type: none"> 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) <ul style="list-style-type: none"> 0: missing 1: eye closing not impaired 2: conjunctival injection in the morning 3: persistent conjunctival injection 4: corneal complications
--	---

42

LEMO Classification

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

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

43

Clinical Activity Score (CAS)

~ Thyroid disease characterized by:

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

~ Studies for Tepezza

~ Payers using CAS for approval

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

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 corneal epithelium
8	Increase of 2 or less in conjunctival lactescence
9	Decrease in visual acuity in last 2-3 months
10	Decrease in eye movements of 48° in last 3-3 months

Visual field (VF), Area 1: 1 peripheral or more quadrants; Area 2: 1 quadrant; Area 3: 2 quadrants; Area 4: 3 quadrants; Area 5: 4 quadrants; Area 6: 5 quadrants; Area 7: 6 quadrants; Area 8: 7 quadrants; Area 9: 8 quadrants; Area 10: 9 quadrants; Area 11: 10 quadrants; Area 12: 11 quadrants; Area 13: 12 quadrants; Area 14: 13 quadrants; Area 15: 14 quadrants; Area 16: 15 quadrants; Area 17: 16 quadrants; Area 18: 17 quadrants; Area 19: 18 quadrants; Area 20: 19 quadrants; Area 21: 20 quadrants; Area 22: 21 quadrants; Area 23: 22 quadrants; Area 24: 23 quadrants; Area 25: 24 quadrants; Area 26: 25 quadrants; Area 27: 26 quadrants; Area 28: 27 quadrants; Area 29: 28 quadrants; Area 30: 29 quadrants; Area 31: 30 quadrants; Area 32: 31 quadrants; Area 33: 32 quadrants; Area 34: 33 quadrants; Area 35: 34 quadrants; Area 36: 35 quadrants; Area 37: 36 quadrants; Area 38: 37 quadrants; Area 39: 38 quadrants; Area 40: 39 quadrants; Area 41: 40 quadrants; Area 42: 41 quadrants; Area 43: 42 quadrants; 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44

Grading Scales

~ New grading scales are trying to be developed to not only grade the severity but also help to determine if inflammatory or passive stage

45

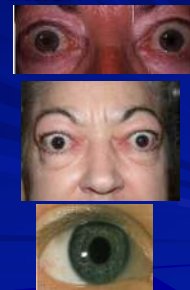
Lid Involvement

- ~ Lid Retraction
- ~ Lid Lag
- ~ Lagophthalmos

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Lid Retraction

- ~ Scleral show in primary gaze
- ~ 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
 - o ~2 mm below the limbus
 - * Lower lid coincident or 1-2mm below the limbus



47

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



48

Lagophthalmos

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

49

Soft Tissue Involvement

- ~ Conjunctiva
- ~ Chemosis
- ~ Periorbital edema

50

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



51

"If it is Red think TED"
Dr. Andy Morgenstern 12-7-2013, OMS-Contemporary Resort



52

Periorbital Edema

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



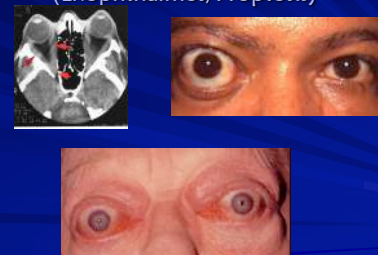
53

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 if 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)

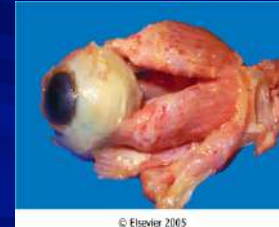


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Infiltrative Orbitopathy (Exophthalmos/Proptosis)



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57

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

58

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



59

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

60

Restrictive Myopathy

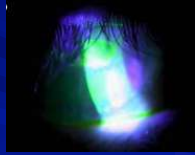


Obvious restrictive myopathy but also note the periorbital edema, and conjunctival hyperemia

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Corneal Exposure

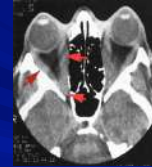
- Exposure keratopathy secondary to exophthalmos and lagophthalmos
- Significant threat to visual function



62

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



63

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
 - 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

65

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

66

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



67

Lid Retractor Surgery



68

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



69

Infiltrative Orbitopathy (Exophthalmos/Proptosis)

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



70

Restrictive Myopathy

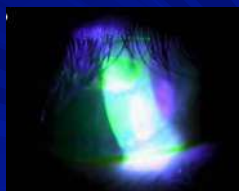
- ~ Non-surgical (while waiting for stability)
 - * Teach proper head position to alleviate diplopia
 - * Prism in spectacle correction (Fresnel or ground in)
 - * Oral steroids
 - * Botulinum toxin injection
- ~ Surgical Consult
 - * Recession of the rectus muscle/s involved
 - * Diplopia in primary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

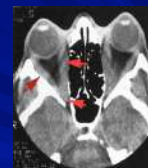
- ~ Manage the corneal defect as first line
 - * Lubricating and antibiotic
 - * Lid taping
 - * Moisture barrier
- ~ Orbital Disease Consult
 - * High dose oral steroids
 - 120-140mg/day x 7 days
 - * Orbital decompression



72

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

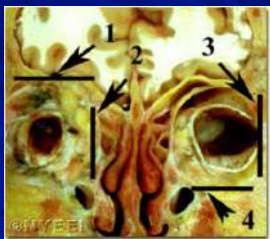


73

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



74

Orbital Decompression (Surgical/Cosmetic)



75

Thyroid Eye Disease and Depression

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



76

Orbital Decompression (Medical/Vision Threatened)



77

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

78

IOP in Thyroid Eye Disease



79

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 (TSH)
 - TSH binding inhibiting immunoglobulins (TBI)
 - 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 FT3 suppression test
 - Sonography
 - Needle biopsy
 - Thyroid Scan

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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 Resp Ab (approx 10% present)
 - Autoimmune atrophic thyroiditis
 - Low FT4, High TSH, Low Anti-TPO Ab, Low levels of Thyroglobulin (Tg) Antibodies (TgAb), Anti-TB Resp Ab (approx 60% present)
 - Treatment: Levothyroxine (*Synthroid, Levothroid, Levoxyl, Unithroid*)
- Hyperthyroid
 - High FT4, Low TSH
 - TSH present


81

February 25, 2019 "Nothing Else Can Be Done"



82

Clinical Activity Score (CAS)



CAS

Clinical Activity Score	
1	Painful tearing/foreign body
2	Pain on attempted gaze
3	Redness of conjunctiva
4	Redness of conjunctiva
5	Chemosis
6	Inflammatory eyelid swelling
7	Refraction of cornea or globe
8	Increase of 2 or more in proptosis in last 3-6 months
9	Decrease in visual acuity in last 3-6 months
10	Decrease in eye movements of 2 or more in last 3-6 months

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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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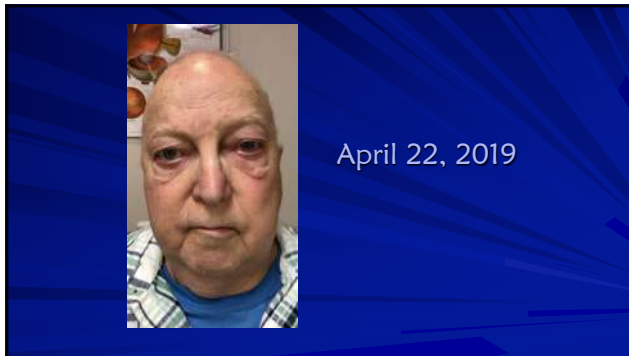
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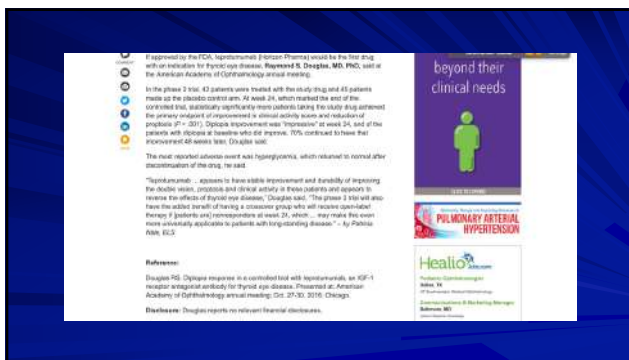
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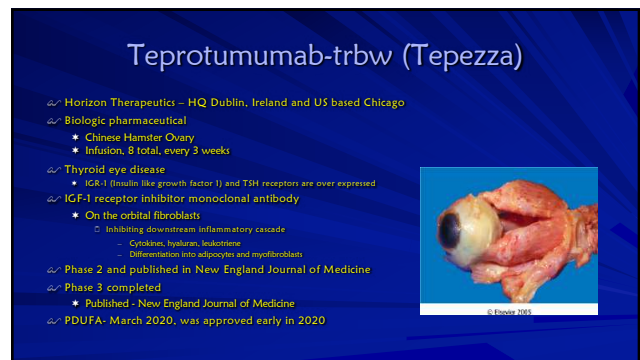
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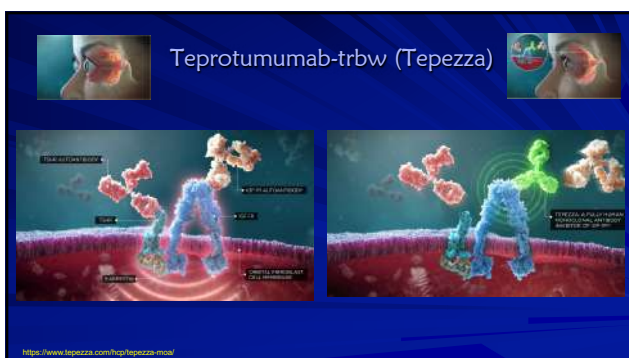
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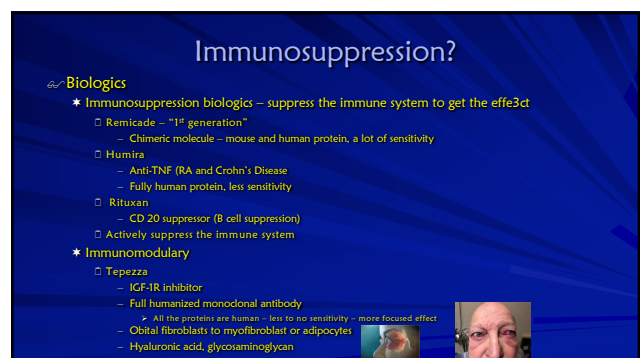
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Teprotumumab-trbw (Tepezza)

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

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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
 - 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

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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

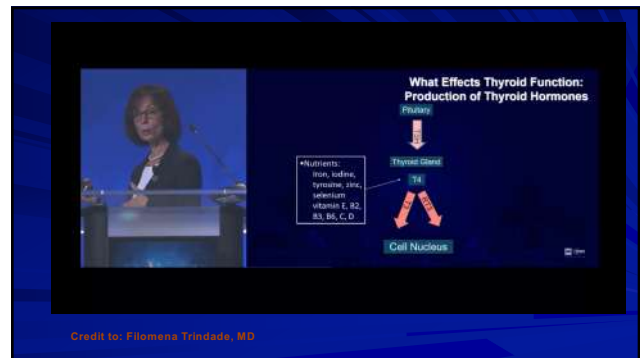
Table 1 | Biologic therapies for TED

Biologic Therapy	Target	Dosing	Findings	Side Effects
Etanercept	TNF- α	2 infusions of 500 mg each, 2 weeks apart	Mean results in improvement of CAS, proptosis, and diplopia	Transfusions of platelets, neutropenia, hepatitis, and myeloma
Abatacept	CD28	Subcutaneous injections of 100 mg every 2 weeks for 12 weeks	6/11 showed decrease in inflammation, no change in symptoms or medication therapy	Diarrhea
Infliximab	TNF- α	Infusions of 5 mg/kg every 8 weeks for 12 weeks	Clinical response observed in reduction of pain and CAS after 12 weeks, no change in symptoms or medication therapy	Infections, leukopenia, lymphopenia, drug-induced lupus
Humira	IL-6	Infusions of 10 mg/kg every 4 weeks for 12 weeks	100% with a 2-point improvement in CAS, mean improvement in CAS of 1.5, no change in diplopia	High risk for serious infections, lymphopenia
Teprotumumab	IGF-1R	Infusions of 10 mg/kg, followed by 20 mg/kg every 3 weeks	Subjected to a 70-80% of patients, improved CAS by 40%, reduced diplopia by 50%	High risk for serious infections, lymphopenia, leukopenia, neutropenia, hyperglycemia, hearing impairment, and dysgeusia. Monitor for early signs of infection or toxicity requiring early withdrawal

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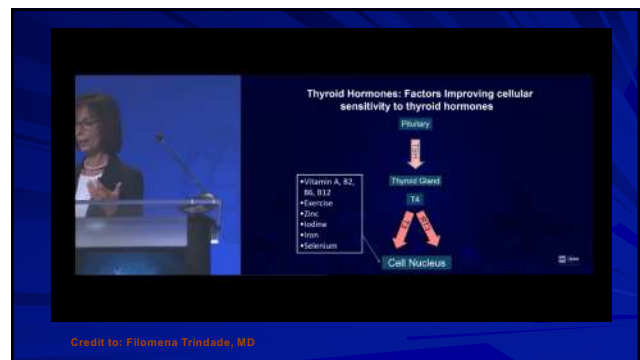
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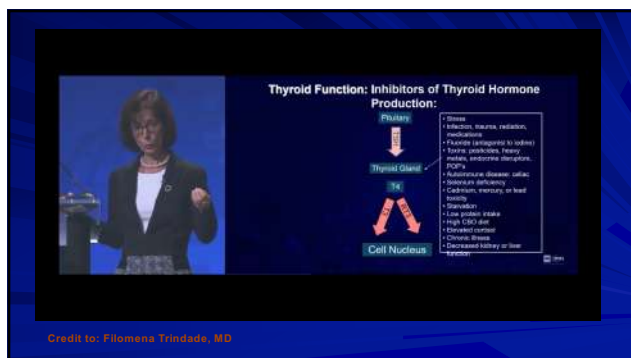
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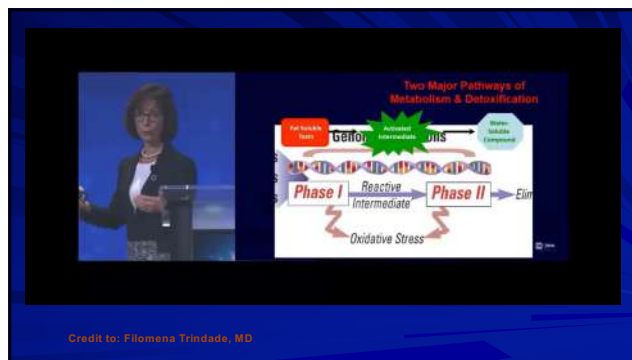
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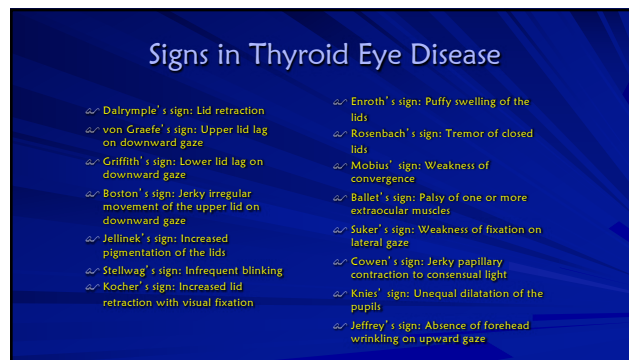
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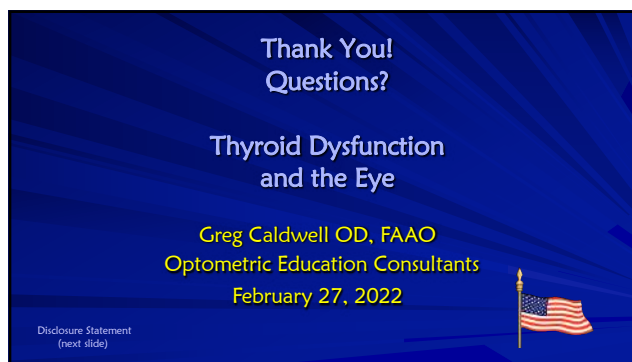
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