

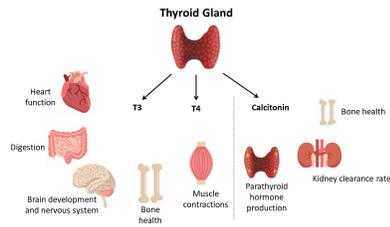
Updates in the Treatment of Thyroid Eye Disease

Donald Hubbard II, MD
Casey Eye Institute

1

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



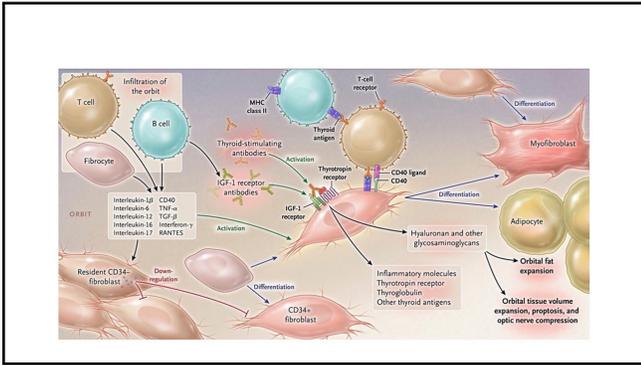
<https://www.hormones-australia.org.au/the-endocrine-system/thyroid/>

2

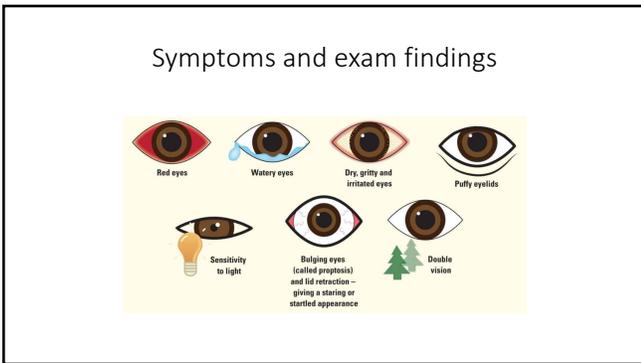
Thyroid Eye Disease

- 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

3



4



5

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

6

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

7

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

8

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

9

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

10

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

11

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

12

References

- Ayabe R, Rootman DB, Hwang CJ, et al. Adalimumab as steroid-sparing treatment of inflammatory-stage thyroid eye disease. *Ophthalmic Plast Reconstr Surg* 2014; 30: 415–419.
- Douglas, R. S., Kahaly, G. J., Patel, A., Sile, S., Thompson, E. H., Perdok, R., ... & Antonelli, A. (2020). Teprotumumab for the treatment of active thyroid eye disease. *New England Journal of Medicine*, 382(4), 341–351.
- Hamed Azzam S, Kang S, Salvi M, et al. Tocilizumab for thyroid eye disease. *Cochrane Database Syst Rev* 2018; 11: CD012984
- Iynouchi SC, Valasevi RW, Harteneck DA. Interleukin-6 stimulates thyrotropin receptor expression in human orbital preadipocyte fibroblasts from patients with Graves' ophthalmopathy. *Thyroid* 2001; 11: 929–934
- Man CJ, Kessler AL, Weister ST. Updates on the understanding and management of thyroid eye disease. *Ther Adv Ophthalmol*. 2021 Jun 30;13:25158414211027760. doi: 10.1177/25158414211027760. PMID: 34263138; PMCID: PMC8252358.
- Perez-Moreiras JV, Gomez-Reino JJ, Maneiro JR, et al. Efficacy of tocilizumab in patients with moderate-to-severe corticosteroid-resistant Graves orbitopathy: a randomized clinical trial. *Am J Ophthalmol* 2018; 195: 181–190
- Sakai M, Vannucchi G, Curio N, et al. Efficacy of B-cell targeted therapy with rituximab in patients with active moderate to severe Graves' orbitopathy: a randomized controlled study. *J Clin Endocrinol Metab* 2015; 100: 432–437
- Stan MN, Garrity JA, Carranza Leon BG, et al. Randomized controlled trial of rituximab in patients with Graves' orbitopathy. *J Clin Endocrinol Metab* 2015; 100: 432–441
- Srikanese D. Updates on Graves disease: advances in treatment of mild, moderate and severe thyroid eye disease. *Curr Opin Ophthalmol* 2017; 8: 706–713.
- [https://www.wikia-ao.org/Thyroid_Eye_Disease#:~:text=Thyroid%20eye%20disease%20\(TED\)%20is,per%20year%20in%20ope%20t](https://www.wikia-ao.org/Thyroid_Eye_Disease#:~:text=Thyroid%20eye%20disease%20(TED)%20is,per%20year%20in%20ope%20t)
