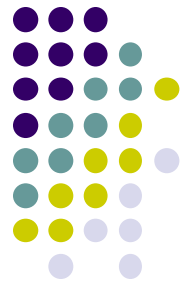


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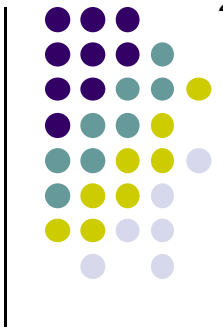
Systemic drugs and ocular toxicity:
Acquired optic neuropathy



Pts with acquired optic neuropathy secondary to systemic drug toxicity will likely present with one (or both) of two complaints/symptoms. What are they?

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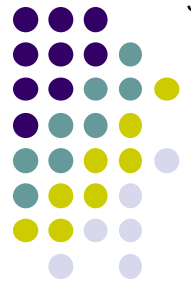
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- Degraded color vision

Q

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--**Degraded color vision**

What color is most likely to be affected?



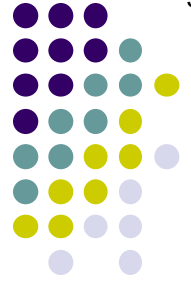
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What color is most likely to be affected?
Red



Q

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What signs will such pts likely manifest?

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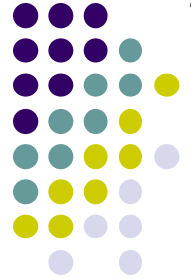
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Q

Systemic drugs and ocular toxicity:
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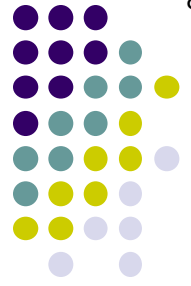
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What sort of VF defect is expected?



A

Systemic drugs and ocular toxicity: Acquired optic neuropathy

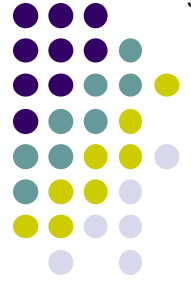
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- A visual field defect**

What sort of VF defect is expected?
A central and/or ceco-central defect



Q

Systemic drugs and ocular toxicity:
Acquired optic neuropathy

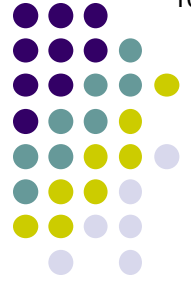
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What about a relative afferent pupillary defect--will one be present?



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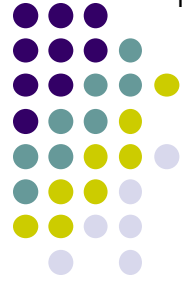
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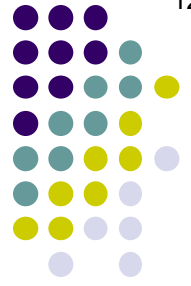
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Acquired toxic optic neuropathies tend to affect both optic nerves equally. So, while both pupils might be sluggish (a soft sign), there will be no **relative** difference in reactivity



Q

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Pts with ... with
one (or ...)
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 Putting it all together, what specific portion of the optic nerve is being affected in an
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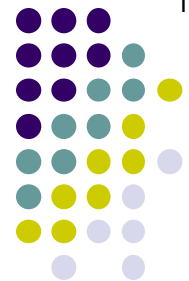
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The **papillomacular bundle (PMB)**

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What signs ...
 Why are fibers of the PMB affected preferentially?

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Systemic drugs and ocular toxicity: Acquired optic neuropathy

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one (or both) eyes. Putting it all together, what specific portion of the optic nerve is being affected in an
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 --Degraded contrast sensitivity.
 acquired toxic optic neuropathy?

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 The **papillomacular bundle (PMB)**

What signs and symptoms are associated with this? Why are fibers of the PMB affected preferentially?

--Decreased acuity, decreased color vision, and a central/cecocentral VF defect.
 --Impaired contrast sensitivity.
 --A visual field defect.
 Think of the PMB fibers as the canary in the coal mine. These fibers are small, have high metabolic activity rates, and are unmyelinated. Taken together, these characteristics make them highly vulnerable to toxins.

What about a relative afferent pupillary defect--will one be present?

No

Why not?

Acquired toxic optic neuropathies tend to affect both optic nerves equally. So, while both pupils might be sluggish (a soft sign), there will be no **relative** difference in reactivity

Q

*Systemic drugs and ocular toxicity:
Acquired optic neuropathy--The 'Big 8'*

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Hints forthcoming...





Q

Systemic drugs and ocular toxicity: Acquired optic neuropathy--The 'Big 8'

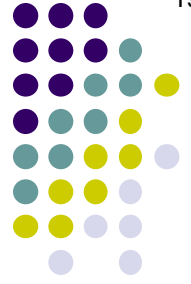
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} These four are used primarily to treat TB

} These two are 'big gun' antibiotics

} This is a 'big gun' acne med

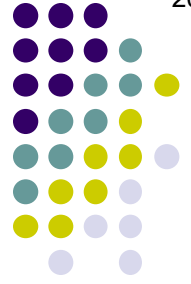
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A

Systemic drugs and ocular toxicity: Acquired optic neuropathy--The 'Big 8'

- Ethambutol
 - Rifampin
 - Isoniazid
 - Streptomycin
 - Linezolid
 - Chloramphenicol
 - Isotretinoin
 - Cyclosporine
- These four are used primarily to treat TB
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Q

*Systemic drugs and ocular toxicity:
Acquired optic neuropathy--The 'Big 8'*

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- This is an immunosuppressive

As you consider this list, what factoid jumps off the screen at you?

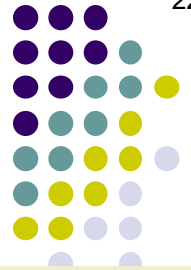


A

Systemic drugs and ocular toxicity: Acquired optic neuropathy--The 'Big 8'

- *Ethambutol*
 - *Rifampin*
 - *Isoniazid*
 - *Streptomycin*
 - *Linezolid*
 - *Chloramphenicol*
 - Isotretinoin
 - Cyclosporine
- These are all antibiotics**
- This is a 'big gun' acne med
- This is an immunosuppressive

As you consider this list, what factoid jumps off the screen at you?
Most of the offending agents are **antibiotics**



Q

Systemic drugs and ocular toxicity: Acquired optic neuropathy--The 'Big 8'

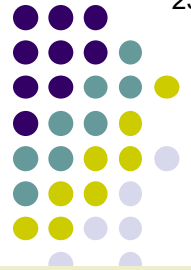
- *Ethambutol*
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What is it about antibiotics that makes them more likely to cause a toxic optic neuropathy?

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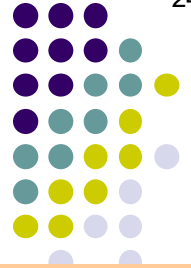
Cells that are highly active metabolically (such as the ganglion cells comprising the PMB) typically contain a lot of mitochondria. Recall that mitochondria are like 'little bacterium' living within cells. (This is more than a metaphor--mitochondrial DNA are similar to that of certain bacterial species. One theory holds that mitochondria originated as independent prokaryotes that entered eukaryotic cells early in evolution.)

Because they share many features with bacteria, mitochondria can be vulnerable to the effects of antibiotics. Thus, mitochondrial-rich tissues (such as the PMB) are at risk for antibiotic-related injury.

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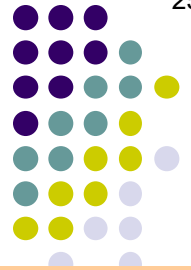


Q

*Systemic drugs and ocular toxicity:
Acquired optic neuropathy--The 'Big 8'*

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Does nutrition status play a role in optic neuropathy secondary to drug toxicity?



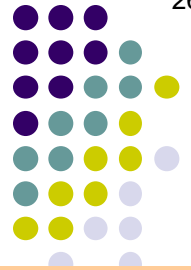
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Does nutrition status play a role in optic neuropathy secondary to drug toxicity?

Yes. Marginal nutritional status makes the PMB fibers vulnerable to damage at drug levels that otherwise might not be significant. Given this, any pt with a suspected toxic optic neuropathy (or any bilateral optic neuropathy, for that matter) should be asked about their dietary habits and relevant GI history.



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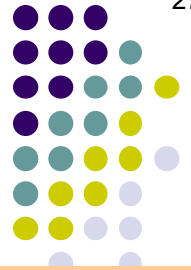
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Which dietary components are thought to be especially critical in this regard?



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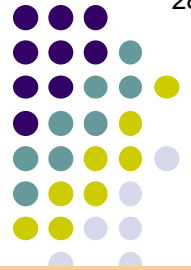
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Which dietary components are thought to be especially critical in this regard?

The B vitamins (especially B₁₂) and folate



Q

*Systemic drugs and ocular toxicity:
Acquired optic neuropathy--The 'Big 8'*

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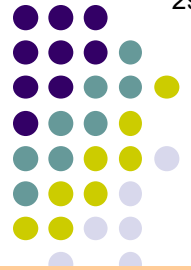
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*Which dietary components are most relevant in this regard?
The B vitamins (*

What dietary habits place a pt at risk?

--
--
--

--(There are plenty of others, of course)



A

Systemic drugs and ocular toxicity: Acquired optic neuropathy--The 'Big 8'

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Which dietary conditions are most concerning in this regard?

The B vitamins (

What dietary habits place a pt at risk?

- Strict veganism
- Fad diets
- Eating disorders
- (There are plenty of others, of course)



Q

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What GI history places a pt at risk?

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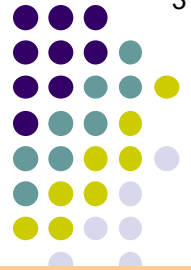
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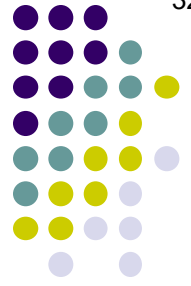
relevant GI history.

What GI history places a pt at risk?

- Gastric bypass surgery
- Short bowel syndrome
- Hyperemesis gravidarum
- (There are plenty of others, of course)

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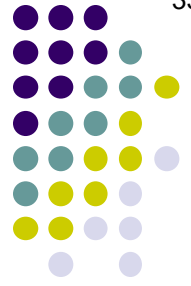
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*Systemic drugs and ocular toxicity:
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● Ethambutol

● *In addition to treating TB (ie, infection with Mycobacterium tuberculosis), infections with what related infectious agents are also commonly treated with ethambutol?*

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-



A

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Q

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- *In addition to treating TB (ie, infection with Mycobacterium tuberculosis), infections with what related infectious agents are also commonly treated with ethambutol?*
- *Mycobacterium avium and its first cousin Mycobacterium intracellulare*
- *Because they are so closely associated, M avium and M intracellulare are collectively referred to by what term?*
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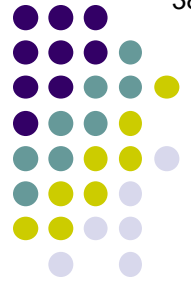


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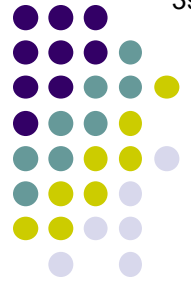


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15 mg/kg/d: **1%**
- *The drug's manufacturer recommends **monthly** vision screenings be performed at what dose?*



A

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● Ethambutol

- *In addition to treating TB (ie, infection with Mycobacterium tuberculosis), infections with what related infectious agents are also commonly treated with ethambutol?*
Mycobacterium avium and its first cousin Mycobacterium intracellulare
- *Because they are so closely associated, M avium and M intracellulare are collectively referred to by what term?*
Mycobacterium avium complex (MAC)
- *Is ethambutol optic neuropathy dose-related?*
Yes
- *What proportion of pts will develop optic neuropathy at the following doses?*
35 mg/kg/d: 20%
25 mg/kg/d: 5%
15 mg/kg/d: 1%
- *The drug's manufacturer recommends **monthly** vision screenings be performed at what dose?*
25 mg/kg/d and above



Q

Systemic drugs and ocular toxicity: Acquired optic neuropathy--The 'Big 8'

● Ethambutol

● In addition to treating TB (ie, infection with *Mycobacterium tuberculosis*), infections with what related infectious agents are also commonly treated with ethambutol?

● *Mycobacterium avium* and its first cousin *Mycobacterium intracellulare*

● How (ie, via what system) is ethambutol cleared by the body?

● Be referred

● to

● My

● Is

● Ye

● W

● 35

● 25 mg/kg/d: 5%

● 15 mg/kg/d: 1%

● The drug's manufacturer recommends **monthly** vision screenings be performed at what dose?

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A

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Renally

- Be to My

- Is Ye

- W

- 35

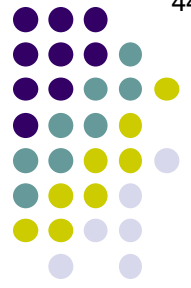
25 mg/kg/d: 5%

15 mg/kg/d: 1%

-

The drug's manufacturer recommends **monthly** vision screenings be performed at what dose?

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Q

*Systemic drugs and ocular toxicity:
Acquired optic neuropathy--The 'Big 8'*

● **Ethambutol**

● *In addition to treating TB (ie, infection with Mycobacterium tuberculosis), infections with what related infectious agents are also commonly treated with ethambutol?
Mycobacterium avium and its first cousin Mycobacterium intracellulare*

● *How (ie, via what system) is ethambutol cleared by the body?
Renally*

● *Does impaired renal function increase the risk of ethambutol optic neuropathy?*

● *Is there a specific dose for patients with renal impairment?
Yes*

● *What is the risk of optic neuropathy at different doses?
35 mg/kg/d: 10%
25 mg/kg/d: 5%
15 mg/kg/d: 1%*

● *The drug's manufacturer recommends **monthly** vision screenings be performed at what dose?
25 mg/kg/d and above*



A

Systemic drugs and ocular toxicity: Acquired optic neuropathy--The 'Big 8'

● Ethambutol

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● Renally

● Does impaired renal function increase the risk of ethambutol optic neuropathy?

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● W

● 35

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● How (ie, via what system) is ethambutol cleared by the body?

● Renally

● Does impaired renal function increase the risk of ethambutol optic neuropathy?

● Yes

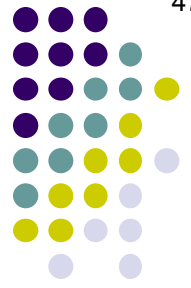
● What parameter of renal function is relevant; ie, what measure of renal function should be assessed in this regard?

● 25 mg/kg/d: 5%

● 15 mg/kg/d: 1%

● The drug's manufacturer recommends **monthly** vision screenings be performed at what dose?

● 25 mg/kg/d and above



A

Systemic drugs and ocular toxicity: Acquired optic neuropathy--The 'Big 8'

● Ethambutol

- In addition to treating TB (ie, infection with *Mycobacterium tuberculosis*), infections with what related infectious agents are also commonly treated with ethambutol?
Mycobacterium avium and its first cousin *Mycobacterium intracellulare*
- How (ie, via what system) is ethambutol cleared by the body?
Renally
- Does impaired renal function increase the risk of ethambutol optic neuropathy?
Yes
- What parameter of renal function is relevant; ie, what measure of renal function should be assessed in this regard?
Glomerular filtration rate (GFR)
- 25 mg/kg/d: 5%
- 15 mg/kg/d: 1%
- The drug's manufacturer recommends **monthly** vision screenings be performed at what dose?
25 mg/kg/d and above