Graves (thyroid eye disease): True/False

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What does it mean to say Graves is associated with thyroid dz, but not caused by it?
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*What does it mean to say Graves is associated with thyroid dz, but not caused by it?*
Thyroid eye dz (TED) is an autoimmune dz. Research suggests that, moreso than those elsewhere in the body, orbital cell type are highly sensitive to circulating TSH-receptor antibodies (TSH-R Ab)--the same circulating antibodies implicated in many forms of autoimmune thyroid disease.
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Stimulation of orbital fibroblasts by TSH-R Ab has what effects on these cells?
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Stimulation of orbital fibroblasts by TSH-R Ab has what effects on these cells?

It induces them to secrete glycosaminoglycans (GAGs), as well as pro-inflammatory cytokines (which attract inflammatory cells to the orbit). Stimulation even causes some fibroblasts to differentiate into adipocytes. Thus, much of the histopathology of TED (ie, an orbit full of ground substance, inflammatory cells, etc) can be traced directly to the effects of TSH-R Ab on orbital fibroblasts.

But to the original question: Note that the above activities are not caused by what’s going on in the thyroid gland itself. Thus, while TED often coincides with thyroid dysfunction, it does not result from it.
Graves orbitopathy is secondary to thyroid disease
Sort of, but not really. Graves is an autoimmune disease that is strongly associated with thyroid dysfunction, but it is not caused by it.

Speaking of thyroid dysfunction... What percent of Graves cases are associated with hyperthyroidism at presentation?
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*Speaking of thyroid dysfunction...* What percent of Graves cases are associated with hyperthyroidism at presentation?
About 90
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**Graves (thyroid eye disease): True/False**

- Graves orbitopathy is secondary to thyroid disease
  - True

**Speaking of thyroid dysfunction…**

*What percent of Graves cases are associated with hyperthyroidism at presentation?*
- About 90

*What percent are euthyroid at presentation?*
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Speaking of thyroid dysfunction…What percent of Graves cases are associated with hyperthyroidism at presentation?
About 90

What percent are euthyroid at presentation?
About 6
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Speaking of thyroid dysfunction... What percent of Graves cases are associated with hyperthyroidism at presentation? About 90

What percent are euthyroid at presentation? About 6

Of the euthyroid presentations, what percent will develop thyroid disease over the next 5 years?
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About half
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Can Graves dz present in association with hypothyroidism?
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Can Graves dz present in association with hypothyroidism?
Yes, albeit uncommonly. Most of these pts have disease (two words)
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Can Graves dz present in association with hypothyroidism?
Yes, albeit uncommonly. Most of these pts have Hashimoto’s thyroiditis
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Graves is aggravated by smoking
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Graves is associated with MS  *(multiple sclerosis)*
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Graves is associated with MS  False; it is associated with MG
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Graves is associated with MS  False; it is associated with MG

What does MG stand for?
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Graves is associated with MS False; it is associated with MG

What does MG stand for? Myasthenia gravis
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Graves myopathy usually results in an ET and/or a hypotropia
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The medial rectus is more likely than the inferior rectus to be affected: False; the order (most to least likely) is (all 4 rectus muscles).
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What is/are the diagnostic criteria for TED?

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How is this defined?
Either the pt has a known autoimmune thyroid condition, or s/he tests positive for one (or more) of a host of anti-thyroid antibodies.
Q

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How is this defined?
Either the pt has a known autoimmune thyroid condition, or s/he tests positive for one (or more) of a host of anti-thyroid antibodies

What are the typical orbital signs?
- Eyelid retraction
- Proptosis
- Restrictive strabismus (in a manner c/w TED myopathy)
- Compressive optic neuropathy
- Edema of the lids and/or conjunctiva

Sort of, but not really. Graves is an autoimmune disease that is strongly associated with thyroid dysfunction, but it is not caused by it.

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Typical orbital signs of TED

- Eyelid retraction
- Proptosis
- Restrictive strabismus (in a manner c/w TED myopathy)
- Compressive optic neuropathy
- Edema of the lids and/or conj (ie, chemosis)

Is the eyelid retraction unilateral, or bilateral?

It can be either

TED is characterized by a particular pattern of retraction—what is it?
Temporal flare

What does temporal flare refer to/mean?
The fact that the retraction is more pronounced at the temporal aspect of the lid

Graves is associated with MS?
False; it is associated with MG

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- Typical orbital signs of TED
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**What are the typical orbital signs?**
- Eyelid retraction
- Proptosis
- Restrictive diplopia

**Is the eyelid retraction unilateral, or bilateral?** It can be either.

**What is temporal flare?** The fact that the retraction is more pronounced at the temporal aspect of the lid.
Graves (thyroid eye disease): True/False

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Either the pt has a known autoimmune thyroid condition, or s/he tests positive for one (or more) of a host of anti-thyroid antibodies.

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- Typical orbital signs of TED
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Typical orbital signs of TED
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- Restrictive strabismus (in a manner c/w TED myopathy)
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Graves is associated with MS? False; it is associated with MG.

Graves myopathy usually results in an ET and/or a hypotropia? True. Graves myopathy more commonly affects the inferotemporal rectus (ITR) and least likely, the superotemporal rectus (STR).

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**Typical orbital signs of TED**

- Eyelid retraction
- Proptosis
- Restrictive strabismus (i.e., convergent TED myopathy)
- Compressive optic neuropathy
- Edema of the lids and/or conj (i.e., chemosis)

**Is the eyelid retraction unilateral, or bilateral?**
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What are the orbital signs?
Graves (thyroid eye disease): True/False

What is/are the diagnostic criteria for TED? Pt must have at least two of the following:

- Autoimmune thyroid dz

Typical orbital signs of TED

- Eyelid retraction
- Proptosis
- Restrictive strabismus (i.e., progressive TED versus the static TED of MG)
- Compressive optic neuropathy
- Edema of the lids and/or conj (i.e., chemosis)

Imaging findings c/w TED

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TED is characterized by a particular pattern of retraction--what is it?

‘Temporal flare’

What does temporal flare refer to/mean?

The fact that the retraction is more pronounced at the temporal aspect of the lid.
**Graves (thyroid eye disease): True/False**

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**What does temporal flare refer to/mean?**
- The fact that the retraction is more pronounced at the temporal aspect of the lid

There is an important exception to the ‘absence of lid retraction indicates it isn’t Graves dz’ contention--in fact, such pts can present with ptosis. Under what circumstance might a Graves pt present with no lid retraction, or even frank ptosis?

‘Temporal flare’

**What is/are the orbital signs?**
- Eyelid retraction
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**What are the typical orbital signs?**
- Eyelid retraction
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- Compressive optic neuropathy

- Restrictive strabismus (in a manner c/w TED myopathy)

- Proptosis

- Eyelid retraction

- Lid edema

- Optic nerve compression

- Limitation of ocular movements

- Chemosis

- Lid edema
Graves (thyroid eye disease): True/False

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**What are the diagnostic criteria for TED?** Pt must have at least two of the following:
- Autoimmune thyroid dz
- Typical orbital signs of TED
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**There is an important exception to the ‘absence of lid retraction indicates it isn’t Graves dz’ contention--in fact, such pts can present with ptosis. Under what circumstance might a Graves pt present with no lid retraction, or even frank ptosis?**
If the pt has concurrent myasthenia gravis.

**What does temporal flare refer to/mean?**
The fact that the retraction is more pronounced at the temporal aspect of the lid.

**TED is characterized by a particular pattern of retraction--what is it?**
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There is an important exception to the 'absence of lid retraction indicates it isn't Graves dz' contention--in fact, such pts can present with ptosis. Under what circumstance might a Graves pt present with no lid retraction, or even frank ptosis?

If the pt has concurrent myasthenia gravis (MG)

What one word best characterizes the clinical course of ptosis in MG?

Variable. That is, one would expect the degree of ptosis to vary from exam to exam.

What are the typical orbital signs?
- Eyelid retraction
- Proptosis

TED is characterized by a particular pattern of retraction--what is it?
'Temporal flare'

What does temporal flare refer to/mean?
The fact that the retraction is more pronounced at the temporal aspect of the lid

What is/are the diagnostic criteria for TED?
- Autoimmune thyroid dz
- Typical orbital signs of TED
- Imaging findings c/w TED

There is an important exception to the 'absence of lid retraction indicates it isn't Graves dz' contention--in fact, such pts can present with ptosis. Under what circumstance might a Graves pt present with no lid retraction, or even frank ptosis?

If the pt has concurrent myasthenia gravis (MG)

What one word best characterizes the clinical course of ptosis in MG?

Variable. That is, one would expect the degree of ptosis to vary from exam to exam.
Graves orbitopathy is secondary to thyroid disease but it is not caused by it.

- Graves is aggravated by smoking: True; Graves patients should be urged to stop smoking.
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Graves (thyroid eye disease): True/False

- What is/are the diagnostic criteria for TED? Pt must have at least two of the following:
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- How is this defined?
  -Either the pt has a known autoimmune thyroid condition, or s/he tests positive for one (or more) of a host of anti-thyroid antibodies

- What are the typical orbital signs?
  - Eyelid retraction
  - Proptosis

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- Temporal flare

- Variable

- Eyelid retraction

- Proptosis

- Restrictive strabismus (in a manner c/w TED myopathy)

- Compressive optic neuropathy

- Edema of the lids and/or conj (ie, chemosis)
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Graves (thyroid eye disease): True/False

What are the typical orbital signs of TED?
-- Eyelid retraction
-- Proptosis
-- Restrictive strabismus (in a manner c/w TED myopathy)

Is the proptosis unilateral, or bilateral?

How is this defined?
Either the pt has a known autoimmune thyroid condition, or s/he tests positive for one (or more) of a host of anti-thyroid antibodies.

What is/are the diagnostic criteria for TED?
Pt must have at least two of the following:
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MS: Multiple Sclerosis
MG: Myasthenia Gravis
TED: Thyroid Eye Disease
ET: Exophthalmos
IR: Inferior Rectus
MR: Medial Rectus
SR: Superior Rectus
LR: Lateral Rectus
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How is this defined?
Either the pt has a known autoimmune thyroid condition, or s/he tests positive for one (or more) of a host of anti-thyroid antibodies.

What are the typical orbital signs?
--Eyelid retraction
--Proptosis
--Restrictive strabismus (in a manner c/w TED myopathy)
--Compressive optic neuropathy
--Edema of the lids and/or conj (ie, chemosis)

Is the proptosis unilateral, or bilateral?
It can be either.

Where does TED rank as a cause of unilateral proptosis in adults?
#1
Graves (thyroid eye disease): True/False

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What is/are the diagnostic criteria for TED? Pt must have at least two of the following:
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- Typical orbital signs of TED
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How is this defined?
- Either the pt has a known autoimmune thyroid condition, or s/he tests positive for one (or more) of a host of anti-thyroid antibodies.

What are the typical orbital signs?
- Eyelid retraction
- Proptosis
- Restrictive strabismus (in a manner c/w TED myopathy)

Is the proptosis unilateral, or bilateral?
- It can be either.

Where does TED rank as a cause of unilateral proptosis in adults?
- #1

Where does TED rank as a cause of bilateral proptosis in adults?
Graves orbitopathy is secondary to thyroid disease. Sort of, but not really. Graves is an autoimmune disease that is strongly associated with thyroid dysfunction but is not caused by it.

Graves is aggravated by smoking. True; Graves patients should be urged to stop smoking.

Graves is associated with MS. False; it is associated with MG.

Graves myopathy usually results in an ET and/or hypotropia. True.

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**Graves (thyroid eye disease): True/False**

How is this defined? Either the pt has a known autoimmune thyroid condition, or s/he tests positive for one (or more) of a host of anti-thyroid antibodies.

What are the typical orbital signs? Eyelid retraction, proptosis, restrictive strabismus (in a manner c/w TED myopathy), compressive optic neuropathy, edema of the lids and/or conjunctiva (ie, chemosis).

Is the proptosis unilateral, or bilateral? It can be either.

Where does TED rank as a cause of bilateral proptosis in adults? #1.

Where does TED rank as a cause of unilateral proptosis in adults? #1.

Pt must have at least two of the following:

- Autoimmune thyroid dz
- Typical orbital signs of TED
- Imaging findings c/w TED
Graves (thyroid eye disease): True/False

What is/are the diagnostic criteria for TED? Pt must have at least two of the following:

- Autoimmune thyroid dz
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How is this defined?
Either the pt has a known autoimmune thyroid condition, or s/he tests positive for one (or more) of a host of anti-thyroid antibodies.

What are the typical orbital signs?
--Eyelid retraction
--Proptosis
--Restrictive strabismus (in a manner c/w TED myopathy)
--Compressive optic neuropathy
--Edema of the lids and/or conj (ie, chemosis)

Is the proptosis unilateral, or bilateral?
It can be either.

Where does TED rank as a cause of unilateral proptosis in adults?
#1

Where does TED rank as a cause of bilateral proptosis in adults?
#1

What about in the pediatric population--is the relationship between proptosis and Graves dz as strong?
No. Graves is rare in children, and when it does occur, only about 10% of pts present with proptosis. (Rule of thumb: In children, proptosis is more likely to be infection or neoplastic than to be inflammatory.)
**Graves (thryoid eye disease): True/False**

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- Sort of, but not really. Graves is an autoimmune disease that is strongly associated with thyroid dysfunction, but it is not caused by it.
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**How is this defined?**
- Either the pt has a known autoimmune thyroid condition, or s/he tests positive for one (or more) of a host of anti-thyroid antibodies.

**What are the typical orbital signs?**
- Eyelid retraction
- Proptosis
- Restrictive strabismus (in a manner c/w TED myopathy)
- Compressive optic neuropathy
- Edema of the lids and/or conj (ie, chemosis)

**Is the proptosis unilateral, or bilateral?**
- It can be either.

**Where does TED rank as a cause of unilateral proptosis in adults?**
- #1

**Where does TED rank as a cause of bilateral proptosis in adults?**
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**Where does TED rank as a cause of unilateral proptosis in kids?**
- #1

**Where does TED rank as a cause of bilateral proptosis in kids?**
- #1
Graves (thyroid eye disease): True/False

What is/are the diagnostic criteria for TED? Pt must have at least two of the following:
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Where does TED rank as a cause of unilateral proptosis in adults?
#1

Where does TED rank as a cause of bilateral proptosis in adults?
#1

kids
Graves orbitopathy is secondary to thyroid disease

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**Graves (thyroid eye disease): True/False**

**What is/are the diagnostic criteria for TED?** Pt must have at least two of the following:
- Autoimmune thyroid dz
- Typical orbital signs of TED
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**How is this defined?** Either the pt has a known autoimmune thyroid condition, or s/he tests positive for one (or more) of a host of anti-thyroid antibodies.

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- Eyelid retraction
- Proptosis
- Restrictive strabismus (in a manner c/w TED myopathy)
- Compressive optic neuropathy
- Edema of the lids and/or conj (ie, chemosis)

**What does this mean, ‘in a manner c/w TED myopathy’?**

---

TED stands for thyroid eye disease.
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What does this mean, ‘in a manner c/w TED myopathy’?
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Graves orbitopathy is secondary to thyroid disease

- True; Graves is an autoimmune disease that is strongly associated with thyroid dysfunction, but it is not caused by it.

- True; Graves patients should be urged to stop smoking.

- False; it is associated with MG, not MS.

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- What is/are the diagnostic criteria for TED?
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- Which of these is the most common orbital sign in TED?
  - Lid retraction

- What percent of TED pts will demonstrate lid retraction at presentation?
  - About 75%

- What percent will demonstrate it at some point during the disease process?
  - Over 90%
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Imaging findings c/w TED

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Q

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What are the typical orbital signs?

- Eye lid retraction
- Proptosis
- Eye lid retraction
- Compressive optic neuropathy
- Lid edema

In the present context, to what does the term lid lag refer?

When a person who doesn’t have TED moves into downgaze, their upper lid margin will follow the globe. In contrast, when a TED pt looks down, their upper lid remains elevated, ie, it “lags.” This is a classic TED finding.

What is the eponymous name for lid lag?
von Graefe’s sign
Graves (thyroid eye disease): True/False

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Typical orbital signs of TED

- Eye lid retraction
- Proptosis
- Non-limiting strabismus (c/w TED myopathy)
- Compressive optic neuropathy
- Edema of the lids and/or conj (ie, chemosis)

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**What is/are the diagnostic criteria for TED?**
Pt must have at least two of the following:
- Autoimmune thyroid dz
- Typical orbital signs of TED
- Imaging findings c/w TED

**It may be classic for TED, but is it pathognomonic?**

**In the present context, to what does the term lid lag refer?**
When a person who doesn’t have TED moves into downgaze, their upper lid margin will follow the globe. In contrast, when a TED pt looks down, their upper lid remains elevated, ie, it ‘lags.’ This is a classic TED finding.

**What is the eponymous name for lid lag?** von Graefe’s sign

**Graves is associated with MG**

**Graves is associated with MS** False; it is associated with MG.

**Graves is aggravated by smoking** True; Graves patients should be urged to stop smoking.

**Graves is usually due to thyroid dysfunction** Sort of, but not really. Graves is an autoimmune disease that is strongly associated with thyroid dysfunction, but it is not caused by it.

**Graves myopathy usually results in an ET and/or hypotropia** True
Graves (thyroid eye disease): True/False

What is/are the diagnostic criteria for TED? Pt must have at least two of the following:
- Autoimmune thyroid dz
- Typical orbital signs of TED
- Imaging findings c/w TED

Sort of, but not really. Graves is an autoimmune disease that is strongly associated with thyroid dysfunction, but it is not caused by it.

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Graves is associated with MS. False; it is associated with MG.

Graves is associated with myopathy. True

Graves myopathy usually results in an ET and/or a hypotropia. True

The medial rectus is more likely than the inferior rectus to be affected. False; the order (most to least likely) is IR > MR > SR > LR.

How is this defined?
Either the pt has a known autoimmune thyroid condition, or s/he tests positive for one (or more) of a host of anti-thyroid antibodies.

What are the typical orbital signs?
- Eyelid retract
- Proptosis
- Eye lid margin will follow the globe. In contrast, when a TED pt looks down, their upper lid remains elevated, ie, it ‘lags.’ This is a classic TED finding.

What is the eponymous name for lid lag?
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It may be classic for TED, but is it pathognomonic?
No

In the present context, to what does the term lid lag refer?
When a person who doesn’t have TED moves into downgaze, their upper lid margin will follow the globe. In contrast, when a TED pt looks down, their upper lid remains elevated, ie, it ‘lags.’ This is a classic TED finding.

What are the typical orbital signs of TED?

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Graves is associated with MS False; it is associated with MG

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The medial rectus is more likely than the inferior rectus to be affected False; the order (most to least likely) is IR>MR>SR>LR

It may be classic for TED, but is it pathognomonic? No

What are the typical orbital signs of TED?
- Lid retraction
- Proptosis
- Ocular motility restriction (TED/Graves
- Compressive optic neuropathy
- Lid oedema (chemosis)

What is the eponymous name for lid lag when it is present in a non-TED pt?

von Graefe’s sign

What is the eponymous name for lid lag?

von Graefe’s sign

In the present context, to what does the term lid lag refer?

When a person who doesn’t have TED moves into downgaze, their upper lid margin will follow the globe. In contrast, when a TED pt looks down, their upper lid remains elevated, ie, it ‘lags’

This is a classic TED finding.
Graves (thyroid eye disease): True/False

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Graves (thyroid eye disease): True/False

What is/are the diagnostic criteria for TED? Pt must have at least two of the following:

- Autoimmune thyroid dz
- Typical orbital signs of TED
- Imaging findings c/w TED

How is this defined?
Either the pt has a known autoimmune thyroid condition, or s/he tests positive for one (or more) of a host of anti-thyroid antibodies

What are these findings?

- Enlargement of the EOMs (in a manner c/w TED myopathy)

What are the typical orbital signs?

- Eyelid retraction
- Proptosis
- Restrictive strabismus (in a manner c/w TED myopathy)
- Compressive optic neuropathy
- Edema of the lids and/or conj (ie, chemosis)

Sort of, but not really. Graves is an autoimmune disease that is strongly associated with thyroid dysfunction, but it is not caused by it. Graves is aggravated by smoking, so patients should be urged to stop smoking.

- Graves is associated with MS False; it is associated with MG
- Graves myopathy usually results in an ET and/or a hypotropia True
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What does this mean, ‘in a manner c/w TED myopathy’?

What are these findings?
Enlargement of the EOMs (in a manner c/w TED myopathy)

Look at the order (most likely):
- Enlargement of the EOMs is fusiform or ‘tendon sparing’
- Involvement of the EOMs occurs in this order:
  - IR>MR>SR>LR

Graves orbitopathy is secondary to thyroid disease, but it is not caused by it. Graves is aggravated by smoking and patients should be urged to stop smoking.

Graves is associated with MG

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What does this mean, 'in a manner c/w TED myopathy'?
It means two things:

- Enlargement of the EOMs is fusiform or 'tendon sparing'
- Involvement of the EOMs occurs in this order:
  - Enlargement of the EOMs
  - Shape
  - 'two words'

- Involution of the EOMs occurs in this order:
  - Inferior rectus (IR) > Medial rectus (MR) > Superior rectus (SR) > Lateral rectus (LR)
Graves orbitopathy is secondary to thyroid disease. Sort of, but not really. Graves is an autoimmune disease that is strongly associated with thyroid dysfunction, but it is not caused by it. Graves is aggravated by smoking; true; Graves patients should be urged to stop smoking. Graves is associated with MS; false; it is associated with MG. Graves myopathy usually results in an ET and/or a hypotropia; true. The medial rectus is more likely than the inferior rectus to be affected; false; the order (most to least likely) is IR > MR > SR > LR.

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What is the natural history of TED?

It is a self-limited disease that tends to 'burn itself out' over time.

How is TED managed?

Other than smoking cessation (which all TED pts should do), management depends upon disease severity:

--Mild disease can be managed symptomatically (ie, maneuvers to lessen surface dryness/irritation)
--Moderate disease requires more aggressive surface protection (eg, moisture goggles), and PO steroids
--Severe disease involves sight-threatening complications such as corneal decompensation, and/or optic neuropathy. This necessitates more aggressive steroid therapy, and consideration should be given to the use of steroid-sparing IMT and/or orbital radiation therapy. Orbital decompression surgery while the pt has floridly active TED is not ideal, and should be considered only as a last resort.

What about treating the concurrent thyroid disease?

Rendering the pt euthyroid is an important goal for TED pts (to be pursued by Endo/IM, of course). However, it is important to note that some treatments in this regard can aggravate the TED by increasing immune activity against the TSH-receptor antigens that are responsible for TED.
Graves (thyroid eye disease): True/False

What is the natural history of TED?
It is a self-limited disease that tends to ‘burn itself out’ over time, but may leave disfiguring sequelae

rectus to be affected  False; the order (most to least likely) is IR>MR>SR>LR
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On average, how long does it take to burn itself out?

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<tr>
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How long for nonsmokers? ~1 year.

How long for smokers? 2-3 years.

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What is the natural history of TED?
It is a self-limited disease that tends to ‘burn itself out’ over time, but may leave disfiguring sequelae.

How is TED managed?
Other than smoking cessation (which all TED pts should do), management depends upon disease severity:

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--- True/False
Graves orbitopathy is secondary to thyroid disease
--- True/False
Graves is aggravated by smoking
--- False; Graves patients should be urged to stop smoking
--- False; it is associated with MG
--- True
Graves myopathy usually results in an ET and/or a hypotropia
--- False; the order (most to least likely) is IR>MR>SR>LR
--- True
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If surgery during active TED is relatively contraindicated, when should it be considered?
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If surgery during active TED is relatively contraindicated, when should it be considered?
Once the pt is euthyroid, and his/her orbital condition has been stable for at least 6 months.
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Suppose a pt meeting those criteria needs orbital decompression, has strabismus, and also has malpositioned eyelids. What should the overall surgical strategy be?

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*Q*
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**Suppose a pt meeting those criteria needs orbital decompression, has strabismus, and also has malpositioned eyelids. What should the overall surgical strategy be?**
Because orbital-decompression surgery will affect both EOM and lid position, the decompression surgery must precede strabismus and/or lid surgery. Likewise, because strabismus surgery will affect lid position, the strabismus surgery must precede the lid surgery. Putting it all together, the surgical order is as follows:

1. Decompression
2. Strabismus
3. Eyelids
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**What about treating the concurrent thyroid disease?**
Rendering the pt euthyroid is an important goal for TED pts (to be pursued by Endo/IM, of course). However, it is important to note that some treatments in this regard can aggravate the TED by increasing immune activity against the TSH-receptor antigens that are responsible for TED.

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