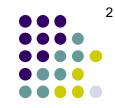


Graves aka Thyroid Eye Disease: True/False



• Graves orbitopathy is secondary to thyroid disease





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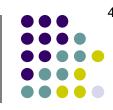


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What does it mean to say Graves is associated with thyroid dz, but not caused by it?

## Q/A

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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 <u>cell type</u> 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.

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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.

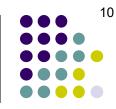
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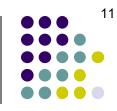
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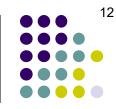


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What percent of Graves cases are associated with hyperthyroidism at presentation?

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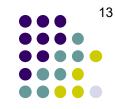


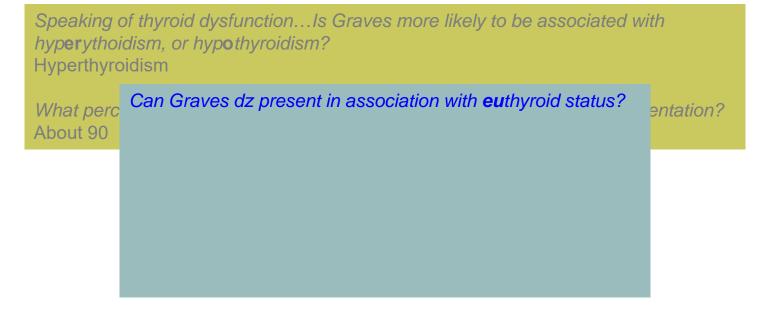
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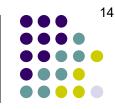
What percent of Graves cases are associated with hyperthyroidism at presentation? About 90

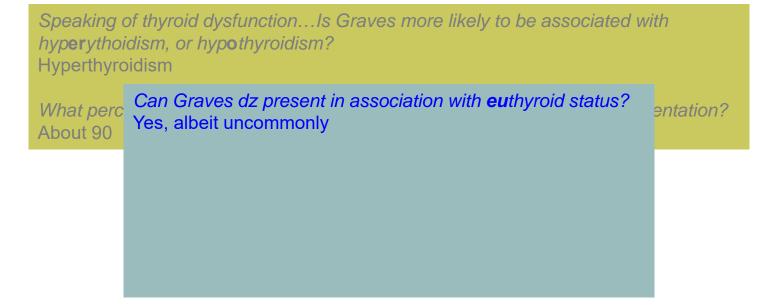
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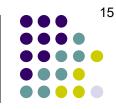


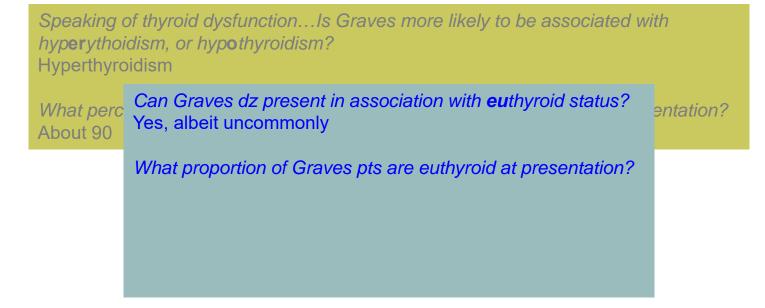
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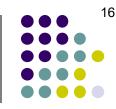


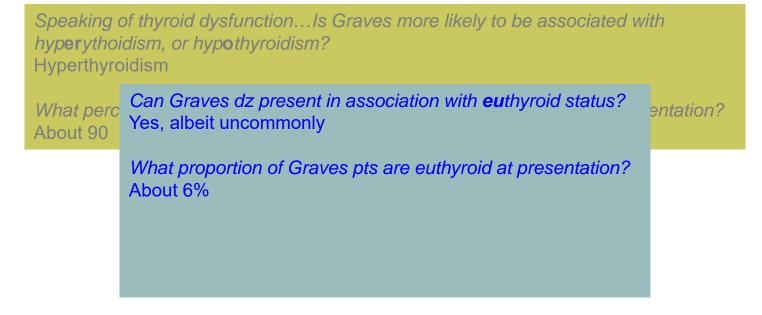
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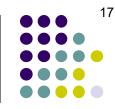


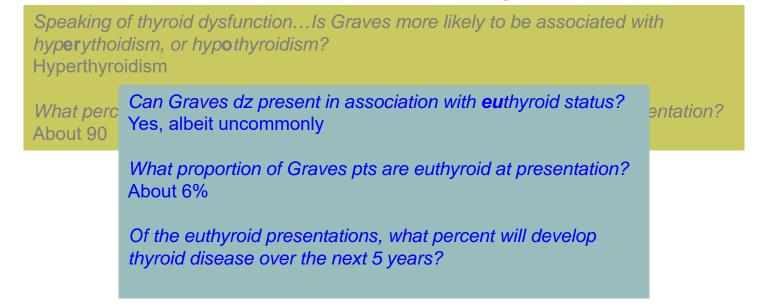
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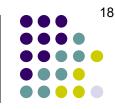


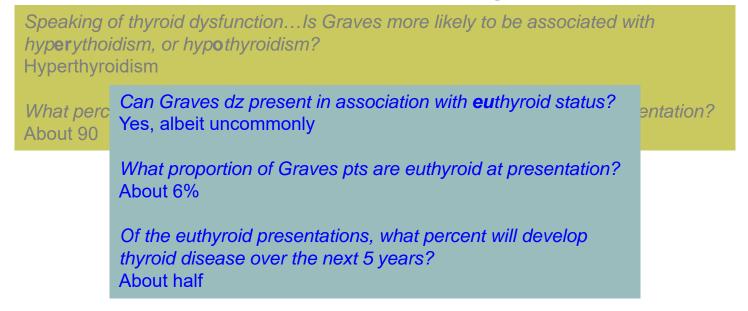
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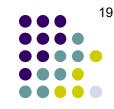


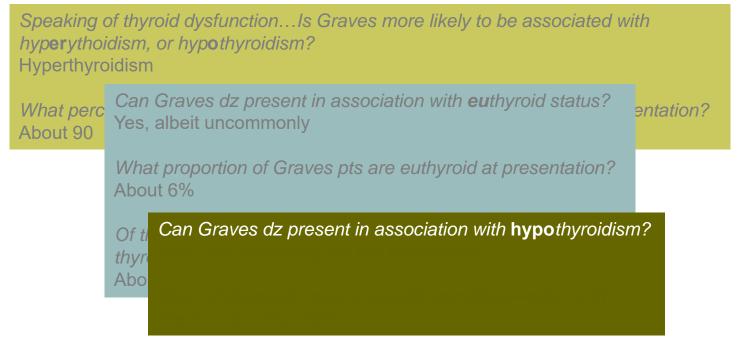
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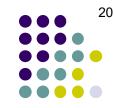


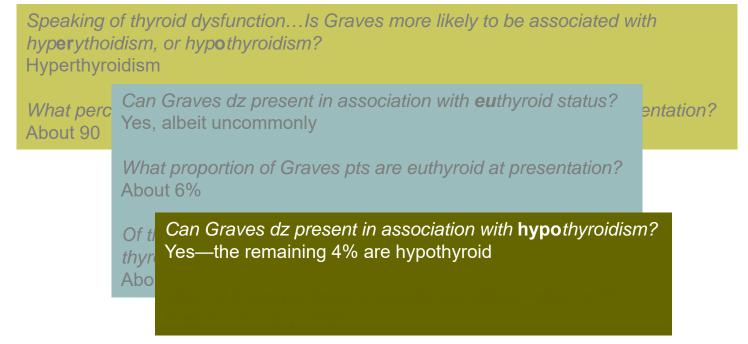
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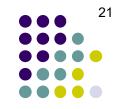


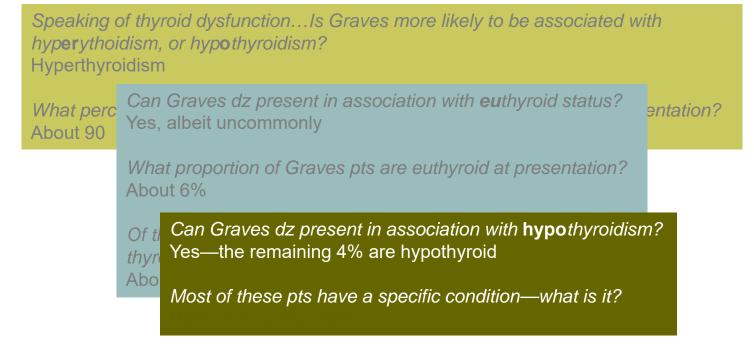
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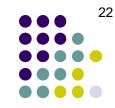


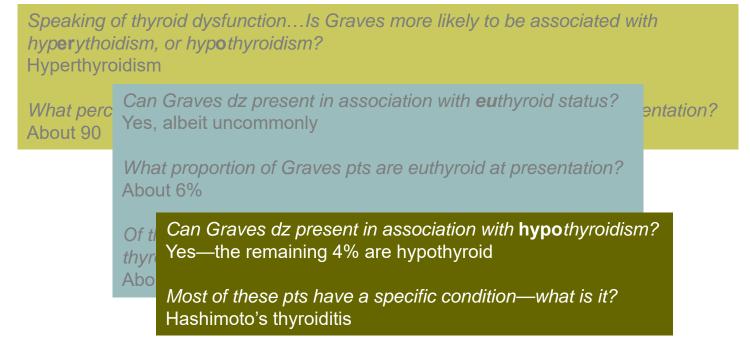
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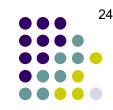
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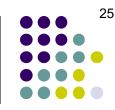


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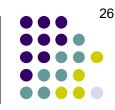
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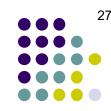
Smoking increases the likelihood of developing TED by how much?

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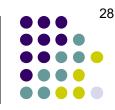
Smoking increases the likelihood of developing TED by how much? A smoker is 7x more likely to develop TED than a nonsmoker!



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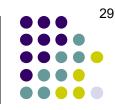
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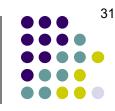
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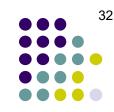
What does MG stand for in this context?

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What does MG stand for in this context? Myasthenia gravis



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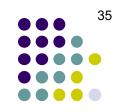




Esotropia

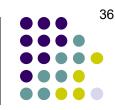
Hypotropia

#### **TED:** Strabismus



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# A/Q



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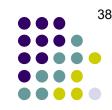
(all 4 rectus muscles)

# Α



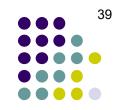
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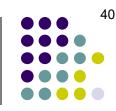


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• The me rectus to likely) is

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Д

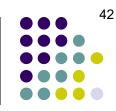
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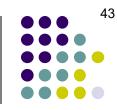
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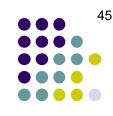
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What is/are the diagnostic criteria for TED?

disease that is strongly associated with thyroid dysfunction, but it is not *caused* by it

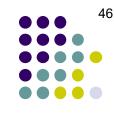
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What is/are the diagnostic criteria for TED? Pt must have at least two of the following:

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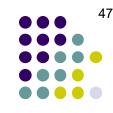


 What is/are the diagnostic criteria for TED? Pt must have at least two of the following:

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

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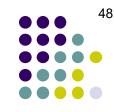
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 How is this defined?
 d by smoking True; Graves

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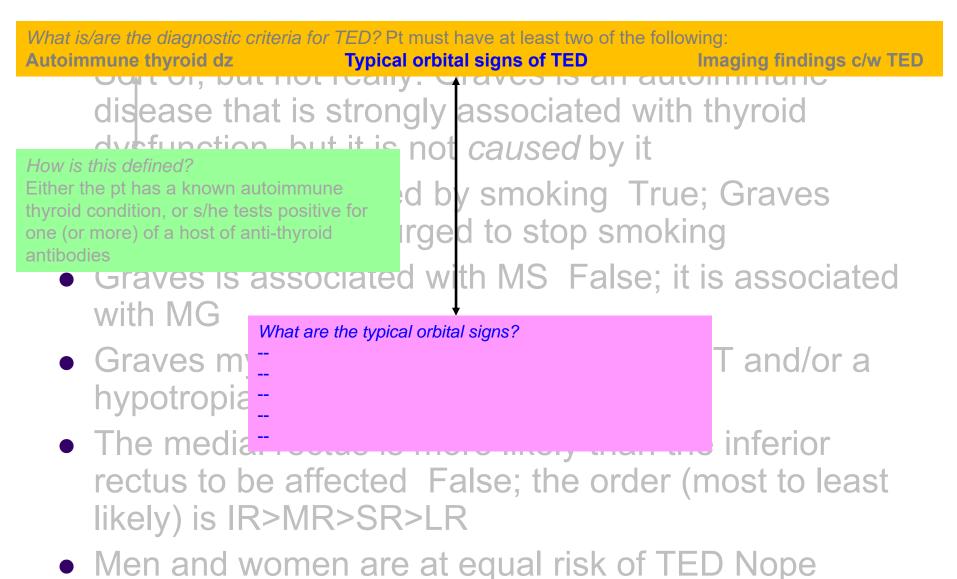
disease that is strongly associated with thyroid dynamics but it is not caused by it

#### 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 d by smoking True; Graves rged to stop smoking

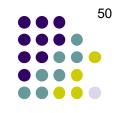
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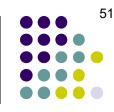


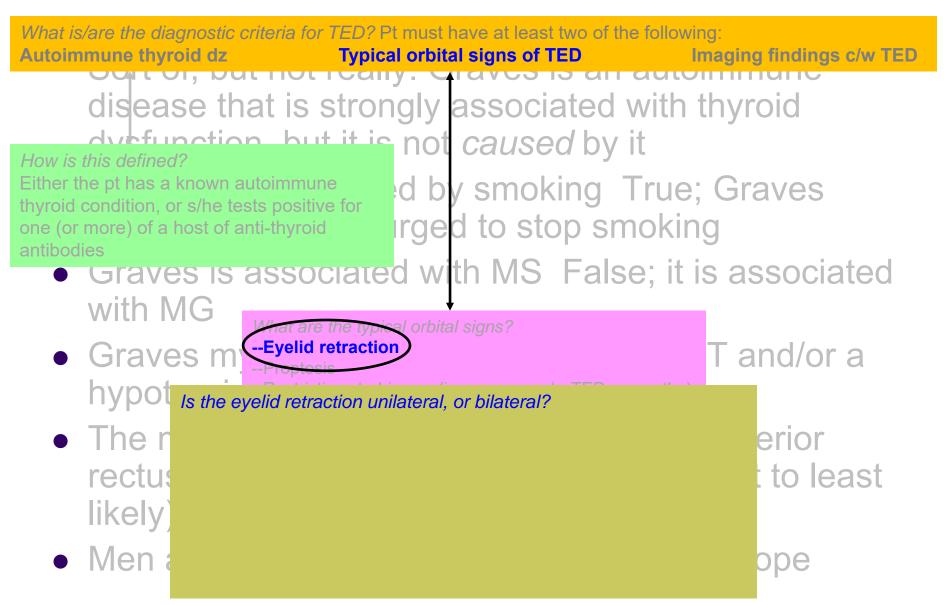
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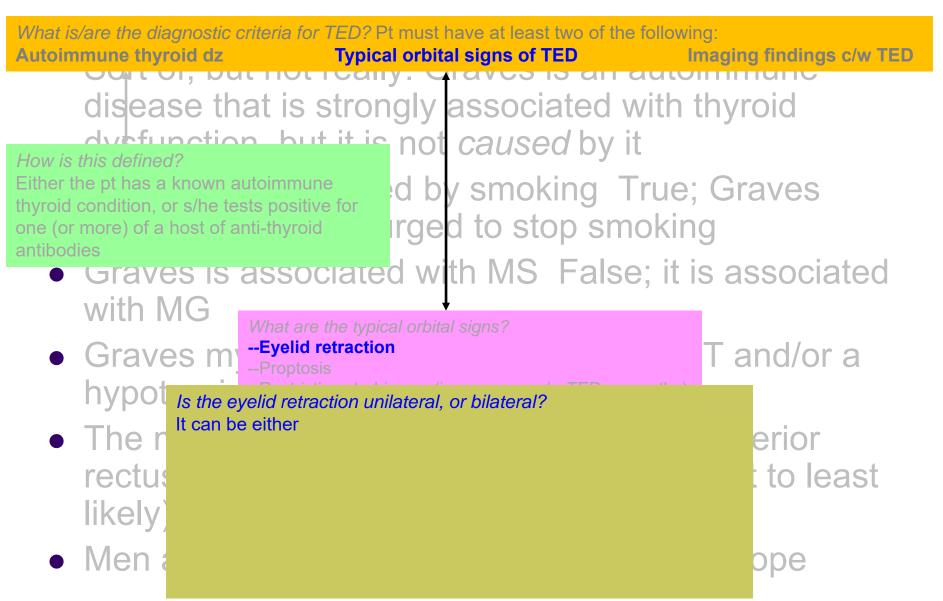
What is/are the diagnostic criteria for TED? Pt must have at least two of the following: Autoimmune thyroid dz Typical orbital signs of TED Imaging findings c/w TED Our OI, but not really. Craves is an autoinmune disease that is strongly associated with thyroid dysfunction, but it is not caused by it How is this defined? by smoking True; Graves Either the pt has a known autoimmune d thyroid condition, or s/he tests positive for irged to stop smoking one (or more) of a host of anti-thyroid antibodies Graves is associated with MS False; it is associated with MG What are the typical orbital signs? Graves m --Eyelid retraction T and/or a hypotropia --Restrictive strabismus (in a manner c/w TED myopathy) --Compressive optic neuropathy • The media--Edema of the lids and/or conj (ie, chemosis) inferior rectus to be affected False; the order (most to least likely) is IR>MR>SR>LR Men and women are at equal risk of TED Nope















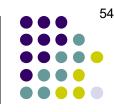
Unilateral\*

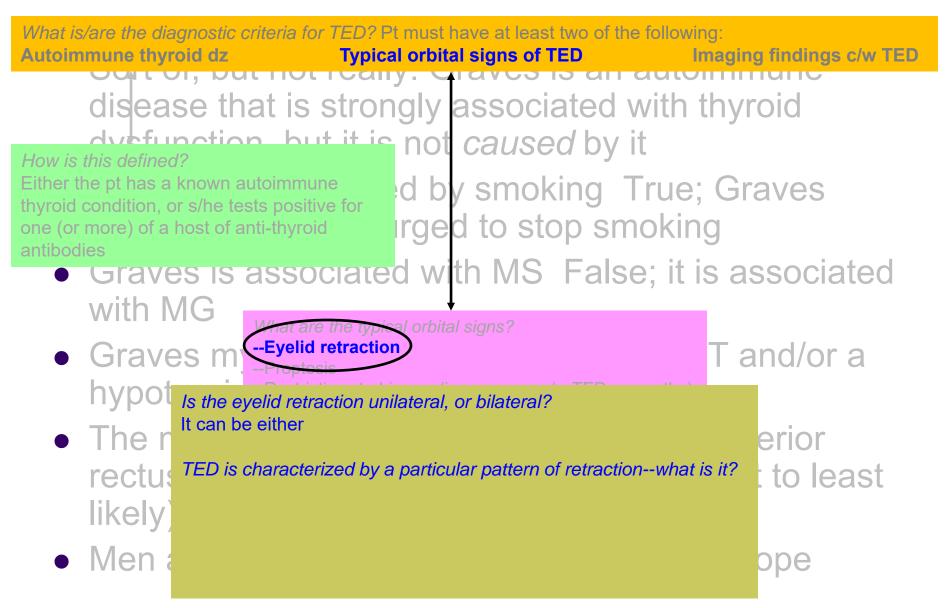


Bilateral

#### **TED: Lid retraction**

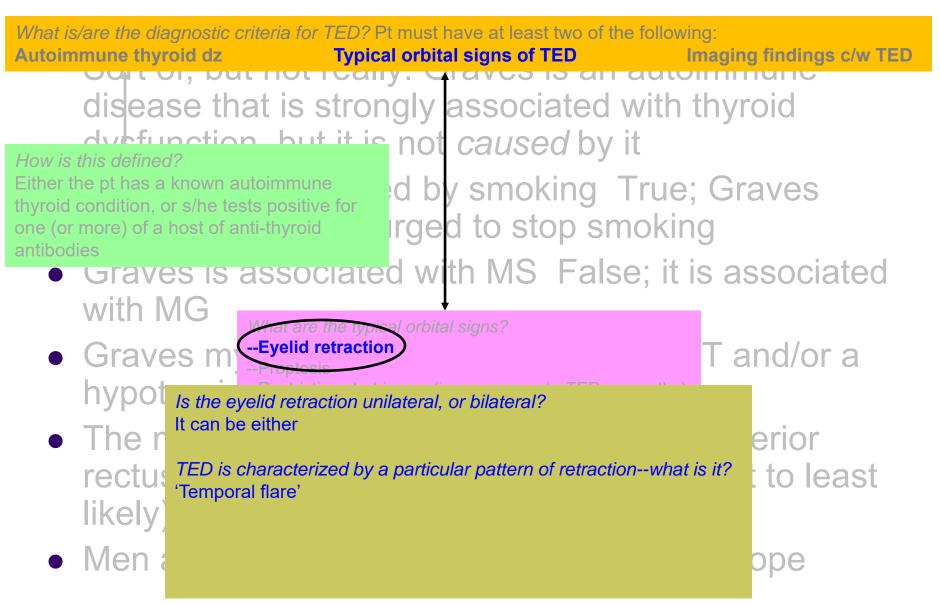
\*Or highly asymmetric, at least

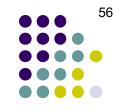


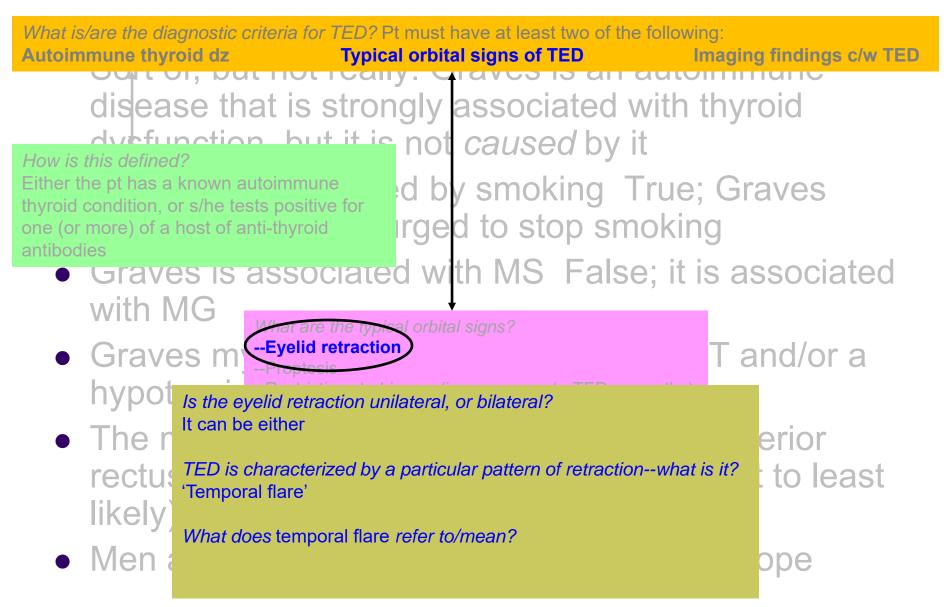




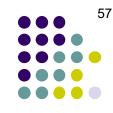


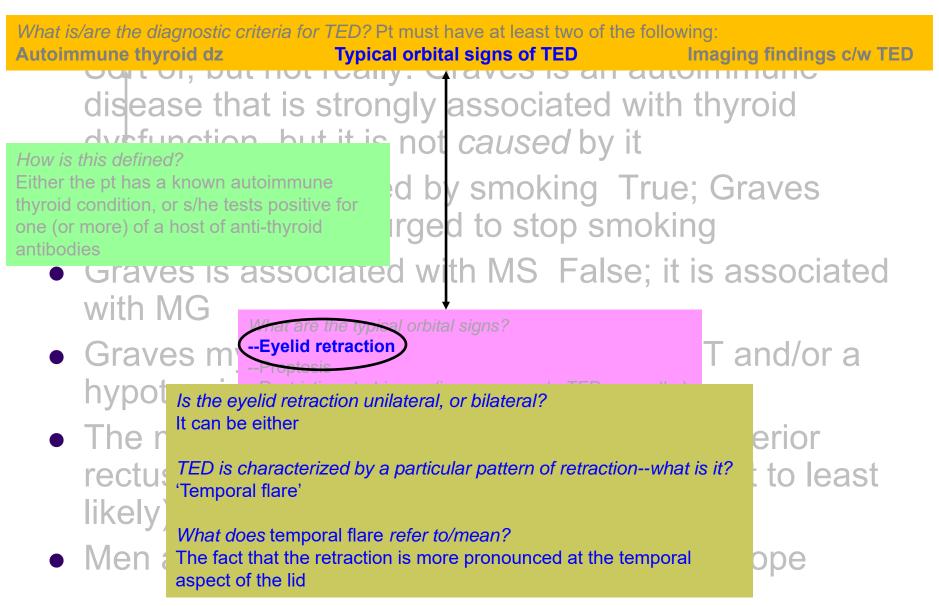














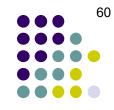
TED: Lid retraction with temporal flare





What is/are the diagnostic criteria for TED? Pt must have at least two of the follo Autoir What well-known brainstem syndrome is associated with lid retraction?		g findings c/w TED
	n thy	roid
one (or antibod	ing	aves ssociated
Graves m     Graves m	Та	and/or a
<ul> <li>hypot Is the eyelid retraction unilateral, or bilateral?</li> <li>The n rectus likely</li> <li>TED is characterized by a particular pattern of retractionwh 'Temporal flare'</li> <li>What does temporal flare refer to/mean?</li> </ul>	at is it?	erior to least
• Men a the fact that the retraction is more pronounced at the tempor aspect of the lid	ral	ope





What is/are the diagnostic criteria for TED? Pt must have at least two of the follo Autoir What well-known brainstem syndrome is associated with lid retraction? Parinaud syndrome	wing: Imaging findings c/w TED thyroid
one (or antibod	e; Graves ing t is associated
Graves m     Graves m	T and/or a
<ul> <li>hypot Is the eyelid retraction unilateral, or bilateral?</li> <li>The r recture likely</li> <li>Men a</li> </ul>	. 10 16431



What is Autoir	s/are the diagnostic criteria for TED? Pt must have at least two of the follo What well-known brainstem syndrome is associated with lid retraction? Parinaud syndrome What is the eponymous name for lid retraction in Parinaud syndrome?		g findings c/w TED Toid
How is Either thyroid one (or antibod		ing	aves ssociated
•	Graves m hypot is the eyelid retraction unilateral, or bilateral?	Та	nd/or a
•	The n rectuse likely	at is it?	erior to least
٠	What does temporal flare <i>refer to/mean?</i> The fact that the retraction is more pronounced at the temporal aspect of the lid	al	ope





What is/are the diagnostic criteria for TED? Pt must have at least two of the Autoir         Autoir         What well-known brainstem syndrome is associated with lid retraction         Parinaud syndrome         What is the eponymous name for lid retraction in Parinaud syndrome         How is         Either         thyroid         one (or	ion? Imaging findings c/w TE	D
<ul> <li>antibod</li> <li>WILLI IVIG</li> <li>WILLI IVIG</li> <li>Graves m</li> </ul>	t is associated T and/or a	
<ul> <li>hypot Is the eyelid retraction unilateral, or bilateral? It can be either</li> <li>The recture recture likely</li> <li>Men</li> <li>Men</li> <li>Is the eyelid retraction unilateral, or bilateral? It can be either</li> <li>TED is characterized by a particular pattern of retraction 'Temporal flare'</li> <li>What does temporal flare refer to/mean? The fact that the retraction is more pronounced at the temporal flare</li> </ul>	. 10 16451	



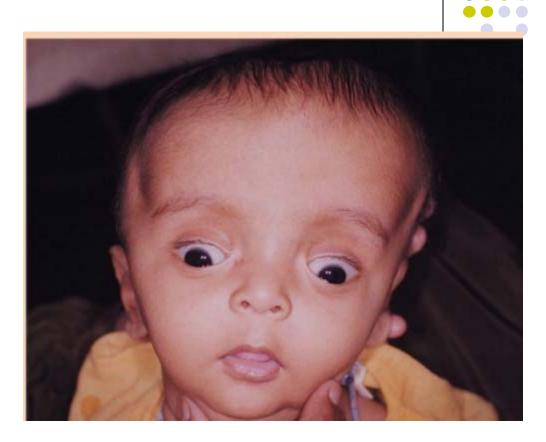
What is Autoir How is	s/are the diagnostic criteria for TED? Pt must have at least two of the follo What well-known brainstem syndrome is associated with lid retraction? Parinaud syndrome What is the eponymous name for lid retraction in Parinaud syndrome? Collier's sign	ing: Imaging findings c/w TED thyroid
Either thyroid one (or antibod	Lid retraction  	e; Graves ng is associated
•	Graves m	T and/or a
•	<ul> <li>Typot Is the eyelid retraction unilateral, or bilateral?</li> <li>The n</li> <li>the eyelid retraction unilateral, or bilateral?</li> <li>It can be either</li> <li>TED is characterized by a particular pattern of retractionwhen 'Temporal flare'</li> <li>What does temporal flare refer to/mean?</li> <li>Men a fact that the retraction is more pronounced at the temporal aspect of the lid</li> </ul>	. 10 16431





What is/are the diagnostic criteria for TED? Pt must have at least two of the follow         Autoir         What well-known brainstem syndrome is associated with lid retraction?         Parinaud syndrome         What is the eponymous name for lid retraction in Parinaud syndrome?         Online is associated with lid syndrome?	wing: Imaging findings c/w TED Official Control of the second sec
Light-near dissociation Impaired upgaze Convergence-retraction nystagmus	e; Graves ing t is associated
<ul> <li>Graves m</li> <li>Graves m</li> </ul>	T and/or a
<ul> <li>hypot is the eyelid retraction unilateral, or bilateral?</li> <li>The right can be either</li> <li>The right can be either</li> <li>TED is characterized by a particular pattern of retractionwho the temporal flare?</li> <li>What does temporal flare refer to/mean?</li> <li>Men a fact that the retraction is more pronounced at the temporal aspect of the lid</li> </ul>	. 10 16431



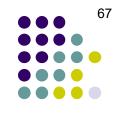


Parinaud syndrome. The combination of lid retraction + impaired upgaze gives rise to a characteristic appearance known as *setting sun sign* 



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 Our OI, but not really. Craves is an autoinmune disease that is strongly associated with thyroid dysfunction, but it is not caused by it How is this defined? Either the pt has a known autoimmune d by smoking True; Graves thyroid condition, or s/he tests positive for rged to stop smoking one (or more) of a host of anti-thyroid antibodies Graves is associated with MS False; it is associated with MG --Eyelid retraction T and/or a Graves m 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? least 'Temporal flare' likely What does temporal flare refer to/mean? Men The fact that the retraction is more pronounced at the temporal pe aspect of the lid





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disease that is strongly associated with thyroid

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by smoking True; Graves d rged to stop smoking

Graves is associated with MS False; it is associated

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Graves m

--Eyelid retraction

T and/or a

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 ... least

likelv

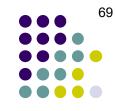
Men

Gotor 'Temporal flare'

What does temporal flare refer to/mean?

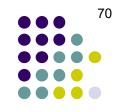
The fact that the retraction is more pronounced at the temporal aspect of the lid

pe



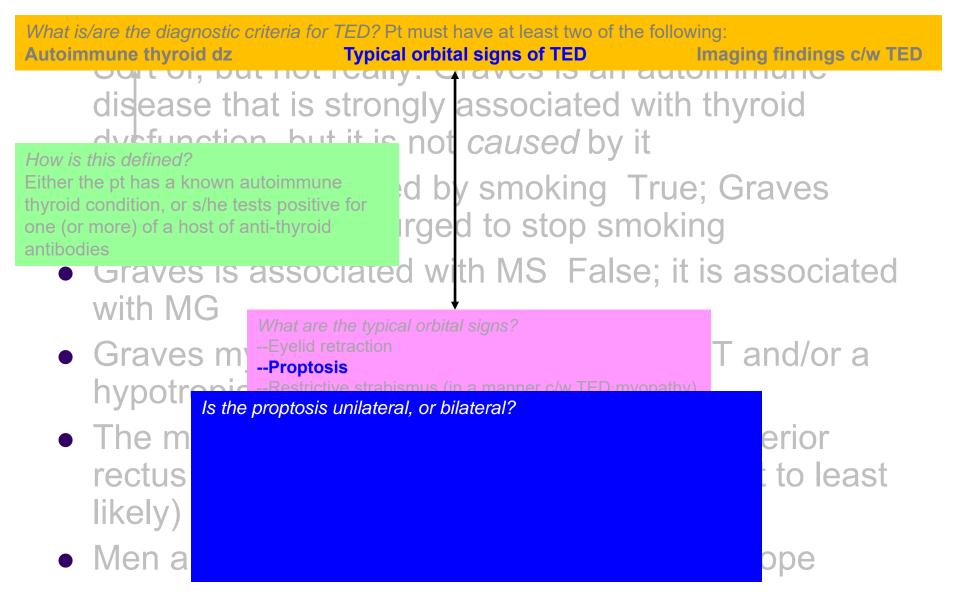
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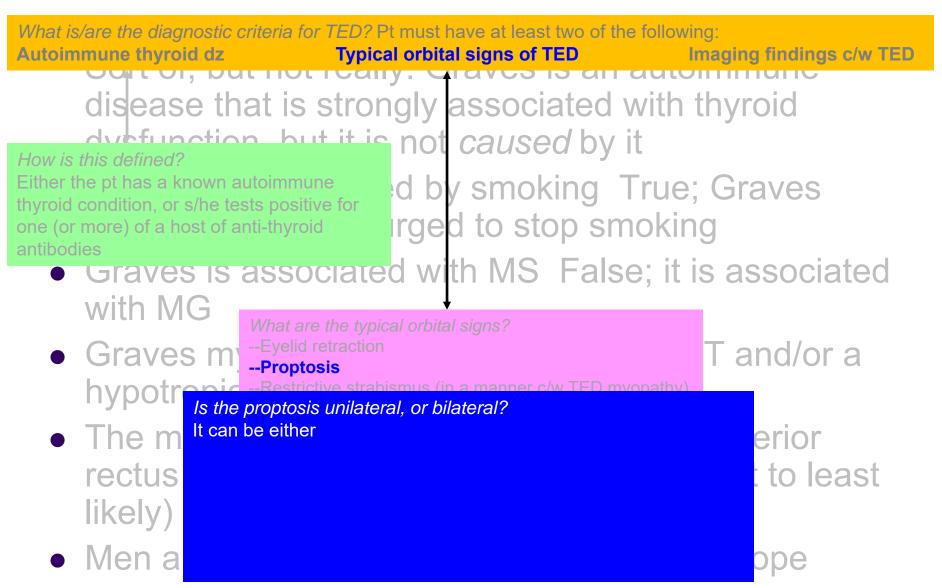
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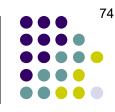
Unilateral\*

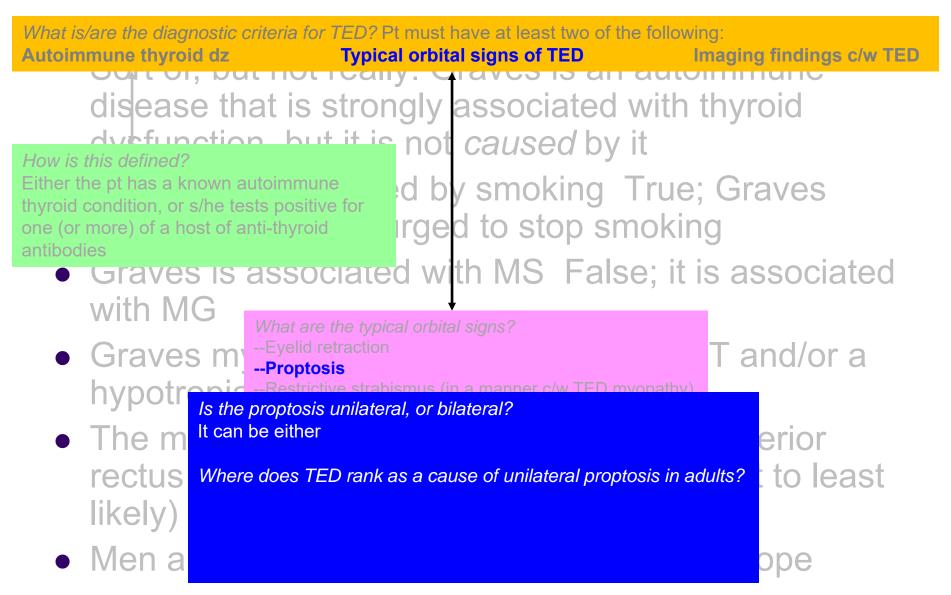


Bilateral

### **TED:** Proptosis

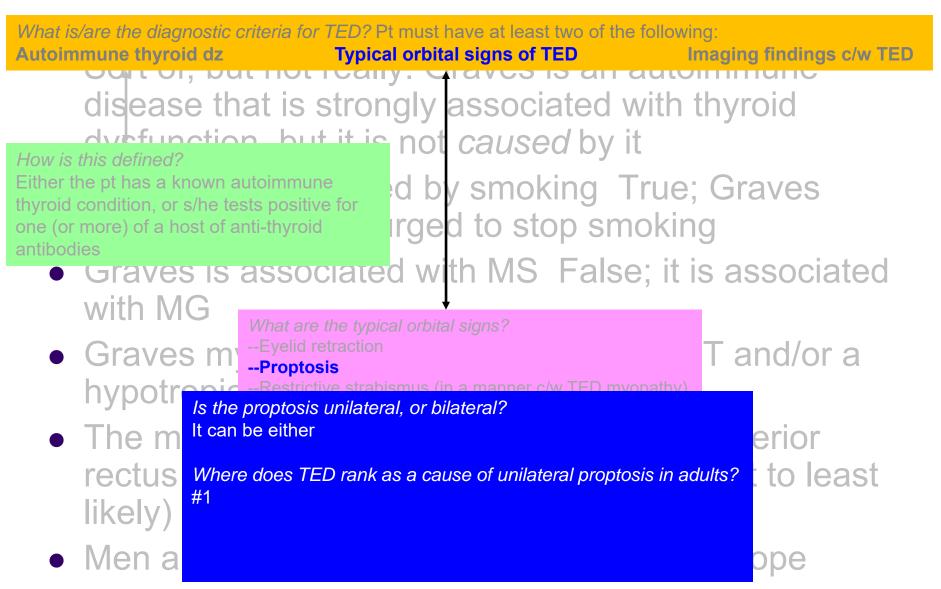
\*Or highly asymmetric, at least

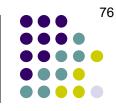


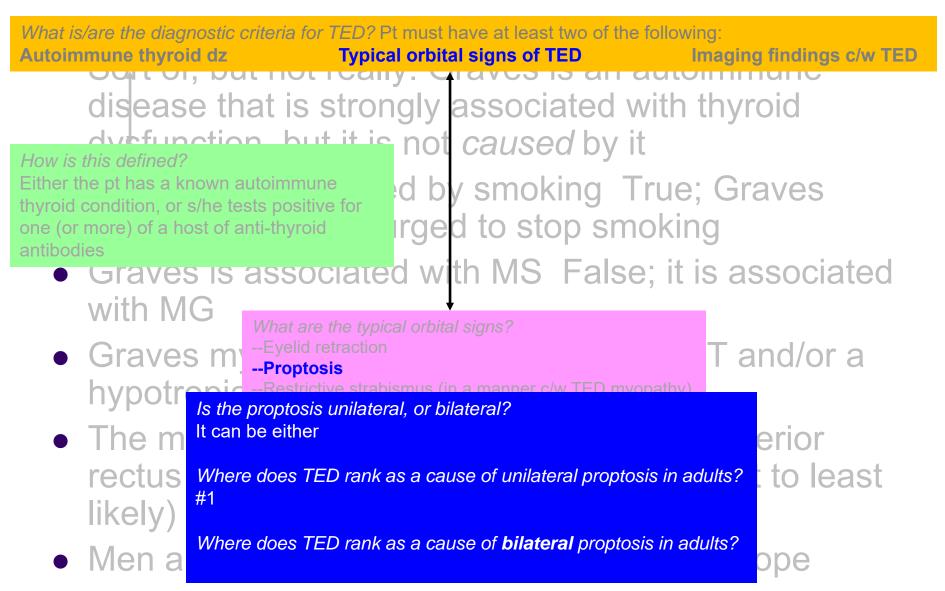






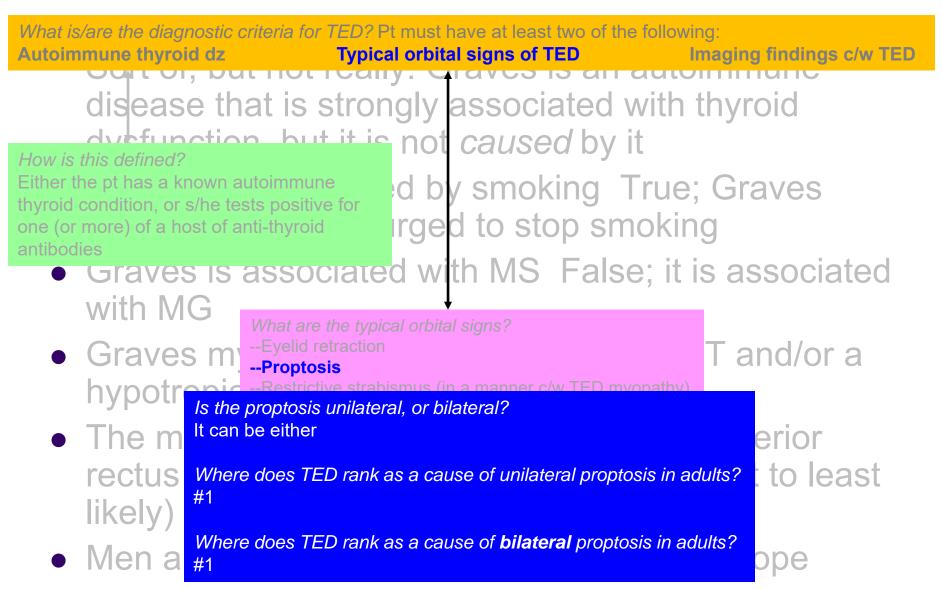


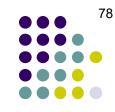


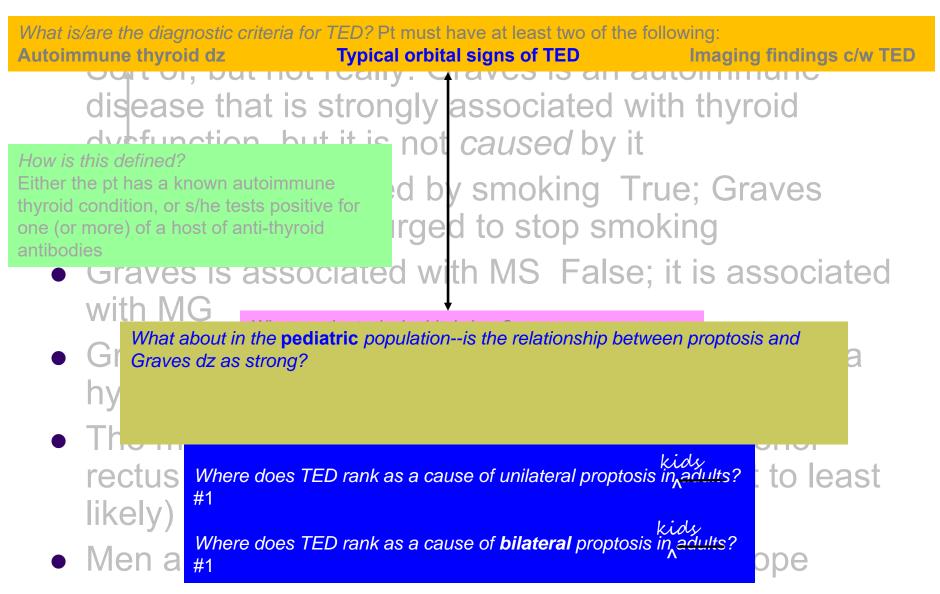






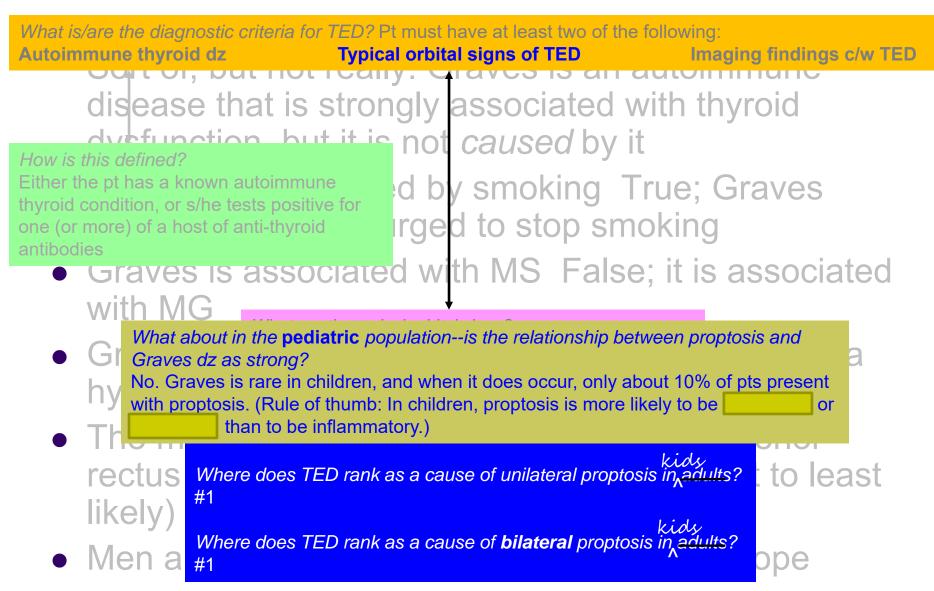




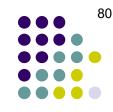


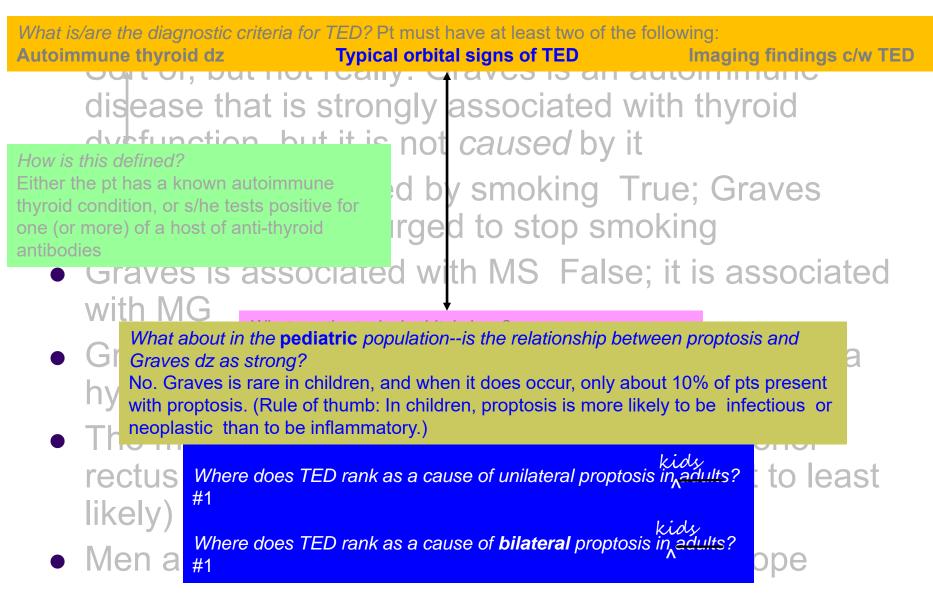










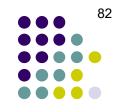




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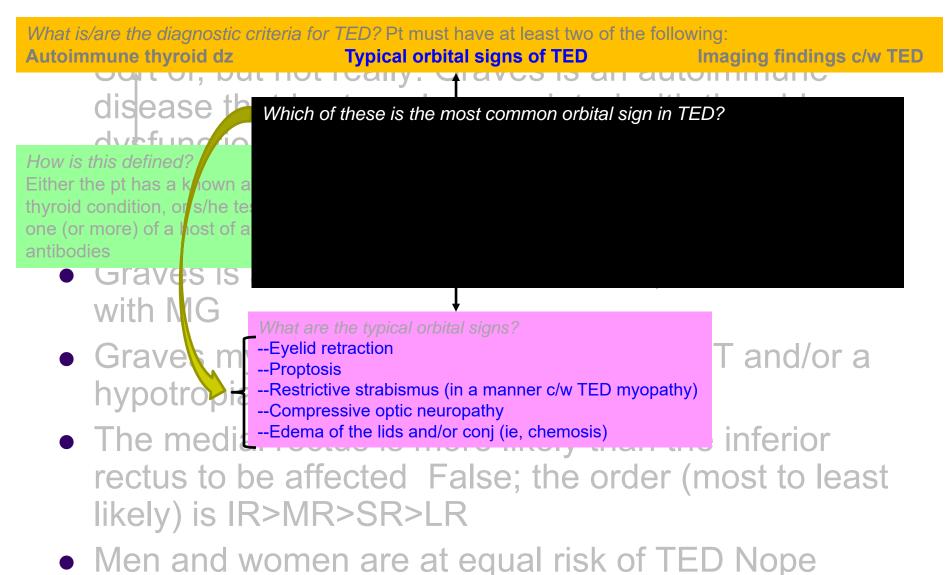
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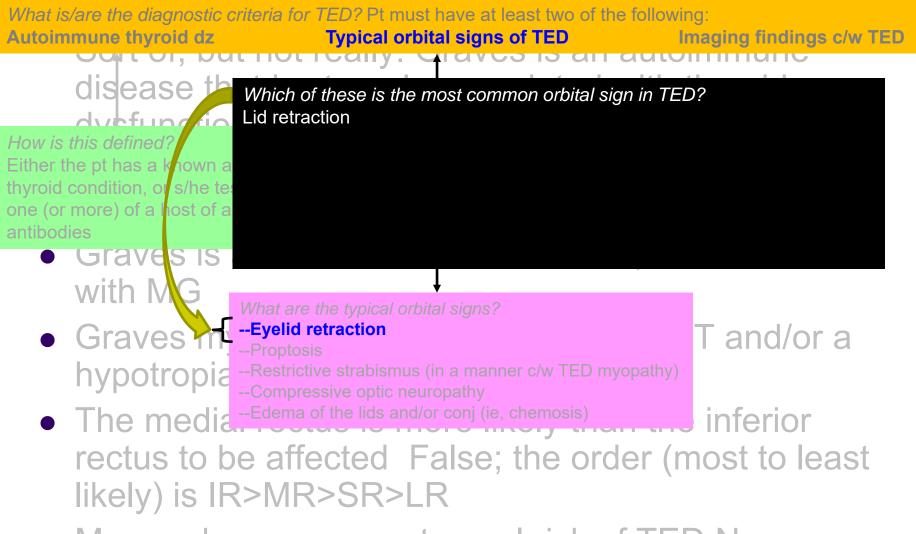
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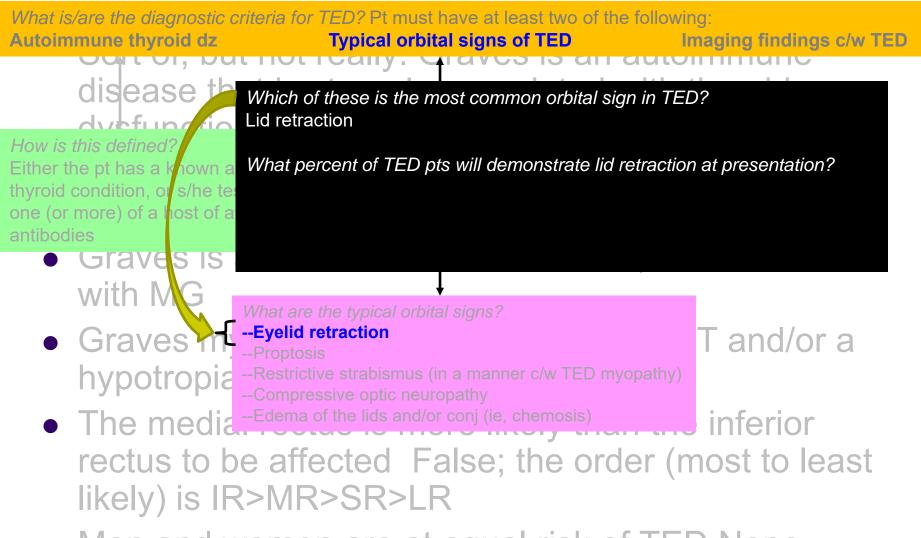






• Men and women are at equal risk of TED Nope





• Men and women are at equal risk of TED Nope

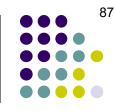


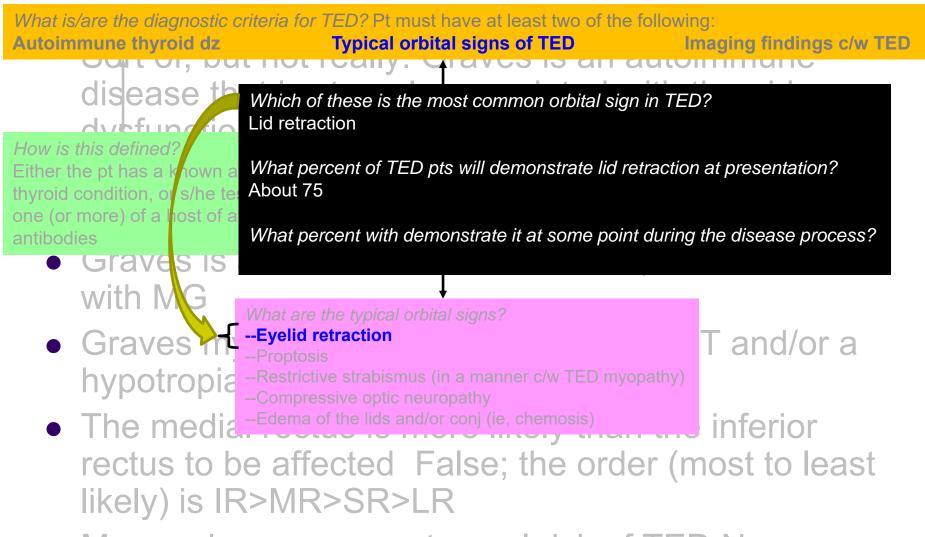


What is/are the diagnostic criteria for TED? Pt must have at least two of the following the following of the fo	maging findings c/w TED	
disease the Which of these is the most common orbital sign in TED? Lid retraction		
How is this defined? Either the pt has a known a thyroid condition, or s/he ter one (or more) of a host of a	n at presentation?	
<ul> <li>Graves IS</li> </ul>		
What are the typical orbital signs?	Tandlara	
Graves inEyelid retraction    Proptosis     hypotropia    Restrictive strabismus (in a manner c/w TED myopathy)    Compressive optic neuropathy	T and/or a	
• The mediaEdema of the lids and/or conj (ie, chemosis)	inferior	
rectus to be affected False; the order (most to least likely) is IR>MR>SR>LR		
<ul> <li>Mon and woman are at equal rick of TED Nana</li> </ul>		

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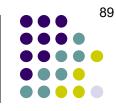
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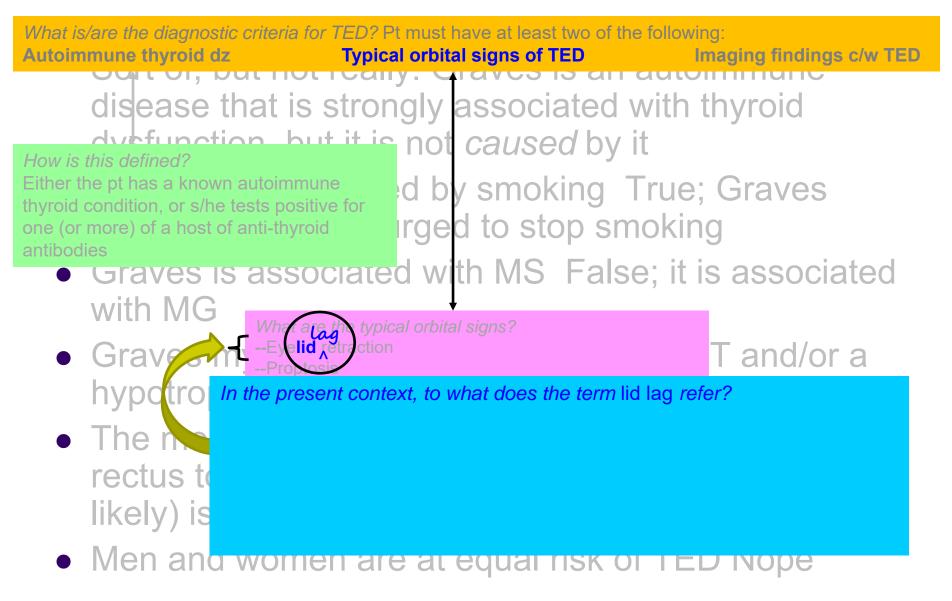




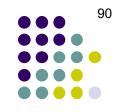
What is/are the diagnostic criteria for TED? Pt must have at least two of the followinAutoimmune thyroid dzTypical orbital signs of TED	maging findings c/w TED	
disease the Which of these is the most common orbital sign in TED?		
How is this defined? Either the pt has a known a what percent of TED pts will demonstrate lid retraction at presentation? Thyroid condition, or s/he tere About 75		
one (or more) of a lost of a antibodies • Graves IS • Graves IS		
<ul> <li>What are the typical orbital signs?</li> <li>Graves in Proptosis</li> </ul>	T and/or a	
hypotropia Restrictive strabismus (in a manner c/w TED myopathy)		
• The mediaEdema of the lids and/or conj (ie, chemosis) rectus to be affected False; the order (most to least		
likely) is IR>MR>SR>LR		

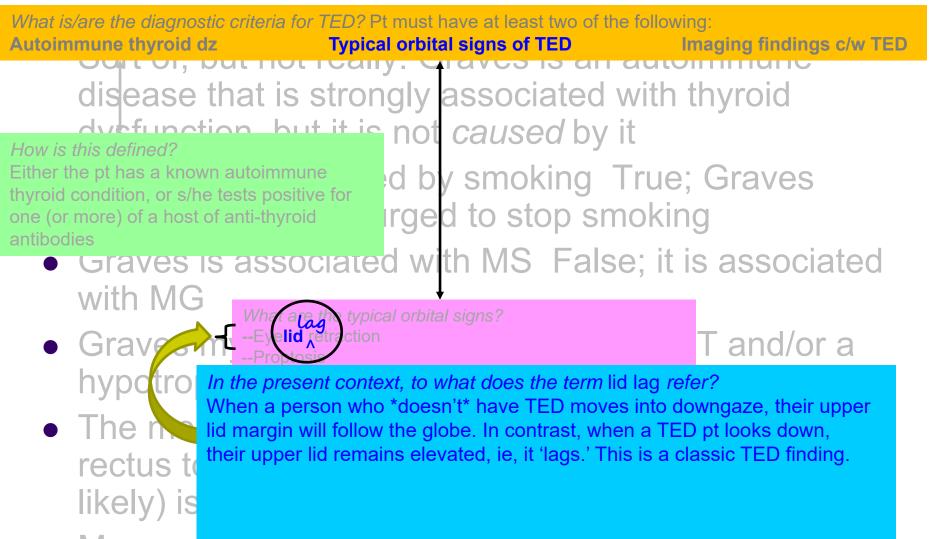
• Men and women are at equal risk of TED Nope











• Men and women are at equal risk of TED Nope

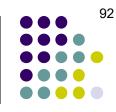


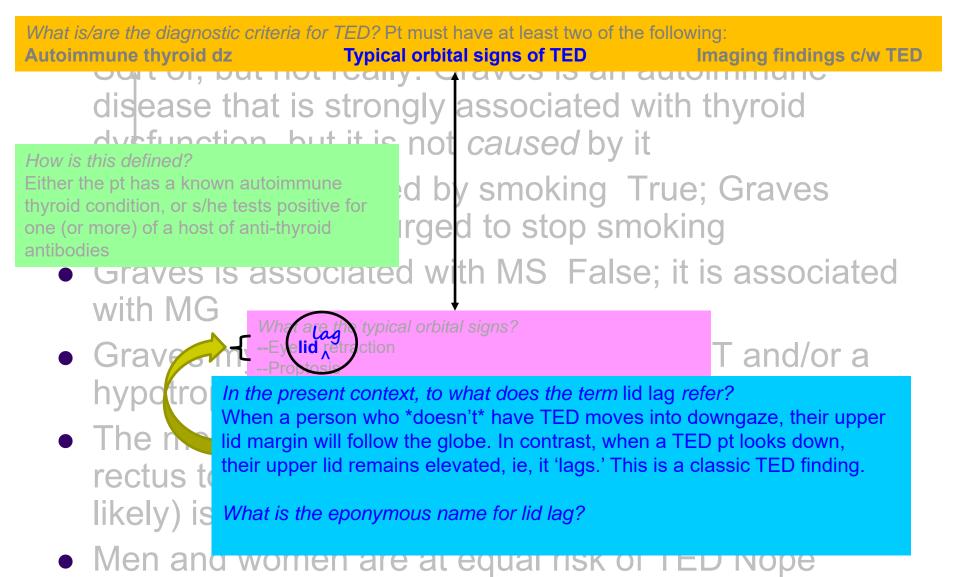


Unilateral. Note how the normal right upper lid 'follows' the eye into downgaze

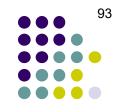
Bilateral

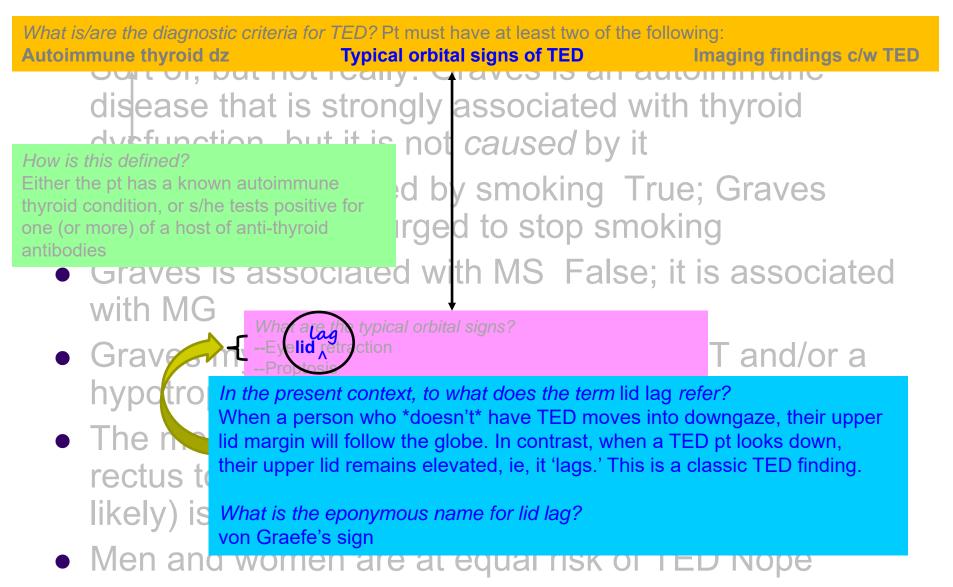
### TED: Lid lag

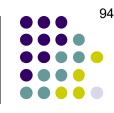


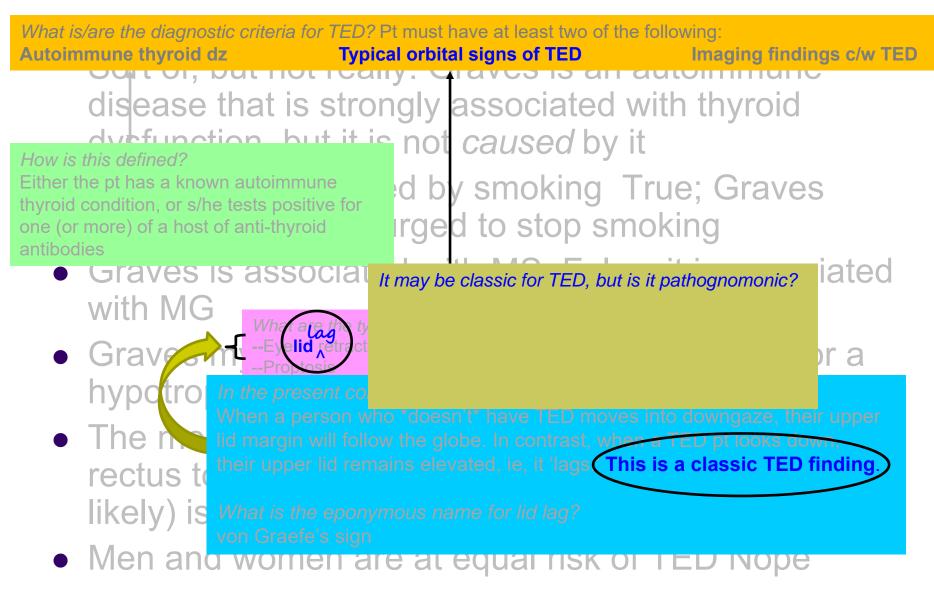






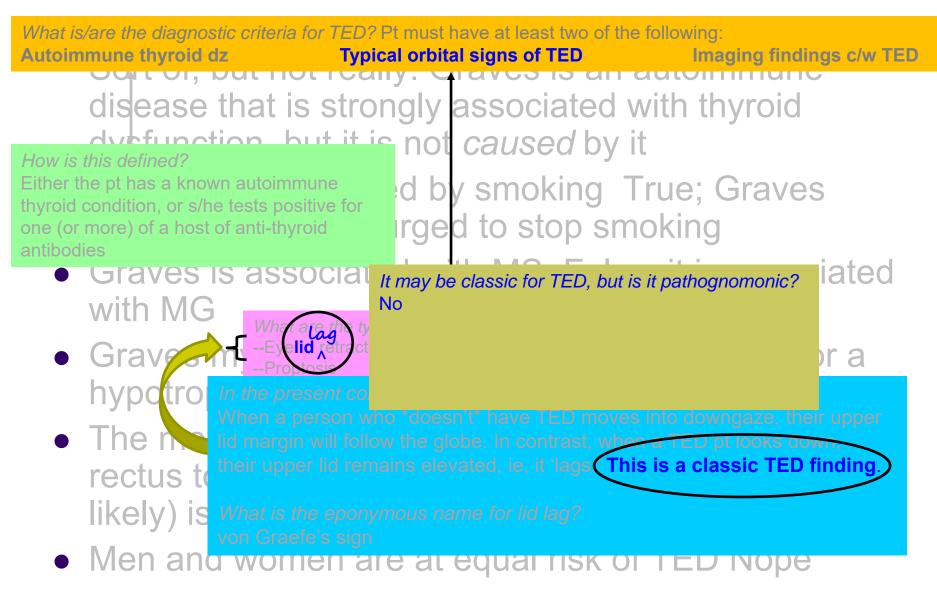




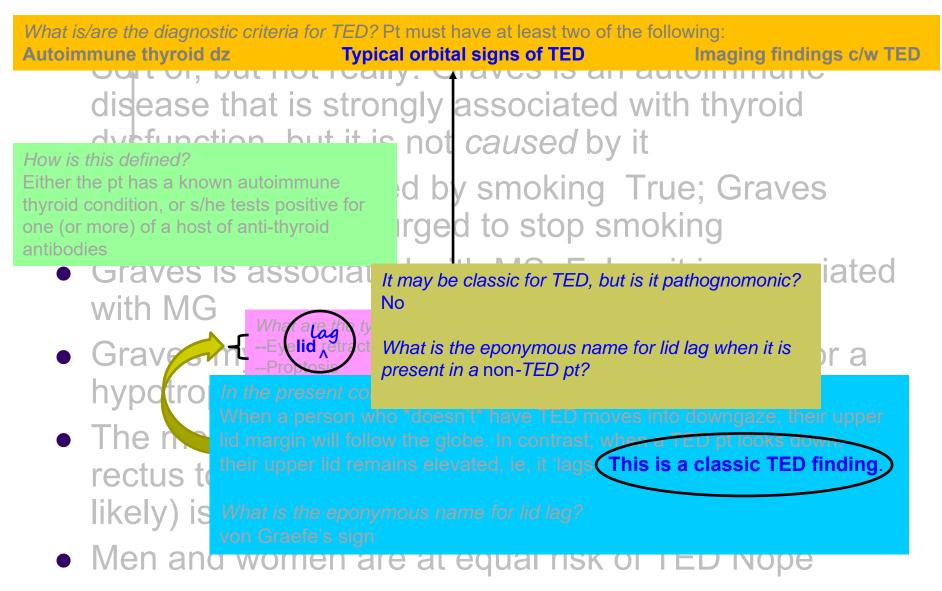






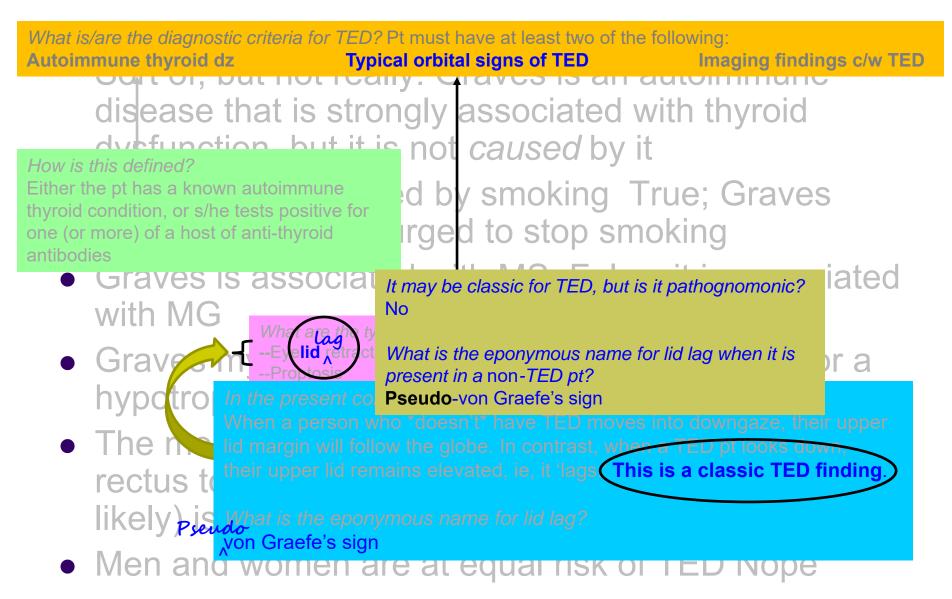








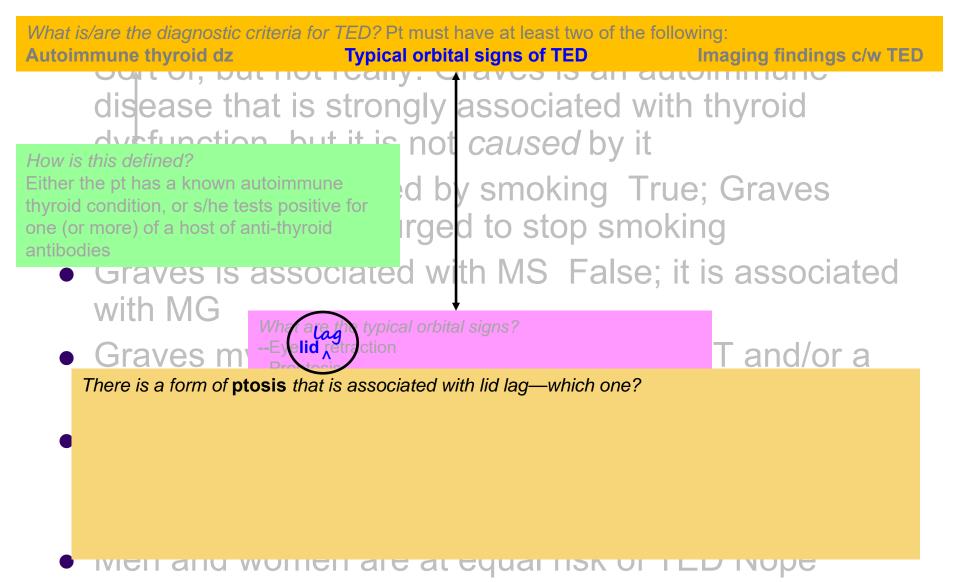




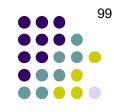
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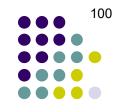






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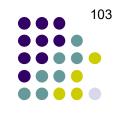
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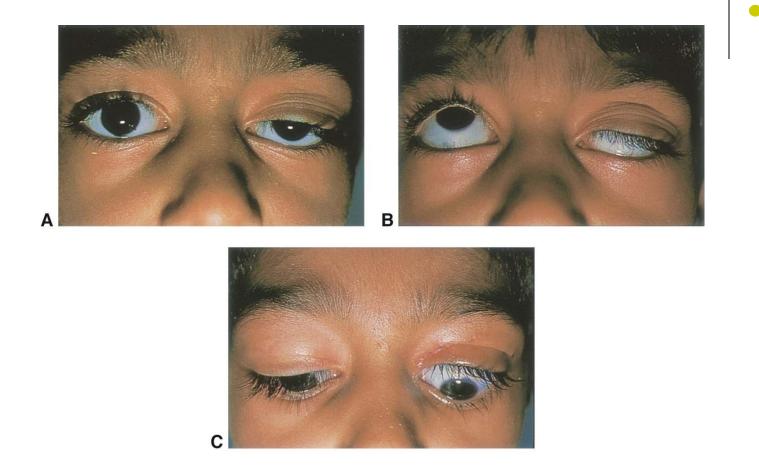
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Congenital myogenic ptosis. A, ptosis. B, failed elevation in upgaze. C, lid lag in downgaze

Thursd Fue Diseas What well-known phenomenon associated with a cranial-nerve palsy frequently manifests with lid lag?

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--Attempted adduction or depression → eyelid retraction

--Attempted globe adduction, elevation or depression → miosis of the pupil

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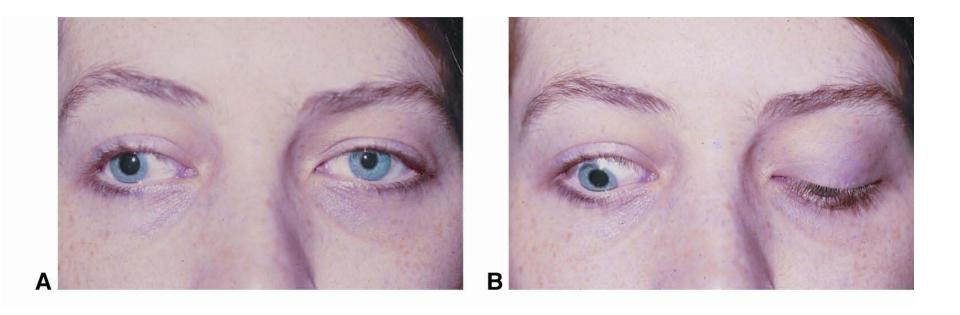
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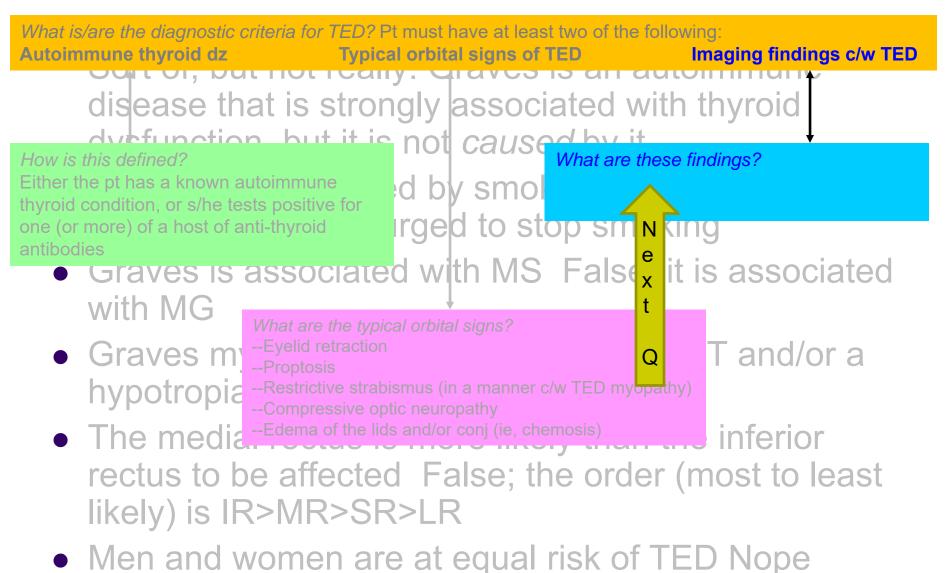
Aberrant regeneration of the right third nerve. A, In primary gaze, there is mild ptosis, pupillary mydriasis, and exotropia, all on the right.

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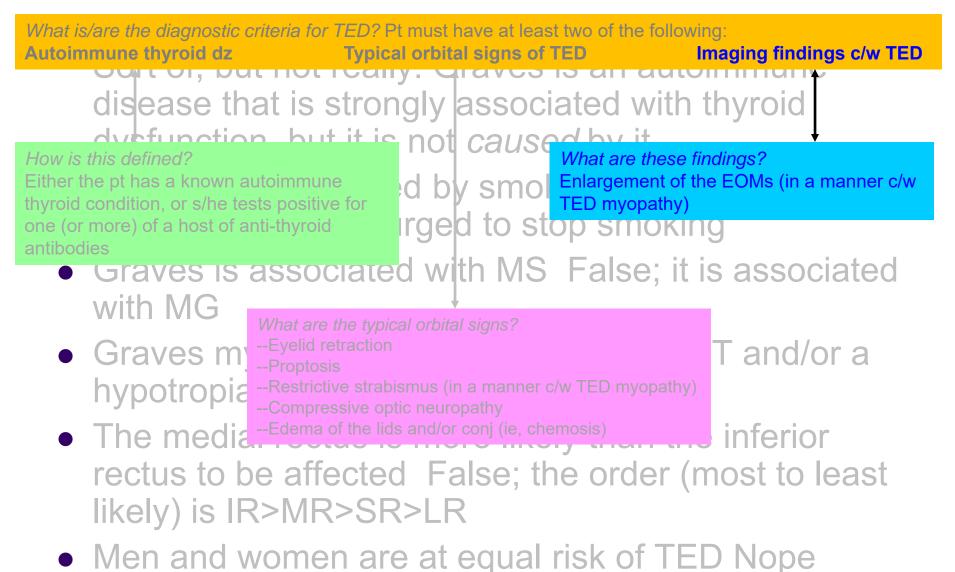
Aberrant regeneration of the right third nerve. A, In primary gaze, there is mild ptosis, pupillary mydriasis, and exotropia, all on the right. B, With attempted downward gaze, the right eyelid retracts as fibers of the right third nerve supplying the inferior rectus now also innervate the levator muscle



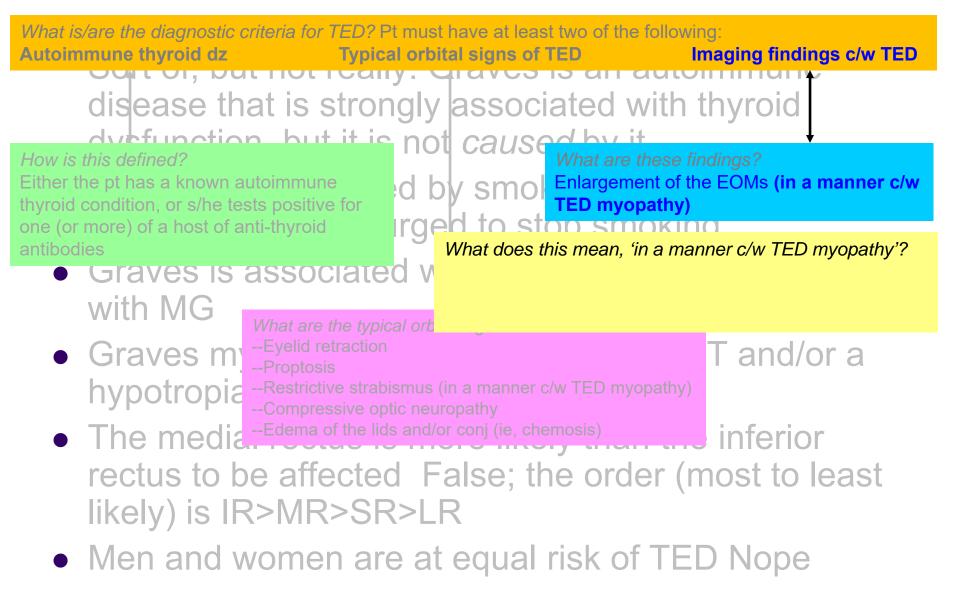




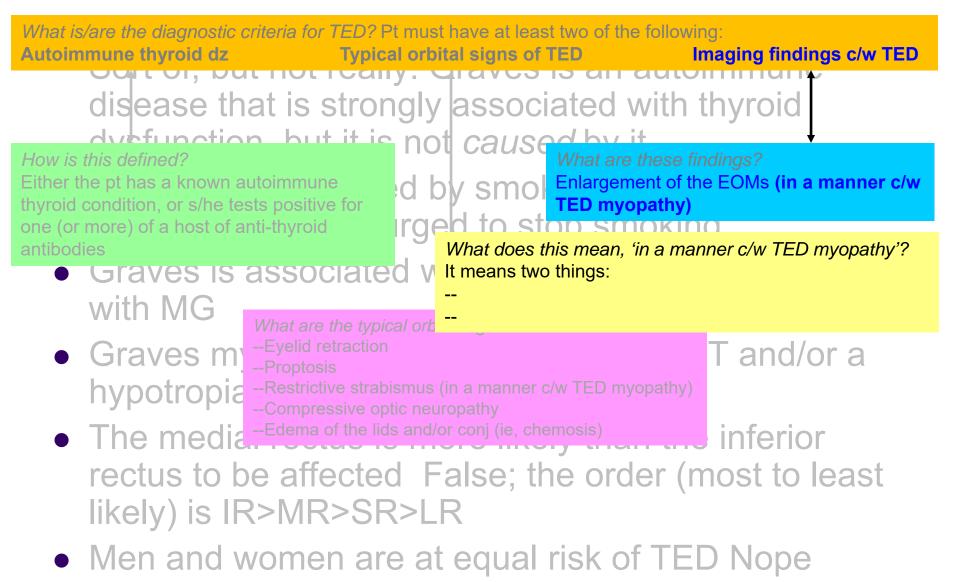






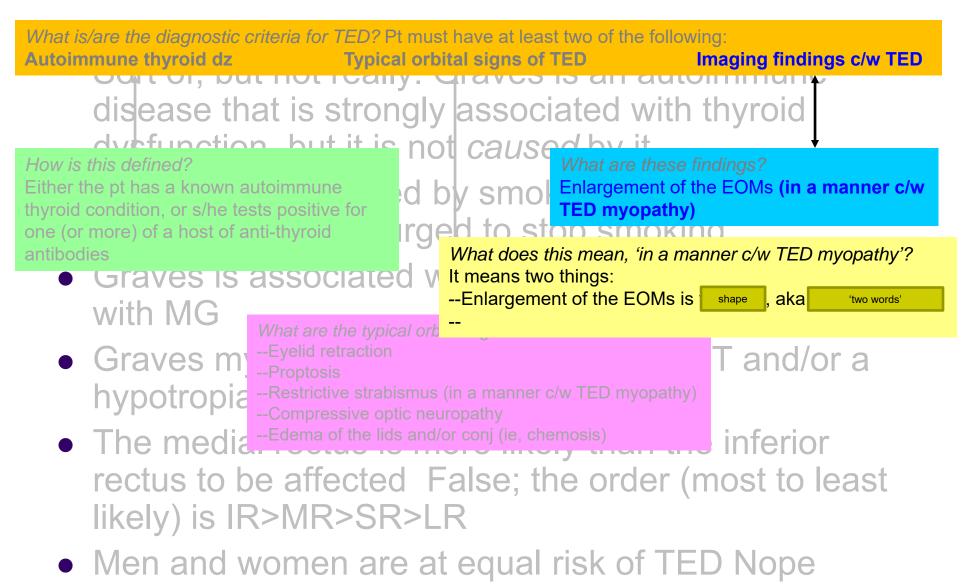






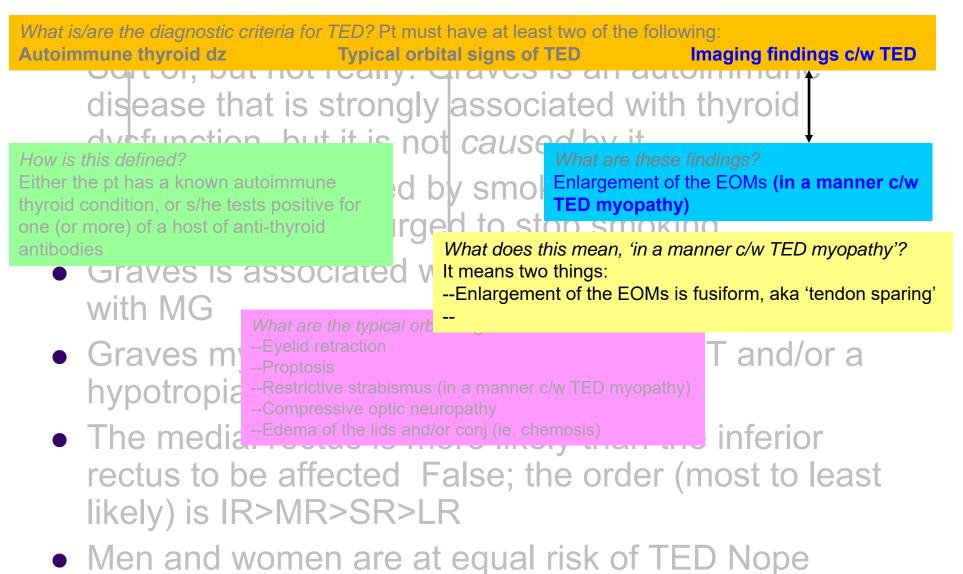










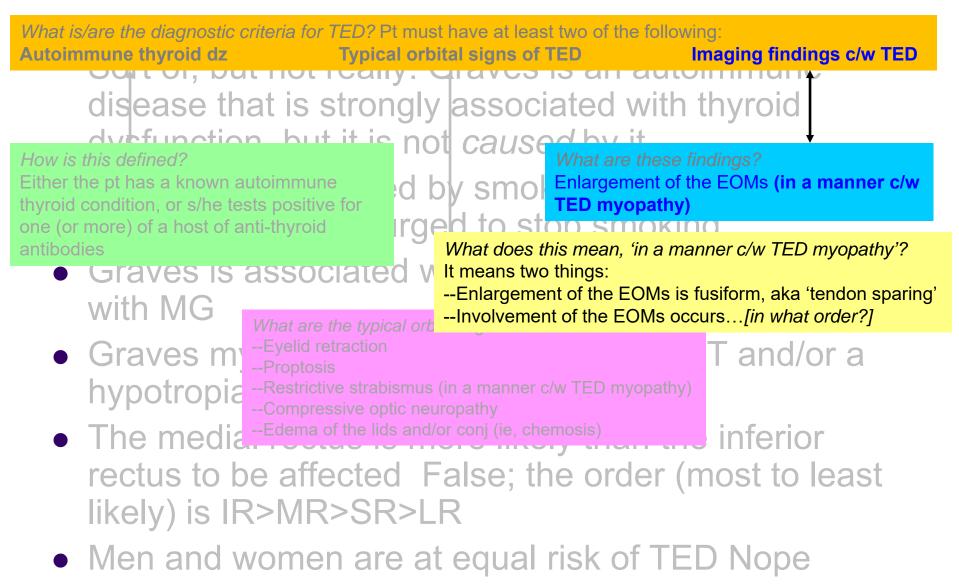






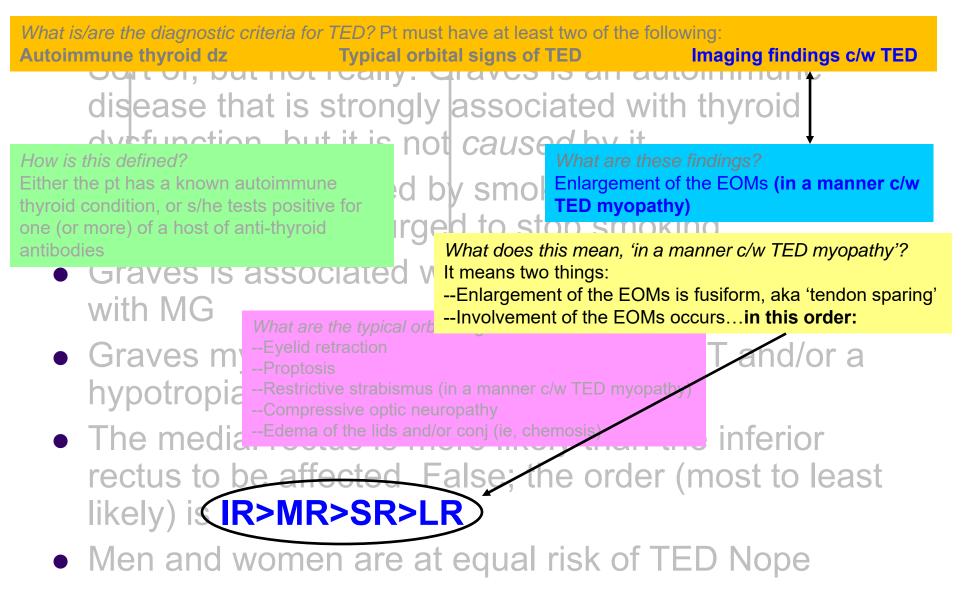
TED: Tendon-sparing EOM enlargement

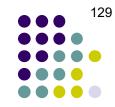


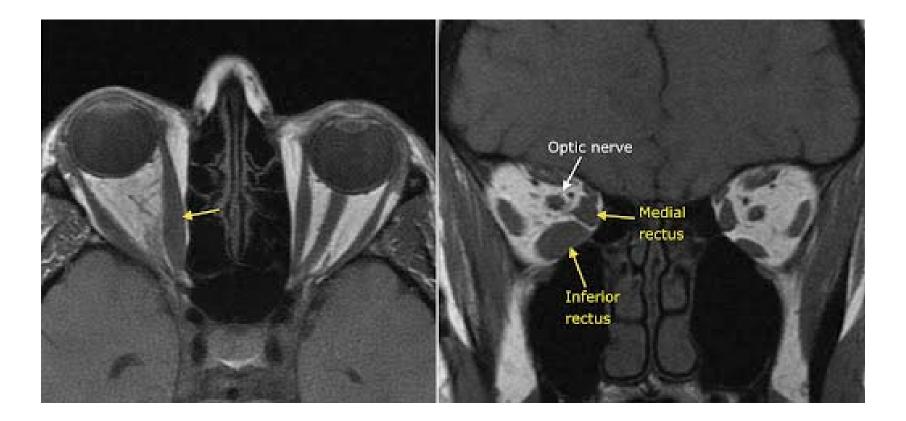






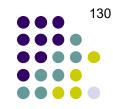






#### TED: Tendon-sparing EOM enlargement involving the IR > MR





What is the natural history of TED?

- 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
- Men and women are at equal risk of TED Nope





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

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On average, how long does it take to burn itself out?

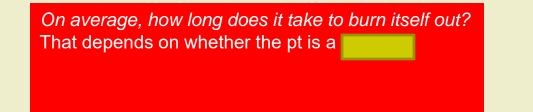
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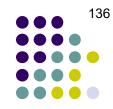
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How long for nonsmokers? How long for smokers?

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How long for nonsmokers? ~1 year How long for smokers? 2-3 years

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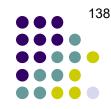
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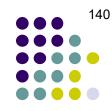
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--Severe disease involves sight-threatening complications such as corneal decompensation, and/or optic neuropathy. This necessitates (?)

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--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.

- 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
- Men and women are at equal risk of TED Nope



What is the natural history of TED?

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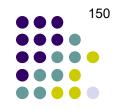




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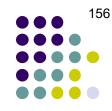


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		sease seventy.
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Severe disease		and/or optic
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#### How is TED managed?

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

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Moderate disease	What about orbital surgery? Why not just bust up in there and address these issues directly?	), and PO steroids
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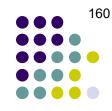
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If surgery during active TED is relatively contraindicated, when should it be considered?





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If surgery during active TED is relatively contraindicated, when should it be considered? Once the pt is one word, and his/her orbital condition has been stable for at least amount of time





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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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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.





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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. <u>Putting it all together, the surgical order is as follows</u>:

- 1. Decompression
- 2. Strabismus
- 3. Eyelids



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?

What about treating the concurrent thyroid disease?

--Severe disease involves signt-inreatening 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.

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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).

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#### How is TED managed?

- 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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