

# Updates in the Treatment of Thyroid Eye Disease

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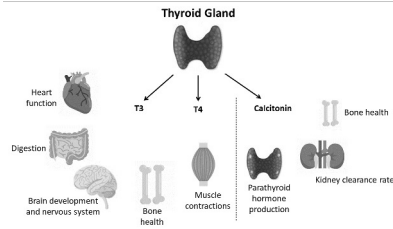
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## Thyroid Gland Functions

- Endocrine gland located in the neck
- Produces thyroxine (T4), triiodothyronine (T3), and calcitonin, which have impact on a large amount of bodily functions



<https://www.hormones-australia.org.au/the-endocrine-system/thyroid/>

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## Thyroid Eye Disease

- Autoimmune diseases involving the thyroid can have impacts on the eye
  - Eg) Graves disease, Hashimoto thyroiditis
- In these conditions, antibodies are produced which can stimulate thyroid hormone receptors
  - Receptor is present in many organs of the body
    - But of note, in many tissues in the orbit
- End result to eye includes muscle enlargement and expansion of orbital fat

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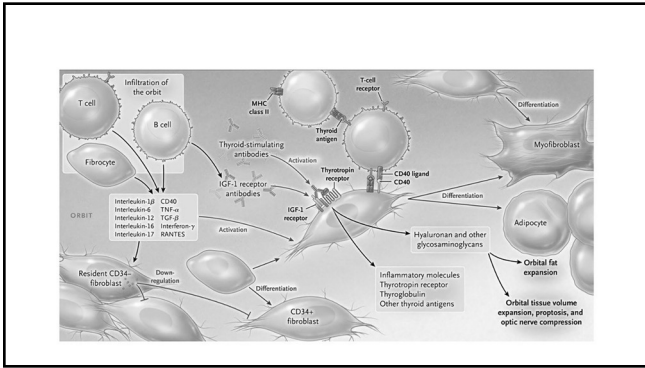
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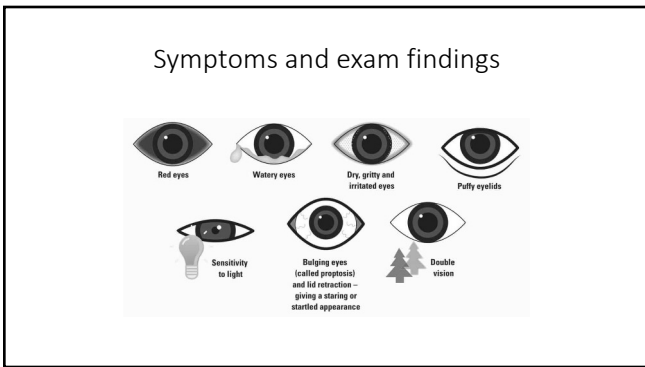
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For initial CAS score items 1-7	
1	Spontaneous orbital pain
2	Gaze evoked orbital pain
3	Eyelid swelling that is considered to be due to active GO
4	Eyelid erythema
5	Conjunctival redness considered due to active GO
6	Chemosis
7	Inflammation of caruncle 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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### Treatment Overview

- Older treatments that are still in use today include:
  - Orbital radiation: has anti-inflammatory effect due to radiosensitivity of lymphocytes
  - IV steroids: Eg) methylprednisolone also reduce inflammation by inhibiting lymphocytes
  - Both are often used together for synergistic effect
- These treatments come with significant side effects
- Over the past decade, newer treatments have investigated biologic agents

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### Teprotumumab

- First Food and Drug Administration (FDA) approved therapy for TED
- Antibody targeted against the IGF-1 receptor
- Regimen is 1 infusion every 3 weeks x8 (24 weeks total)
- Resulted in significant improvement in proptosis compared to placebo group (83% vs 10%)
- Many quality of life metrics improved as well

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### Rituximab

- Monoclonal antibody against CD20 (B-lymphocyte marker)
- Inhibits B-cells (responsible for producing) autoantibodies in thyroid eye disease
- Mixed results
  - Several RCTs have reported improvement in symptoms of, moderate-to-severe TED. Others have found no improvement in clinical activity score, proptosis, or diplopia

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### Adalimumab (Humira®), Infliximab

- Tumor necrosis factor-alpha (TNF-α) inhibitors
- Limited data, retrospective study of adalimumab found 4/10 patients had improvement in diplopia, pain, and swelling, but no objective measurements were taken
- Infliximab: case reports reporting various levels of efficaciousness
  - Case series of 3 cases reported complete resolution of symptoms in studied patients

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### Tocilizumab

- Monoclonal antibody targeting IL-6
- IL-6 has been found to stimulate the expression of TSHR in orbital fibroblasts, which binds thyroid autoantibodies
- RCT data found significantly reduced CAS by 2 points or greater in patients receiving tocilizumab vs placebo in patients with corticosteroid-resistant TED
- Diplopia didn't improve and CAS score was not significantly lower at 40 weeks as well as high rate of recurrence

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### Biologics Summary

- While biologics may show promising results, many are potent immunosuppressive medications
- Risk benefit ratio of these medicines should be evaluated, and potential side effects discussed with patients
- Much research continues to be done on these medications and will likely see them becoming more utilized in the treatment of TED

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