A multidisciplinary (MDT) approach to Graves Orbitopathy (GO) Thyroid Eye disease (TED) the most common inflammatory disease of the orbit

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TEAMed
Thyroid Eye Disease Amsterdam Declaration Implementation Group UK

BOPSS
BRITISH OCULOPLASTIC SURGERY SOCIETY
One patient’s journey

40+ year old NIDDM Asian lady Graves Hyperthyroidism 2014 Thyroidectomy Normal TFT levels non smoker

3 day history of intermittent sudden loss of vision pain and double vision

Euthyroid Post thyroidectomy Uncontrolled NIDDM HbA1c >100

pain proptosis loss of left vision when trying to look up unable to move her eye constant double vision
Day 1
Urgent Referral from another hospital

Day 2
MDT Thyroid eye clinic CXH
Sight Threatening disease left eye

Day 2
MRI orbit to confirm diagnosis

Day 3 - 5
3 days of high dose intravenous steroids in Endocrine Day Unit
Optimisation diabetic control

Day 6
Eye Clinic review
Decision for urgent decompression

Day 7
Urgent orbital decompression
Discharge day 8

Day 14
Start mycophenolate Mmolecules
Weekly Intravenous Steroids

No Radiotherapy due to diabetes

Ongoing Rx
Monthly review in MDT Thyroid eye clinic
with immunosuppression eye clinic
Day 1
- pain
- proptosis
- transient visual obscurations
- unable to move her eye
- constant double vision

Day 8
- no pain
- less proptosis
- no transient visual obscurations
- improved eye movements
- no double vision
Recurrence of orbital inflammation despite orbital decompression IVMP & ongoing immunosuppression with mycophenolate
Decreasing vision increasing pain

Switched to prednisolone & ciclosporin to try to maintain her vision
Poorly controlled diabetes, diabetic eye disease not suitable for radiotherapy
Graves Orbitopathy GO
Thyroid Associated Orbitopathy TAO
Thyroid eye disease TED

50% GD disease have clinically relevant GO
Can worsen despite good thyroid control
Can blind or cause severe double vision
Disfigurement & Impact on QOL usually much worse than clinical severity

poor clinical outcome
no effective medical cure
No animal model
How is immune tolerance broken?
Learning Outcomes

1 Aetiology & Pathogenesis

2 Risk Factors and how to modify them

3 Principles of management of Thyroid Eye Disease (including TEAMed 5)

4 A case study to illustrate the need for a multidisciplinary approach
Aetiology & Pathogenesis
Graves Disease

60-80% of all cases of hyperthyroidism
Autoimmune condition stimulating the TSH receptor
Defined typically by hyperthyroidism, TSH R antibody or diffuse uptake on a Tc NM scan
Pathognomonic features, eye disease, thyroid bruit
Muscle & fat expansion in a confined space ‘Orbital Cushings’
Estimated Prevalence of GO

<table>
<thead>
<tr>
<th>PREVALENCE (per 10,000 population)</th>
<th>PROPORTION OF PATIENTS WITH VARIANT</th>
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<tbody>
<tr>
<td>(a)</td>
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<tr>
<td>All cases of GO</td>
<td>8.97</td>
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<td></td>
<td>15.48</td>
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<tr>
<td>Mild GO</td>
<td>5.83</td>
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<td></td>
<td>11.03</td>
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<tr>
<td>Moderate-to-severe GO</td>
<td>2.96–4.45</td>
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<tr>
<td>Sight-threatening GO</td>
<td>0.18</td>
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<tr>
<td>(b)</td>
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<tr>
<td>Euthyroid/hypothyroid GO</td>
<td>0.02–1.10</td>
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<tr>
<td>GO associated with demyopathy</td>
<td>0.15</td>
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<tr>
<td>GO with cognitive impairment</td>
<td></td>
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<tr>
<td>Asymptomatic</td>
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<tr>
<td>Unilateral</td>
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</table>

1 in 10 will not have any thyroid hormone problems of these about half will go on to have thyroid hormone problems about 1 in 10 will only be affected in one eye socket

EUGOGO Position Statement  Perros et al 2017
Who is at risk?

- Family history
- Age
- Gender

Radioiodine

Thyroid control

Smoking

High TSH antibody
(normal <1.75 IU/L)

High risk for progression if >8.8 IU/L
Smoking

- Prummel & Wiersinga 1993
- x7 risk of visual loss
- Higher relapse rate on stopping anti-thyroid drugs
- x4 GO progression post I-131
- poorer response to immunosuppression
GO does not necessarily parallel thyroid activity but important to render euthyroid
Can worsen post radio iodine treatment

75% eye and thyroid onset within the same year

Do not give radio-iodine if there is significant eye disease
cover high risk groups with oral steroids
The disease does ‘burn out’
Lasts on average 1 yr in non smokers 2-3 yrs smokers
Reactivation 5-10%
Risk of blindness uncommon 2-5%
Prevent visual loss
Modifying severity of residual disease with timely intervention

Possible effect of early, effective anti-inflammatory treatment in thyroid eye disease

Disease activity
Modified disease severity
Unmodified disease severity
Assessing Activity & Severity
<table>
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<tr>
<th>Sight threatening (2-5%)</th>
<th>Optic neuropathy/ corneal breakdown</th>
<th>Immediate treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate to severe (29-33%)</td>
<td>Not sight threatening but sufficient impact on daily life Lid retraction ≥ 2mm Moderate to severe soft tissue involvement ≥ 3mm proptosis (corrected for race/gender) diplopia</td>
<td>Immunosuppression (If active) Surgery (if inactive)</td>
</tr>
<tr>
<td>Mild (65-73%)</td>
<td>Minor impact on daily life Minor lid retraction mild soft tissue involvement, &lt;3mm exophthalmos no diplopia</td>
<td>Lubricants and other simple measures</td>
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</tbody>
</table>
GO is self-limiting disease but you need to ask for every patient which severity curve are they on? where are they on their disease course?
Sight Threatening Disease

2-5%

Corneal exposure keratopathy

DON is a Clinical diagnosis
no single gold standard sign

One study found that in patients with optic neuropathy
28% had other co-morbidities causing poor vision
25% CAS <3
33% no proptosis
Management
Amsterdam Declaration for Thyroid Eye Disease 2009

• halving the time from presentation to diagnosis
• referral to a centre of excellence for optimal treatment of thyroid disease

• appropriate use of radioiodine
• avoidance of hypothyroidism
• vigorous anti-smoking measures
TEAMEd-5 Improving outcomes in Thyroid Eye Disease

1. **DIAGNOSE** Graves' disease accurately
   - Measure TSH receptor antibody (TRab)

2. **SCREEN** all Graves' patients for TED
   - Use the DiaGO clinical assessment tool

3. **ALERT** all Graves' patients to the risk of TED
   - Give patients TEAMEd Early Warning Cards

4. **PREVENT** TED
   - Encourage smoking cessation
   - Achieve and maintain euthyroidism rapidly
   - Avoid hypothyroidism after I-131
   - Avoid I-131 in active TED

5. **REFER** to a specialist clinic early
   - Refer patients with TED to a specialist multidisciplinary joint thyroid-eye clinic

For more information, visit: [http://www.btf-thyroid.org/teamed-5](http://www.btf-thyroid.org/teamed-5)
Achieve & maintain Euthyroidism

- Carbimazole: titration
- Thyroidectomy
- Block & Replace

Imperial College Healthcare NHS Trust
2. **SCREEN** all Graves’ patients for TED

- Use the **DiaGO clinical assessment tool**

**TeaMed DiaGO**

- 20 questions
- 13 Q patient
- 7 Q doctor

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**Table 1: Vancouver Orbitopathy Rule (VOR) – A positive response to question 1 or 2 and one of 3, 4 or 5**

1. Swelling or feeling of fullness in one or both of your upper eyelids?
2. Bags under the eyes?
3. Redness in your eyes or eyelids?
4. Do your eyes seem to be too wide open?
5. Is your vision blurry (even with glasses/contacts)?

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**Vancouver Orbitopathy Rule (VOR)**
3. ALERT all Graves’ patients to the risk of TED
   - Give patients TEAMed Early Warning Cards

For more information on TED go to www.btf-thyroid.org/teamed
or visit
Thyroid Eye Disease Charitable Trust
www.TEDct.org.uk
British Thyroid Foundation
www.btf-thyroid.org

Thyroid Eye Disease Early Warning Card

If you have been diagnosed with Graves’ Disease (an overactive thyroid gland) you have a 20% chance of developing Thyroid Eye Disease (TED).

©TEAMed Thyroid Eye Disease Amsterdam Declaration Implementation Group UK

Common symptoms are:
- Redness in the eyes or lids
- Swelling or feeling of fullness in one or both upper eyelids
- Bags under the eyes
- Eyes seem to be too wide open
- Pain in or behind the eyes
- Gritty eyes; sensitivity to light
- Blurred vision or double vision

TED may develop months or even years after Graves’ disease has been diagnosed.

Smoking increases the risk of TED.

If you develop any of these symptoms contact:

Name .................................................................
Tel .................................................................
Referral to smoking cessation services
Discourage passive smoking
Do not give radio-iodine to patients with significant eye disease requiring immunosuppression.

Good evidence that oral steroid cover and rapid treatment of post RAI hypothyroidism mitigates risk in patients with low risk of GO / mild GO.

RAI
Can worsen GO
Prummel & Wiersinga 1993
PREGO demonstrates that MDT clinic setup improves time to diagnosis (6 vs 16 months), time from first symptoms to first consultation (9 vs 16 months).

UK Multicentre audit (Orbit 2017) demonstrates similar findings.
Not enough ophthalmologists work in thyroid Eye MDT clinics in the UK
There are not enough clinics to accommodate this recommendation
MDT Thyroid Eye Network
@ Central Middlesex Hospital (since 2011)
@ Western Eye Hospital (since 2015)
@ Charing Cross Hospital (starting Jan 2018)

Endocrinologist

Oculoplastic Surgeon

MDT Clinic

Radiotherapist
Orbital Radiotherapy

Radiologist
DWI MRI

Thyroid surgeons
Thyroidectomy

Sight saving
urgent orbital decompression
(ENT/ Eyes )

immunosuppression
specialist

Oculoplastic Surgeon
Functional Decompression surgery

Squint
+ lid surgery

active

inactive
Mild disease 60%+

Tear Supplements + Selenium
There is currently no available treatment to effectively reverse the protruding eyes in the acute stage.
Immunosuppression reduces

- Soft tissue inflammation (70-80%)
- Double vision (55%)
- DON (77%)

little change in proptosis
Orbital decompression surgery treats proptosis and can save vision

Urgent sight threatening disease
DON unresponsive to IV steroids
Ulceration or infection of the cornea

Removal of walls of the orbit to expand the orbital volume to ease pressure or allow tissues to settle back into the orbit

Rehabilitation
Severe proptosis (disease should be inactive)
Generally post thyroidectomy
Potential complications

- Blindness
- Haemorrhage
- Double vision
- Periorbital numbness
- Sinusitis
- Asymmetry
  - globe malposition
  - lid malposition

Post single medial wall decompression
A study among 250 consecutive GO patients seen in an interdisciplinary thyroid-eye clinic in Germany reports significant occupational disability:
- 36% were on sick leave
- 28% were disabled
- 5% had gone into early retirement
- 3% had lost their jobs

Ponto et al 2009

Many GO patients are unhappy and this may not reflect our clinical impressions of disease activity/severity.
We collect QOL every visit

only 1 in 5 units treating TED in a UK wide survey collect QOL data

TED-QOL questionnaire

This questionnaire is designed to assess quality of life in thyroid eye disease. Please answer by circling the number that best describes your position.

1) How is your eye disease currently interfering with your overall quality of life?

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2) How is your eye disease currently affecting your ability to carry out daily activities?

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3) How is your eye disease currently affecting your satisfaction with your appearance?

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Rehabilitation Surgery improves QOL

1 Orbital Decompression
2 Squint Surgery
3 Eyelid surgery
MDT approach improves diagnosis and optimises management

Endocrinologist

Radiotherapy

Radiologist
  DWI MRI

Ophthalmologist
  Oculoplastic Surgeon

Thyroidectomy
  (thyroid surgeons)

Sight saving urgent orbital decompression
  (ENT/ Eyes)

Functional orbital Decompression surgery
  Oculoplastic surgeons

Squint & lid surgery

immunosuppression specialist

active

inactive
One patient many specialists

Endocrinologist

Ophthalmologist
Oculoplastic Surgeon

Radiologist
DWI MRI

Thyroidectomy
(thyroid surgeons)

Sight saving urgent orbital decompression
(ENT/ Eyes)

immunosuppression
specialist

Functional orbital Decompression surgery
Oculoplastic surgeons

Squint & lid surgery

active disease

inactive disease
Prevent visual loss
Modifying severity of residual disease with timely intervention

Possible effect of early, effective anti-inflammatory treatment in thyroid eye disease
special thanks to

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