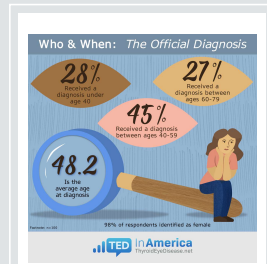




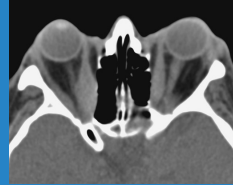
## WHO GETS TED?

More common in individuals with hyperthyroidism or Grave's disease  
 History of other autoimmune conditions  
 Women >> Men  
 Middle age most common – 30-60 years of age  
 Median age of onset ~48  
 Family history and genetics  
**SMOKERS!!**  
 Stress  
 RAI



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## COMMON FINDINGS IN TED



### RADIOGRAPHICAL EVIDENCE

- Orbital fat expansion
- Enlargement of the extraocular muscles
  - Often sparing of the tendons
  - Inferior and medial rectus muscle tend to be the most commonly effected
  - However, any muscle can enlarge and can be the one to lead to compression of optic nerve
- I'M SLOW
- CT vs MRI – when?

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## DIAGNOSTIC CRITERIA FOR TED DIAGNOSIS?

2 of 3 of the following are needed

- 1. Concurrent or recently treated immune-related thyroid dysfunction – laboratory testing
- 2. Typical ocular signs
- 3. Matching Radiographical evidence



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## COMMON ASSOCIATION IN TED

### ASSOCIATED SYSTEMIC CONDITIONS

- Grave's disease – autoimmune disease attacking thyroid gland leading to overactive thyroid
- Hashimoto's Disease - autoimmune disease attacking thyroid gland leading to inability to produce thyroid hormones, leading to underactive thyroid
- Euthyroid – no systemic condition associated
  - Even if thyroid testing normal at presentation - thyroid abnormalities, if present, typically demonstrated within 18-24 months of clinical presentation

\*\*\*10% will be Euthyroid or Hypothyroidism, remaining 90% often Grave's associated

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## COMMON FINDINGS IN TED

### SYMPTOMS

- Retro-orbital ache\*\*
- Prominent eyes or eyes bulging – most common symptom patient notices
- Diplopia, more specifically gaze-evoked
- Watery eyes
- Eyelid swelling

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## COMMON FINDINGS IN TED

### LABORATORY TESTING

- TSH (Thyroid Stimulating Hormone) – if associated with Grave's often suppressed
- Autoantibodies
  - TRAb (Thyrotropin Receptor antibodies): antibodies that direct against TSH receptors; Mimics TSH and causes the thyroid to release excess hormones (T3 and T4)
  - One of the most common in Grave's and often used to correlate disease activity
  - TSI (Thyroid stimulating immunoglobulins) – stimulate the thyroid; High levels very common in active Grave's disease
  - TPOAb (thyroid peroxidase antibodies) - autoantibodies that attack thyroid peroxidase, an enzyme crucial for thyroid hormone production. Can be high in Grave's but often more in Hashimoto's disease
  - TgAb (thyroglobulin antibodies) – sign of thyroid being attacked by immune system

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|          | Hashimoto's disease | Graves' disease |
|----------|---------------------|-----------------|
| TSH      | LOW                 | HIGH            |
| T3       | Low/normal          | High/normal     |
| T4       | Low/normal          | High/normal     |
| Anti-TPO | ++/+++              | ++/+++          |
| TgAb     | ++/+++              | ++/+++          |
| TRAb     | ++/+++              | ++/+++          |

### COMMON LABS IN GRAVE'S ASSOCIATED UNCONTROLLED TED

TSH – LOW (often undetectable)  
 T3/T4 – HIGH  
 TRAb\*\* – ELEVATED  
 TSI\*\* – ELEVATED  
 TgAb – can be elevated

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| CLINICAL SIGNS OF TED   |
|---|
| <ul style="list-style-type: none"> <li>• <b>Upper eyelid signs</b> <ul style="list-style-type: none"> <li>• <b>Stellwag sign</b> – incomplete or frequent blink</li> <li>• <b>Gifford sign</b> – difficulty everting upper eyelid</li> <li>• Periorbital edema/swelling</li> <li>• Incomplete lid closure - lagophthalmos</li> </ul> </li> <li>• <b>Lower eyelid signs</b> <ul style="list-style-type: none"> <li>• <b>Enroth sign</b> – lower lid edema</li> <li>• <b>Griffith sign</b> – lid lag on upgaze</li> </ul> </li> </ul> |

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| CLINICAL SIGNS OF TED  |
|--|
| <p><b>Generalized eye findings</b></p> <ul style="list-style-type: none"> <li>• <b>Proptosis/Exophthalmos</b> <ul style="list-style-type: none"> <li>• Bulging of eye</li> </ul> </li> <li>• <b>Dalrymple sign</b> <ul style="list-style-type: none"> <li>• Eyelid retraction</li> <li>• Most common presenting <b>clinical sign**</b> of TED, found in up to 90% of patients</li> <li>• Widened palpebral tissue (lid retraction) or lid spasm</li> <li>• Visible sclera is visible at the upper margin of the cornea and can include lower margin of cornea</li> </ul> </li> </ul> |



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| CLINICAL SIGNS OF TED   |
|---|
| <ul style="list-style-type: none"> <li>• <b>Conjunctival signs</b> <ul style="list-style-type: none"> <li>• <b>Goldziher sign</b>: conjunctival injection</li> <li>• Chemosis</li> <li>• Inflammation of caruncle or plica</li> </ul> </li> </ul> |



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| CLINICAL SIGNS OF TED  |
|--|
| <p><b>Generalized eye findings</b></p> <p><b>Von Graefe sign</b> – Delay of upper eyelid movement in down gaze</p> <p><b>Kocher sign</b> – staring appearance</p> <p><b>Vigouroux sign</b> – eyelid fullness</p> |



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| CLINICAL SIGNS OF TED   |
|---|
| <ul style="list-style-type: none"> <li>• <b>Extra ocular movements findings</b> <ul style="list-style-type: none"> <li>• <b>Mobius sign</b> – unable to converge</li> <li>• <b>Ballet sign</b> – muscle restriction of I or more muscles</li> <li>• <b>Suker sign</b> – poor fixation in abduction</li> </ul> </li> </ul> |

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### CLINICAL SIGNS HIGHLIGHTS

- Eyelid retraction\*
- Lid lag (Von Graefe's sign)
- Periorbital and eyelid edema
- Unilateral/bilateral proptosis
- Injection, exposure keratopathy
- EOM restriction (\*TM SLOW)
- Compressive optic neuropathy 2/2 compartment syndrome (decreased vision, color, RAPD)

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### SEVERITY OF DISEASE

- Mild
  - minor lid retraction
  - slight proptosis
  - no diplopia
- Moderate-severe
  - significant soft-tissue signs
  - diplopia
  - proptosis >3 mm
- Severe/sight threatening
  - optic neuropathy
  - corneal breakdown

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### SEVERITY/ACTIVITY LEVEL

- **Determine Stage** – mild, moderate, severe
- **Determine Activity level** - Active or Non-active (Stable) or concern for Reactivation

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### ACTIVE VS. STABLE DISEASE

- Must attempt to determine at every visit
  - Document in chart
- Using Scoring system to show activity level

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### SEVERITY OF DISEASE/STAGING

- **Severity**
  - Mild
  - Moderate
  - Severe/Sight-Threatening
- **Activity Level**
  - Active
  - Non-Active, Quiescent or stable
- **Reactivation**
  - Triggers? Clinical activity?
  - **Reactivation (disease relapse) can occur in ~5-10% of affected patients over their lifetime\*\***

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### SCORING SYSTEMS

- European Group on Grave's Orbitopathy (EUGOGO)
- VISA
- NO SPECS
- CAS

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## EUGOGO GRADING

| Score         | Features   |
|---------------|--|
| Mild          | Minor impact on daily life<br>Minimal indication for immunomodulation or surgical treatment<br>21 of the following signs:<br><ul style="list-style-type: none"> <li>• minor lid retraction (&lt;2 mm)</li> <li>• mild soft-tissue involvement</li> <li>• exophthalmos &lt;3 mm above normal for race and gender</li> <li>• no or intermittent diplopia</li> <li>• corneal exposure responsive to lubricants</li> </ul> |
| Moderate      | Not sight-threatening but has a sufficient impact on daily life<br>Indication for immunosuppression (if active) or surgery (if inactive)<br>22 of the following signs:<br><ul style="list-style-type: none"> <li>• lid retraction ≥ 2 mm</li> <li>• moderate or severe soft-tissue involvement</li> <li>• exophthalmos ≥ 3 mm above normal for race and gender</li> <li>• inconstant or constant diplopia</li> </ul>   |
| Severe (1-2%) | Patients with dysthyroid optic neuropathy and/or corneal breakdown   |

## NO SPECS

- **N:** No signs or symptoms.
- **O:** Only signs (e.g., eyelid retraction, proptosis).
- **S:** Soft tissue involvement (e.g., eyelid swelling, conjunctival injection).
- **P:** Proptosis (bulging eyes).
- **E:** Extraocular muscle involvement (e.g., double vision, restricted eye movements).
- **C:** Corneal involvement (e.g., corneal ulcers or dryness).
- **S:** Sight loss (due to optic nerve compression).

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## VISA SCORING

Vision (V), Inflammation (I), Strabismus (S), Appearance (A)

- Vision – Monitor for concerns of compressive optic neuropathy (CON)
- Inflammation/congestion – Based on documented change in inflammation rather than absolute value
- Strabismus/Motility – measuring ductions and alignment
- Appearance/exposure –
- \*\* SCORE OF 5 or more indicates active disease

## NO SPECS

- **Does not assess disease activity:** It doesn't distinguish between active inflammation and the chronic, fibrotic stage of TED.
- **Not directly linked to treatment:** Treatment decisions are not solely based on the NOSPECS classification.
- **NOT RECOMMENDED FOR MONITORING**

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## VISA SCORING

## GRADING – CLINICAL ACTIVITY SCORE (CAS)

Purpose: distinguish active vs stable phases of disease

CAS ≥ 3/7 indicates active disease

## For initial CAS score items 1-7

- 1 Spontaneous orbital pain
- 2 Case evoked orbital pain
- 3 Eyelid swelling that is considered to be due to active GO
- 4 Eyelid erythema
- 5 Conjunctival redness considered due to active GO
- 6 Chemosis
- 7 Inflammation of caruncle or plica

## Follow-up after 1-3 months score items including 8-10

- 8 Increase of > 2 mm proptosis
- 9 Decrease in unocular ocular excursion in any one direction of > 8 degrees
- 10 Decrease of acuity equivalent to 1 Snellen line

One point is given for the presence of each of the parameters assessed. The sum of all points define clinical activity: Active ophthalmopathy if score is > 3/7 at first examination or > 4/10 in successive examination. GO – Graves' orbitopathy

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### EXPECTED DISEASE COURSE

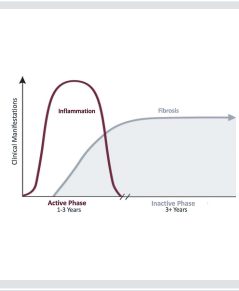
**Initial phase:** inflammatory, progressive phase duration may last from 6 to 18 months, with orbital and periorbital signs including proptosis and retraction

**Static phase:** decrease in inflammation but minimal improvement in orbital tissue - hits a plateau

- Very few patients return to their pre-disease state when inflammation subsides
- EOM and orbital tissue expansion do not regress but symptoms may improve slightly
- Fibrotic scarring very common by this point

**\*\* Most Common reason for extension to Rundle's curve → SMOKING**

### Rundle's Curve



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### MANAGEMENT – ACTIVE, MODERATE-SEVERE

- **Systemic corticosteroids \*\* MOST COMMON way to start with concern for CON or severe progression in CAS\*\***
- Prednisone
  - 1- 1.5-mg/ kg (recommended maximum period of 2 months)
  - Pulse-dosed IV dexamethasone followed by oral prednisone can be considered as an alternative when oral prednisone alone fails to control inflammation.
- Intravenous methylprednisolone (IVMP) – often vision threatening disease
  - Intermediate dose (500mg once weekly for six weeks followed by 250mg weekly for six weeks)
  - High dose (750mg weekly for six weeks followed by 250mg weekly for six weeks)
  - 20% to 30% of cases may show poor or no response, and in 20% of cases, there may be a relapse after discontinuation of medication

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### CONSERVATIVE TREATMENTS

- Education and Counseling – Set Expectations!!
- Smoking cessation!!!
- **Aim for euthyroid state\*\***
- Corneal exposure: lubricants, taping, and protective shields/goggles, and tarsorrhaphy (severe cases)
- Diplopia: Fresnel prisms or occlusion therapy/patching may be considered
- Diet/Lifestyle modifications:
  - **sodium restriction to reduce water retention and tissue edema\*\***
  - **Cool compresses, sleeping with the head of the bed elevated to decrease orbital edema\*\***
  - Oral NSAIDs for periorbital pain.
  - Selenium - some benefit in patients with mild, noninflammatory orbitopathy

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### MANAGEMENT – ACTIVE, MODERATE-SEVERE

- **Radiotherapy**
  - This method can be used alone or in conjunction with corticosteroids
  - Radiation therapy works on the similar mechanism of decreasing inflammation and studies show it appeared to facilitate tapering of steroids
  - Standard radiation treatment involves 20 Gy in 10 fractions (for total 200 cGy for each orbit)
  - Side effects can occur
    - Minor side effects - dry eye (7% to 25%) and cataracts (1 to 10%)
    - Very Rare - Radiation retinopathy
    - Diabetic are at higher risk for retinopathy after radiation, so orbital radiation generally is often avoided in this population

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### STEROIDS AND RADIATION

#### Goal: reduce inflammation

- Often does not have sustainable, significant long-term effects on disease outcomes
  - i.e. proptosis (approx 1mm) and diplopia

#### Systemic steroids: \*\*

- Pros: readily available, decrease inflammation
- Cons: well known comorbidities

#### Radiation:

- Pros: decrease inflammation, improves vertical motility
- Cons: minimal effect on proptosis, CAS, and lid symptoms

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### MANAGEMENT – ACTIVE, MODERATE-SEVERE

- **Tepezza (Teprotumumab)**
  - Human monoclonal antibody
  - FDA approval 2020
  - Targets IGF-1R, a tyrosine kinase receptor; found on orbital fibroblasts
  - IGF-1R forms a physical and signaling complex with TSHR
  - Mechanism: not fully understood; reduces levels of TSHR and IGF-1R on the fibrocytes and attenuates TSH-mediated IL-6, IL-8, TNF- $\alpha$ .
  - Side effects: muscle spasms, fatigue, nausea, diarrhea, hyperglycemia, hearing impairment, alopecia
  - Significant improvement ("dramatic") in proptosis and diplopia

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## OPTIC TRIAL

- Multi-centered, randomized, double-masked, placebo-controlled phase III clinical trial
- N = 83, active moderate to severe TED
- Inclusion: at least 1: lid retraction  $\geq 2$  mm, moderate/severe soft tissue involvement, proptosis  $\geq 3$  mm above normal value for race/sex, diplopia, ocular symptoms that began within 9 months, CAS at least 4, euthyroid
- Exclusions: previous irradiation, surgery for TED, CON, previous toxi or rituximab
- Dosing: q3 weeks, 8 total doses, 10mg/kg (initial), 20mg/kg (subsequent 7)
- Results: reduced proptosis in 80% of patients, improved CAS in 69%, reduced diplopia in 68%

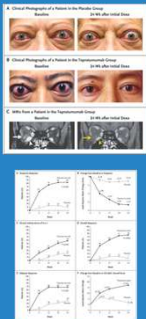
37

## TEPEZZA

- Tepezza (Teprotumumab)
  - Dosing: q3 weeks, 8 total doses<sup>\*\*\*</sup>, 10mg/kg (initial), 20mg/kg (subsequent 7)
  - A single 500 mg injection of Tepezza typically costs around \$16-\$17,00
  - Full course of treatment: A full course of treatment, typically involving eight infusions over 24 weeks, is estimated to cost around \$200,00
  - Often requires insurance prior authorization and sometimes use of corticosteroids prior
  - Side effects: muscle spasms, fatigue, nausea, diarrhea<sup>\*\*\*</sup>, hyperglycemia, hearing impairment, alopecia
  - Hearing test needed prior to beginning treatment, mid-point, and after completion
  - Contraindicated in Diabetics, pregnancy, Irritable bowel disease, hearing loss

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## OPTIC TRIAL



Primary outcome: proptosis response (reduction  $\geq 2$  mm) at week 24

Secondary outcome: overall response ( $\geq 2$  CAS), proptosis reduction, diplopia response, mean change in quality-of-life questionnaire.

Response: Tepezza group 83% vs placebo 10%

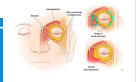
NNT = 1.36

-3.32 mm ~ single wall orbital decompression

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## MANAGEMENT: SURGICAL REHABILITATION

- #1 Decompression
  - Urgent - orbital decompression should be performed when there are severe surgical indications such as optic neuropathy, dramatic ocular surface disease, and subluxation of the globe.
  - Non-urgent - orbital decompression indications are diplopia, orbital pain, proptosis, and ocular hypertension as a mechanical result of proptosis
    - Should not be performed within the active phase of thyroid eye disease
- #2 Strabismus surgery - correct misalignment and should occur after decompression
- #3 Eyelid retraction repair
  - Surgical release or recession of eyelid retractors, with or without use of spacers or grafts
  - If surgery is not option - Transconjunctival Botox injections have been used for the medical management of upper eyelid retraction



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## OPTIC-X TRIAL

- Patients who initially received placebo in the OPTIC study and then received teprotumumab in OPTIC-X (first-time treatment) showed a significant reduction in proptosis.
- Confirming initial results seen in the OPTIC study
- Provided evidence that retreatment can be beneficial for those with an insufficient initial response or disease flare.
- Brings the question - Can teprotumumab be used in those with inactive disease?
  - Due to a small number of patients who experienced proptosis reduction even when they had a CAS score of zero or one at baseline

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## ALTERNATIVE THERAPIES - BIOLOGICS

- Adalimumab (Humira):
  - Subcutaneous TNF- $\alpha$  antagonist - targets/blocks TNF- $\alpha$ , a cytokine, that plays a role in inflammation.
  - A small retrospective study suggested that adalimumab may be beneficial for patients with active TED, particularly those with a high level of inflammation at the beginning of the study.
  - Another small study published in ARVO, demonstrated adalimumab to be effective in some of those who were steroid-resistant or couldn't tolerate steroids
    - Limits: both of these studies were small in sample size and a larger randomized controlled trial is needed to confirm findings.

Formal Peri-d. Invest Ophthalmol & Vis Sci 2021

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### ALTERNATIVE THERAPIES - BIOLOGICS

- **Infliximab (Remicade)**
  - Monoclonal antibody that also targets TNF- $\alpha$
  - Case reports have suggested that infliximab might be effective in treating severe, steroid-resistant TED, including cases with optic nerve compression.
  - In some instances, it has been used successfully after steroids and even surgical decompression have failed.
  - Again small sample size without good controls, larger studies needed

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### SUBCUTANEOUS TOCILIZUMAB

- Previous reports of tocilizumab for TED have used IV administration based on the rheumatology literature (4mg/kg q 4 weeks)
  - Weight based dosing, therapy driven by response
- Subcutaneous tocilizumab 162mg standardized single use vial – case report of 2 patients
  - Improvement of disease activity, decrease in CAS, reduction of proptosis by 2-3mm
  - Patient 1: good response > thyroidectomy > reactivation > retreated > good response again > stable after 6 months

Vignelli PR, et al. Ophthalmic Plast Reconstr Surg. 2019

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### ALTERNATIVE THERAPIES - BIOLOGICS

- **Tocilizumab (Actemra)**
  - Off label treatment for TED
  - Recombinant humanized monoclonal antibody that works by blocking the interleukin-6 (IL-6) receptor
  - Binds and blocks soluble and membrane bound IL-6R
  - IL-6 is a pro-inflammatory cytokine that directly results in expression of TSHR (autoantigen) on orbital fibroblasts
  - Prompt reduction of CAS and subjectively improved QOL score vs natural disease course

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### MULTIDISCIPLINARY APPROACH

- Multidisciplinary approach is crucial for effective management of Thyroid Eye Disease (TED), involving collaboration between primary care, endocrinologists, optometrists/ophthalmologists, oculoplastic surgeons, and in some cases other specialists.
  - Primary care – smoking cessation, generalized health management (diabetes, hypertension, etc), assist with additional laboratory testing, assist with side effects of medications/treatments
  - Endocrinology – management of medications and treatment options for thyroid abnormalities
  - Optometry/Ophthalmology – monitoring activity levels and severity of ocular complication
  - Oculoplastics surgeons – surgical intervention or needed management in sight threatening cases

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### IV TOCILIZUMAB

- Literature exists regarding treatment if IV tocilizumab for severe and/or refractory cases of TED
  - i.e. after failed IV steroid and decompression
- Adverse reactions: fatigue (most common), neutropenia, URI
- Improvements: VA, hyperemia, chemosis, eyelid edema, proptosis, EOMs, decrease in TSI
- Orbital fat biopsies
  - Before toc: dispersed lymphoid infiltrate and aggregates
  - After: absence of inflammatory cells
- Dose: 3 infusions 8mg/kg q 4 weeks
- Results: 93% with >2 point improvement in CAS, mean proptosis reduction of 1.5mm, no change in double vision
- Side effects: high recurrence rate, transaminitis, pyelonephritis

Sy A et al. Ophthalm Plast Reconstr Surg. 2017

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### ENDOCRINOLOGY – TREATMENTS

- **Medications**
  - Antithyroid medications – Most common meds used methimazole\*\* (MMI) and at times propylthiouracil (PTU)
  - Antithyroid drugs work by inhibiting the thyroid peroxidase
- B-blockers – Most commonly used Propranolol
  - Helps reduce increased heart rate, tremors, anxiety associated with Grave's
  - Propranolol can also inhibit the conversion of the less active thyroid hormone T4 to the more active T3.

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## ENDOCRINOLOGY – TREATMENTS

- **Radioactive Iodine (RAI)**
  - RAI utilizes the thyroid gland's natural ability to absorb iodine.
  - Radioactive iodine is swallowed then absorbed by the thyroid cells → delivers radiation that destroys the overactive thyroid cells → reduces the amount of thyroid hormone produced → improving symptoms of hyperthyroidism
- Can worsen or trigger Thyroid Eye Disease (TED)\*\*
  - Contraindicated in Severe TED
  - **Must monitor patients undergoing RAI closely for activation/worsening or reactivation\*\***

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## EXAM TESTING: TED

Visual acuity  
Pupils (watch closely for APD) – can be indicative of optic nerve compression/optic neuropathy  
Color plates  
EOMs – muscle enlargement/restriction  
IOP – important for monitoring orbital congestion and increased risk of optic nerve changes  
External photos (9 gaze and Worm's eye view)  
**Exophthalmometry\*\* (Hertel) – need for proptosis progression**  
Slit lamp exam and cornea, conjunctiva evaluation  
External exam – eyelid position, resistance to retropulsion  
Visual field – monitoring for enlargement changes with optic nerve compression  
Optic nerve evaluation (document details)  
OCT of nerve/RNFL in more moderate-advanced stages  
Orbital imaging CT of orbits and if needed MRI – moderate to advanced stage  
Progression tracking: CAS, VISA

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## ENDOCRINOLOGY – TREATMENTS

- **Thyroidectomy**
  - Surgical removal of entire thyroid gland → leading to a permanent cure of hyperthyroidism and related symptoms.
  - Results in hypothyroidism → requiring lifelong thyroid hormone replacement
- Who is a good candidate?
  - Those with moderate-severe TED (RAI can worsen clinical course)
  - Smokers
  - Medication ineffectiveness or intolerance
  - Pregnant patients
  - Progressive, compressive enlargement of thyroid gland

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## CASE HISTORY

- Are they diagnosed with hyperthyroidism or Grave's disease?
  - If so, try to determine month and year of diagnosis
  - What were the symptoms at time of diagnosis
  - Are they on treatment or have history of treatment? If so, what med/dosage OR what Treatment
  - When were recent thyroid labs and what were the results?
- Do they have any eye symptoms?
  - If so, what were the symptoms? List all
  - **When did first notice symptoms/ when did they start? Month/Year\*\* - (Narrow down) – WANT Day 0**
  - Symptoms stable or progressive

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## EYE EXAM TESTING

- As eye providers, we must know what testing to perform and why
  - It is more than just visual acuity and documenting proptosis
- Needs to be approached methodically
- Testing should be repeated each visit
  - How often depends on the exam findings

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## CASE HISTORY???

- Specific eye symptoms
  - Orbital ache
  - Diplopia – in primary gaze? Gaze evoke pain?
  - Eyelid swelling
  - Worsening bulging of eyes
- How do you document this?

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## CASE HISTORY DOCUMENTATION

### TED History

- Initially diagnosed with Grave's:
- Current Treatment:
- First had eye symptoms:
- What were the initial eye symptoms:
- Smoker: Yes or No



### Review of systems - TED:

- 1. pain or ache behind eyes at rest (I): YES or NO; with eye movement: YES or NO
- 2. double vision (I): yes (monocular or binocular), present in primary ... present in other gaze ...
- 3. eyelid swelling (I):
- 4. Increased bulging (I):
- 5. Dry eyes/burning/occasional frequency of artificial tear use:
- 6. Change or loss of vision(I):

THIS along with exam - helps indicate ACTIVITY LEVEL

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## CASE REVIEW #1

58 yo female with recent diagnosis of Grave's disease presents today as new patient referral from endocrinology. Complains of noticing that her eyes seem to be bulging more R>L

What information do we want to know on this patient?

What clinical signs do you see based on the external photo alone? Does she have TED?

If TED, what is needed to determine activity level and stage of disease?

Management for this patient? Follow-up schedule?



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## WHEN TO REFER?

- Active, Severe stage TED → Oculoplastic specialist
- Does not have to be same day but can request within couple weeks
- Any concern for Sight-threatening disease → Oculoplastic specialist
- Request that be seen within a few days
- Inability to properly monitor for progression → find an optometry or ophthalmology colleague that will help manage until/if oculoplastics is needed

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## CASE #2

- 39 yo female with negative medical and ocular history, married, mother of 2 younger children, and has active lifestyle and is not a-smoker
- Presents with complaint eye ache/pain OD worse with movement x 10 days
- Associated with headaches, "small, dark grey/black spot" OD
- Denies trauma, recent illness, fevers, double vision
- Other: recent tick bite, currently on abx for sinus infection, similar symptoms approx 1 year ago

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## MAKING THE REFERRAL

- Give detailed information about exam testing and data already obtained
- Give more than a referral stating "More proptosis"
- Be specific on why you are referring to and who would prefer they see – get to know your referring providers that can and will handle these patients
  - Optometry colleague
  - General Ophthalmologist
  - Oculoplastic specialist

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## CASE #2

- Now what....What exam information do I need?
  - Full exam (Lids, Anterior segment, Posterior segment), EOMs, IOP, pupils, color plates, external photos
  - Scleritis measurements
  - Hertel measurements
  - Visual field
  - OCT

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### CASE #2 – PHYSICAL EXAM

OD

VA (cCL) 20/30, ph 20/25  
Pupils: 4/3, no RAPD  
IOP: 12  
Ishihara: 11/11

OS

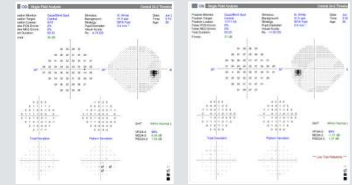
VA (cCL) 20/25, ph NI  
Pupils: 4/3, no RAPD  
IOP: 12  
Ishihara: 11/11

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### Additional testing

- Hertel: Base 110 - OD: 21mm OS: 20mm
- Measured at Small angle Esotropia right eye – in primary
- Visual field: as pictured
- OCT: mild inferior thinning both eyes – symmetrical between eyes

### CASE #2 – EXAM FINDINGS



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### CASE #2 – PHYSICAL EXAM

OD

Lids: Mild upper lid retraction (MRD1 = 5mm)  
no edema  
Cornea: clear  
Conjunctiva:  
Iris: normal  
AC: deep and quiet  
Optic nerve: 0.4 pink, flat, no pallor  
Macula: flat, dry  
Vessels: normal  
Vitreous: clear  
Periphery: flat, attached

OS

Lids: Mild upper lid retraction (MRD1 = 5.5mm), no edema  
Cornea: clear  
Conjunctiva:  
Iris: normal  
AC: deep and quiet  
Optic nerve: 0.4 pink, flat, no pallor  
Macula: flat, dry  
Vessels: normal  
Vitreous: clear  
Periphery: flat, attached

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### DIFFERENTIAL DIAGNOSIS (DDX)

- Vascular
- Infectious/Inflammatory
- Neoplastic
- Drugs
- Iatrogenic
- Congenital
- Autoimmune
- Trauma
- Endocrine

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### DIFFERENTIAL DIAGNOSIS (DDX)

- Vascular: CC fistula
- Infectious/Inflammatory
- Neoplastic: orbital tumor**
- Drugs
- Iatrogenic
- Congenital
- Autoimmune: myositis, IgG4, optic neuritis**
- Trauma
- Endocrine: thyroid eye disease**

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### CASE #2 – A/P

- What is my assessment?
  - Diplopia, non-concomitant
  - Retro-orbital ache
  - Suspected myositis right eye –
    - Unknown etiology – suspect thyroid eye disease, vs. orbital inflammation vs. other orbital process
- What is my plan for this patient?
  - Lab testing: CBC, BMP, ESR, RF, ANCA, ANA, ACE, IgG4, syphilis, toxo, bartonella, Lyme, RMSF, Ehrlichiosis, TSH, TSI.
  - Orbital imaging: CT of orbits w/ and w/o contrast – thin cuts
  - Recs: PO NSAIDs, ibuprofen 600mg TID until follow-up
  - Follow-up in clinic within a week with these results
  - Notify PCP of exam findings/complaints today

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### CASE #3 – PHYSICAL EXAM

OD

VA (cc) 20/40, ph 20/25  
 Pupils: no RAPD  
 IOP: 21  
 Ishihara: 9/11

OS

VA (cc) 20/30, ph 20/25  
 Pupils: no RAPD  
 IOP: 19  
 Ishihara: 10/11

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### CASE #2 – DIAGNOSIS UPDATE

- Labs – infectious, inflammatory, thyroid – ALL normal limits
- CT orbit results – “Diffuse thickening of the right inferior rectus muscle with the differential diagnosis including thyroid-associated orbitopathy/IgG4 autoimmune disease, versus less likely lymphoma or sarcoid”
- Had 2 of the 3 to make diagnosis (Radiographical Evidence and Typical Ocular signs)
- Missing laboratory or systematic diagnosis of thyroid dysfunction

**DIAGNOSIS: Euthyroid Thyroid Eye Disease**



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### CASE #3- EXAM FINDINGS

- ANTERIOR EXAM FINDINGS – see photos to follow
- POSTERIOR EXAM FINDINGS –
  - Nerve: C/D 0.3 pink, healthy, no pallor OU
  - Macula: flat, dry
  - Posterior pole: normal
  - Periphery: flat and attached
- Hertel: Base 105mm OD 30mm OS 28mm
- EOMs: some restrictions OU – stable
- HVF: generalized depression OU with mild non-specific loss OU - stable

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### CASE #3

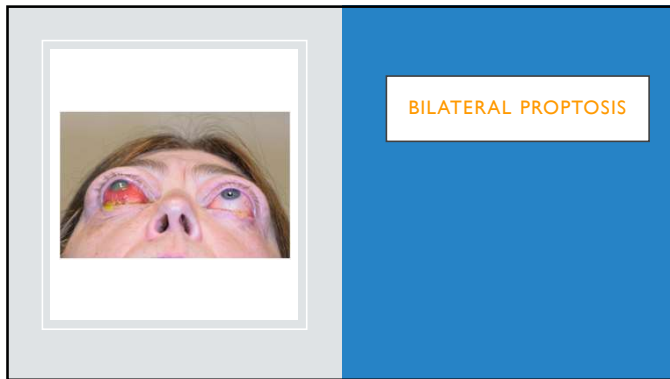
- 67 yo female with a history of Grave's disease and previous mod-severe TED which had been inactive and stable for 10+ years, presents for 6 month follow-up with complaints of increasing watering and redness of right eye over the past month or two
- Using PFAT several times a day, lubricating ointment at night
- Last endocrinology visit was a few months ago. Labs stable – no changes to her medication 10mg MMI continued
- Denies any new pain or ache with eyes, diplopia is stable but continues to have in certain gazes
- No new health issues but did have Covid ~ 2.5-3 months prior to visit

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### LID LAG



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**CAS SCORING**

**Baseline Assessment**

1. **Spontaneous orbital pain:** Pain in the that occurs without any specific trigger. – No
2. **Gaze-evoked orbital pain:** Pain that is triggered by eye movement. – No
3. **Eyelid swelling:** - Yes
4. **Eyelid erythema:** - Yes
5. **Conjunctival redness:** Redness of the - Yes
6. **Chemosis:** Swelling of the conjunctiva - Yes
7. **Inflammation of caruncle or plica:** Inflammation of the caruncle or plica. - Yes

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**CAS SCORING**

**Ongoing Assessment (Follow-up for progression)**

1. **Increase in proptosis:** A measurement increase of 2mm or more is considered significant – Yes, (previously was 28mm OD, 27mm OS)
2. **Decreased eye movements:** A reduction of 8 degrees or more in any direction of eye – No
3. **Decrease in visual acuity:** A reduction of one or more Snellen lines in visual acuity. - No

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**CASE #3**

- Severity level?
- Active or non-active – why?
- Treatment/Management?

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**CASE #3- ANSWERED**

- Severity level?
  - Severe, vision threatening due to corneal surface compromise OD>OS
  - Needs to be monitored very closely for CON development
- Active or non-active – why?
  - Active – CAS Score of 6 out of 10
- Treatment/Management?
  - Urgent referral to Oculoplastic specialist – within 1-2 weeks
  - Aggressive lubrication with thicker PF gels/ointments, taping of eyelids
  - Strong consideration for systemic steroid use and Orbital radiotherapy

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## CASE #4

21 yo female returns to clinic for 3-month follow-up for TED to monitor activity

- Has been noticing more watering of her eyes on both sides. Is not currently using any eye drops. No vision changes or other issues

## TED History

Initially diagnosed with Grave's Oct 2022

Current Treatment: Methimazole 2.5 mg daily

First had eye symptoms: May-June 2024 (patient was not taking meds as prescribed at this time and also changes to TSH with still present TSH antibodies on most recent 7/2025 labs but trending downward) concern for reactivation in summer 2024

Smoker: marijuana use

## Review of systems - TED:

1. Pain or ache behind eyes at rest (I): No ; with eye movement: No
2. Double vision (I): eye (monocular or binocular), present in primary - NO, present in other gazes - No
3. Eyelid swelling/Yes, both sides but stable
4. Increased tearing (I): No
5. Dry eye/burning, occasional frequency of artificial tear use: at times but is not using tears
6. Change or loss of vision(I): No

## ASSESSMENT/PLAN

Thyroid eye disease, bilateral - moderate - stable

Onset of eye disease - October 2022 (proptosis right eye > left - at that time), suspect reactivation/flare in ~ June 2024 based on new symptoms

(left>right) and lab results. Currently appears to be entering quiescent stage

Grave's disease diagnosed Oct 2022 - currently treated with Methimazole

Proptosis, both eyes (left eye > right eye)

Lid retraction, both eyes (left > right) - stable

Bilateral upper eyelid edema - stable

- moderate-severe, appears currently stable and hopefully entering quiescent stage - symptoms now minimal and measurements are stable

- no signs of optic neuropathy - HVF full, full color plates intact, RNFL healthy, no vision changes, no APD

- No diplopia

- CT of orbits 3/2025 medial rectus enlargement but no signs of optic nerve compression

- followed closely with endocrinology with recent Labs - TSH normal limits TSH remains (+)

- Patient is taking medication 2.5 mg Methimazole for management of thyroid levels. Continue medications as prescribed.

- The nature of TED was discussed in depth with the patient, including expected period of activity, potential for vision loss and cosmetic change and worsening of disease activity and severity with smoking.

- The patient was counseled maintaining a euthyroid state.

- Discussed/counseled on importance of smoking cessation - no current tobacco use but smoking marijuana daily

- recommend Restasis BID-QID OU consider ointment at night

- cool compresses, low salt diet, sleep with head elevation to improve periorbital edema and inflammation

- Strict return precautions reviewed

- Patient has some interest in orbital surgery once stable, no active signs of disease for 6+ months then will make surgical referral to Oculoplastics if still interested

## CASE #4- EXAM

- VA sc: 20/25- PH 20/20 OD, 20/20- OS
- IOP 17/18
- ECRs - full OU
- Color plates I/II OD/OS
- 24-2 HVF: Full without defects both eyes
- Hertel 98/94/35: Baze 106 OD 38mm OS 36.5-31mm - stable to 5/2025 and 3/2025 visits
- Lid/sphers: BUL edema with mild erythema - stable, LUL and LLL Lid retraction
- MRD1 OD 2.5-3mm OS 5.0mm
- Cornes: clear OU, no TBUT OU
- Conjunctiva: clear OU, no chemosis, no injection, mild bilateral caruncle redness
- AC: deep and quiet OU
- Iris: normal (JNVI) OU
- Lens: clear OU
- FUNDUS EXAM:
- Vitreous: clear OU
- Optic Nerve: C/D: 0.2 OU (+) sharp margins OU, (-) pallor/edema OU
- Macula: flat dry OU
- CA's markers: No decrease in vision, No increase in proptosis, No decrease in eye movements, No conjunctival injection/chemosis - Score 0

## TAKE AWAY OBJECTIVES

Be aware of demographics - know which patients are at highest risk

Be familiar with the most common symptoms and signs in patients with TED

Laboratory testing and co-management -

- Recent thyroid labs (thyroid levels AND antibodies)

- Work closely with PCP, endocrinology, other specialists

Verify systemic medications/dosages every visit or possible other treatments (RAI vs. thyroidectomy)

Complete the needed ocular testing every visit - Demonstrates stability or progression

External photos - pictures are worth 1000 words in the chart

Discuss modifiable risk factors - Smoking cessation, lifestyle, Medication and follow-up compliance

## CASE #4



- What else do I want to know about this patient?
- Does this patient have active TED?
- What Stage of TED?



## QUESTIONS?

