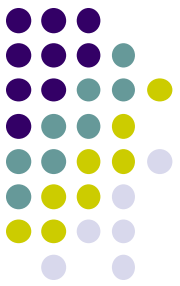


# Q

## *Systemic drugs and ocular toxicity:* *Acquired optic neuropathy*



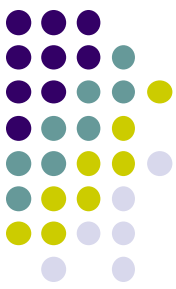
*Pts with acquired optic neuropathy secondary to systemic drug toxicity will likely present with one (or both) of two complaints/symptoms. What are they?*

*--?*

*--?*

# A

## *Systemic drugs and ocular toxicity:* *Acquired optic neuropathy*

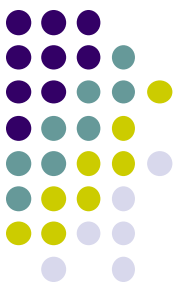


*Pts with acquired optic neuropathy secondary to systemic drug toxicity will likely present with one (or both) of two complaints/symptoms. What are they?*

- Decreased visual acuity*
- Degraded color vision*

# Q

## 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?*

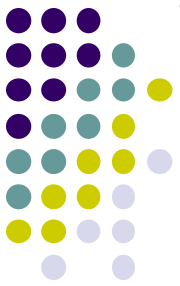
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--**Degraded color vision**

*What color is most likely to be affected?*

# A

## Systemic drugs and ocular toxicity: Acquired optic neuropathy



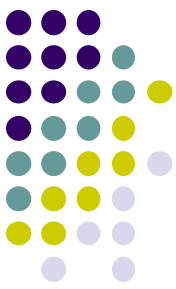
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- Decreased visual acuity
- Degraded color vision**

*What color is most likely to be affected?*  
**Red**

# Q

## 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?*

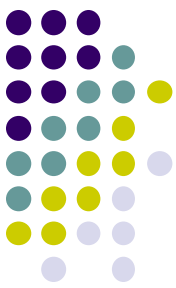
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- Degraded color vision

*What signs will such pts likely manifest?*

- ?
- ?
- ?

# A

## *Systemic drugs and ocular toxicity:* *Acquired optic neuropathy*



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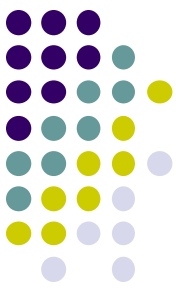
- Decreased visual acuity
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*What signs will such pts likely manifest?*

- Decreased BCVA
- Impaired color vision
- A visual field defect

# Q

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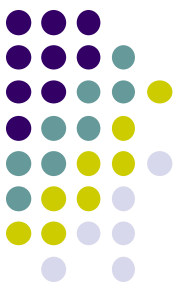
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--**A visual field defect**

*What sort of VF defect is expected?*

# A

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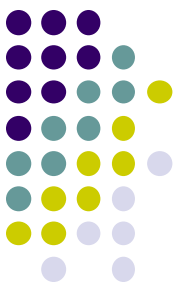
*What sort of VF defect is expected?*

A central and/or ceco-central defect



# Q

## *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?*

- Decreased visual acuity*
- Degraded color vision*

*What signs will such pts likely manifest?*

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- Impaired color vision*
- A visual field defect*

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

# A

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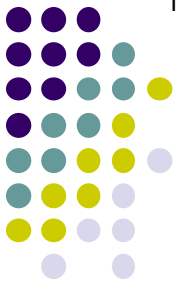
- Decreased BCVA*
- Impaired color vision*
- A visual field defect*

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

*No*

# Q

## 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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- Degraded color vision

*What signs will such pts likely manifest?*

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- A visual field defect

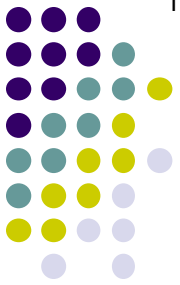
*What about a relative afferent pupillary defect--will one be present?*

No

*Why not?*

# A

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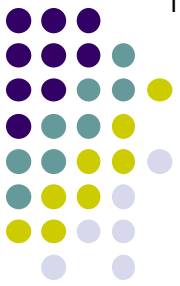
No

*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



Pts with... with  
one (or both) eyes  
--Decreased visual acuity  
--Decreased color vision

Hmm...Decreased acuity, decreased color vision, and a central/cecocentral VF defect.  
Putting it all together, what specific portion of the optic nerve is being affected in an  
acquired toxic optic neuropathy?

What signs and symptoms  
--Decreased visual acuity  
--Impaired color vision  
--A visual field defect

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

**Systemic drugs and ocular toxicity:**  
**Acquired optic neuropathy**

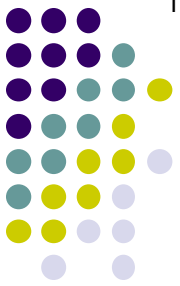
Hmm...Decreased acuity, decreased color vision, and a central/ceco-central VF defect. Putting it all together, what specific portion of the optic nerve is being affected in an acquired toxic optic neuropathy?

## The papillomacular bundle (PMB)

--A visual field defect

No

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Q

## Systemic drugs and ocular toxicity: Acquired optic neuropathy

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--Degraded color vision  
Hmm...Decreased acuity, decreased color vision, and a central/cecocentral VF defect. Putting it all together, what specific portion of the optic nerve is being affected in an acquired toxic optic neuropathy?

The **papillomacular bundle (PMB)**

What signs...  
--Decreased visual acuity  
--Impaired color vision  
--A visual field defect  
Why are fibers of the PMB affected preferentially?

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

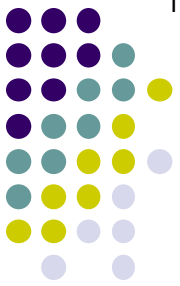
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# A

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Putting it all together, what specific portion of the optic nerve is being affected in an acquired toxic optic neuropathy?  
The **papillomacular bundle (PMB)**

What signs...  
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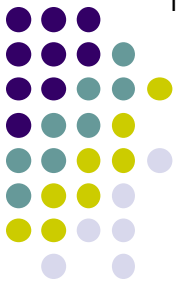
Why are fibers of the PMB affected preferentially?  
Think of the PMB fibers as the canary in the coal mine. These fibers are small, have high metabolic activity rates, and are unmyelinated. Taken together, these characteristics make them highly vulnerable to toxins.

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



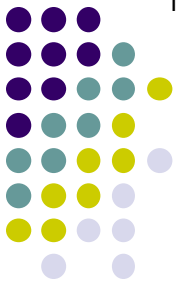


# Q

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

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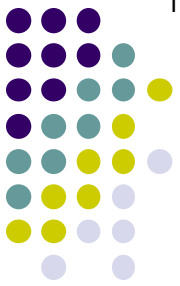
*Hints forthcoming...*



# Q

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

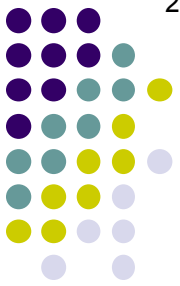
- - 
  - 
  - 
  - 
  - 
  -
- } These four are used primarily to treat TB
- } These two are 'big gun' antibiotics
- } This is a 'big gun' acne med
- } This is an immunosuppressive



# A

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

- Ethambutol
  - Rifampin
  - Isoniazid
  - Streptomycin
  - Linezolid
  - Chloramphenicol
  - Isotretinoin
  - Cyclosporine
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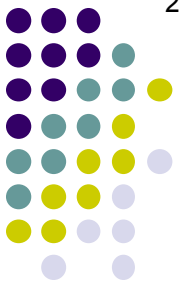


# Q

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*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'*

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

This is a 'big gun' acne med

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# Q/A

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



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

Cells that are highly active metabolically (such as the ganglion cells comprising the PMB) contain a lot of organelle

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- *Chloramphenicol*
- Isotretinoin
- Cyclosporine

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

Cells that are highly active metabolically (such as the ganglion cells comprising the PMB) contain a lot of mitochondria

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# A

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

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

Cells that are highly active metabolically (such as the ganglion cells comprising the PMB) 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.)

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## A

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Cells that are highly active metabolically (such as the ganglion cells comprising the PMB) 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.

This is a 'big gun' acne med

This is an immunosuppressive

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## Q

*Systemic drugs and ocular toxicity:*  
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*Does nutrition status play a role in optic neuropathy secondary to drug toxicity?*



# A

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## Q

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

# Q/A

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

The B vitamins, especially [ ] and [ ]

# A

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

The B vitamins, especially B<sub>12</sub> and folate



Q

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*What dietary habits place a pt at risk?*

*Which dietary c*  
*in this regard?*  
 The B vitamins

--?  
 --?  
 --?

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

*critical*

# A

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*Which dietary conditions place a pt at risk 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)

*critical*

Q

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

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**relevant GI history**

*What GI history places a pt at risk?*

--?

--?

--?

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

*ought to be especially critical*

*and folate*

# A

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

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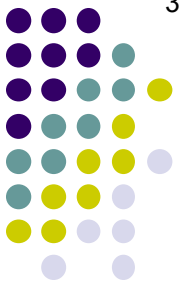
**relevant GI history**

*What GI history places a pt at risk?*

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

*ought to be especially critical*

*and folate*



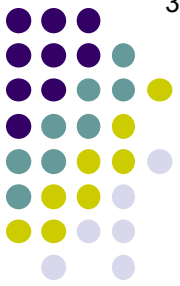
# Q

## 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?*

● Cyclosporine



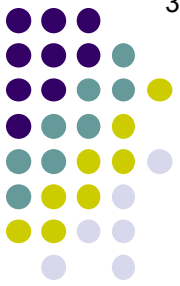
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## Systemic drugs and ocular toxicity: Acquired optic neuropathy--The 'Big 8'

### ● 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*

● Cyclosporine



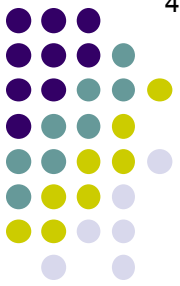
# Q

## 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*
- *Because they are so closely associated, M avium and M intracellulare are collectively referred to by what term?*
- 
- 
- 
- 
- 

Cyclosporine



# A

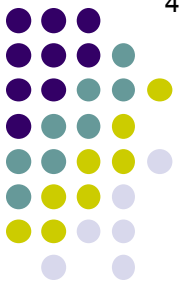
## Systemic drugs and ocular toxicity: Acquired optic neuropathy--The 'Big 8'

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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?*
- **Mycobacterium avium complex (MAC)**
- 
- 
- 
- 
- 

Cyclosporine





# Q

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

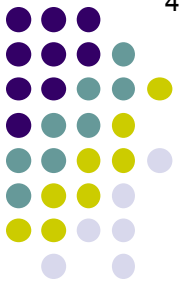
### ● Ethambutol

- *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*
- *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?*
- 
- 
- 
- 

Cyclosporine

# A

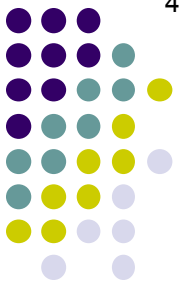
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Cyclosporine



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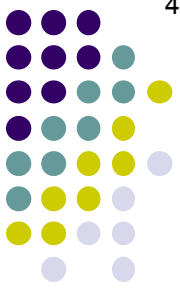
## Systemic drugs and ocular toxicity: Acquired optic neuropathy--The 'Big 8'

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**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:  
25 mg/kg/d:  
15 mg/kg/d:

## A

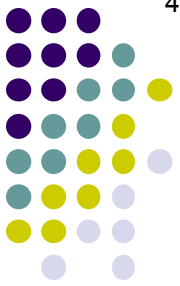
*Systemic drugs and ocular toxicity:*  
*Acquired optic neuropathy--The 'Big 8'*



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Cyclosporine



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

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● 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

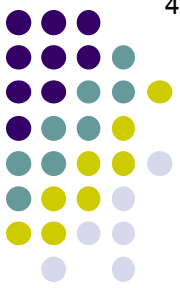
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● 35 mg/kg/d: **20%**

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Per the BCSC: At what dose is monthly screening exams warranted?



# A

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

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What proportion of pts develop optic neuropathy at the following doses?

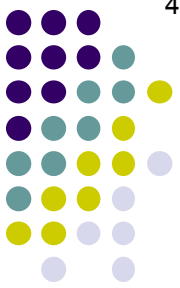
35 mg/kg/d: **20%**

25 mg/kg/d: **5%**

15 mg/kg/d: **1%**

Screen monthly

Per the BCSC: At what dose is monthly screening exams warranted?  
Greater than 15 mg/kg/d



Q

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

### ● Ethambutol

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

*Mycobacterium avium* complex (MAC) is first considered for treatment of what infection?

Because they are so commonly associated with MAC, what infections are often referred to by what term?

*Mycobacterium avium* complex (MAC) is first considered for treatment of what infection?

Is ethambutol optic neuropathy dose-related?

Yes

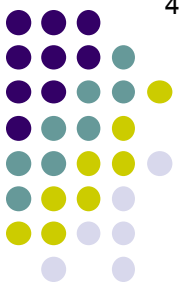
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Per the BCSC: At what dose is monthly screening exams warranted?  
Greater than 15 mg/kg/d



# A

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

### ● Ethambutol

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

*Mycobacterium avium* complex (MAC) is first co

What constitutes an appropriate baseline exam?

--DFE

--Amsler grid

--VA

--Color vision

--Formal VF testing

Because they are so commonly associated with what term?

*Mycobacterium avium* complex (MAC)

Is ethambutol optic neuropathy dose-related?

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What proportion of pts develop optic neuropathy at the following doses?

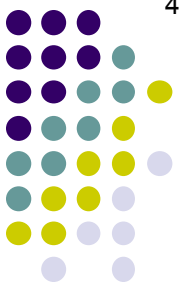
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Per the BCSC: At what dose is monthly screening exams warranted?  
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Q

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In addition to treating infection with *Mycobacterium tuberculosis*), infections with what related infectious agents are also commonly treated with ethambutol?  
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Because they are so closely associated, what term is used to describe the association?  
to by what term?  
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Is ethambutol optic neuropathy dose-related?  
Yes

What proportion of patients develop optic neuropathy at the following doses?

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What constitutes an appropriate baseline exam?

--DFE?

--Amsler grid?

--VA?

--Color vision?

--Formal VF testing?

Which must be checked monthly?

--?

--?

--?

Per the BCSC: At what dose is monthly screening exams warranted?  
Greater than 15 mg/kg/d

# A

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



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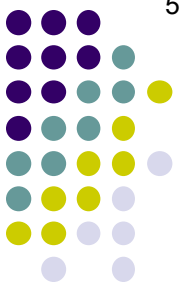
Which must be checked monthly?

--VA

--Color vision

--Formal VF testing

Per the BCSC: At what dose is monthly screening exams warranted?  
Greater than 15 mg/kg/d



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*Mycobacterium avium* complex (MAC)

Is ethambutol optic neuropathy dose-related?  
Yes

What proportion of patients develop optic neuropathy at the following doses?

35 mg/kg/d: **20%**

25 mg/kg/d: **5%**

15 mg/kg/d: **1%**

Screening

What constitutes an appropriate baseline exam?

--DFE

--Amsler grid

--**VA**

--**Color vision**

--**Formal VF testing**

Which must be checked monthly?

--VA

--Color vision

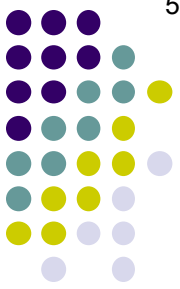
--Formal VF testing

If one of these is found to be diminished, what should be done?

Per the BCSC: At what dose is monthly screening exams warranted?  
Greater than 15 mg/kg/d

# A

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



### ● Ethambutol

- In addition to treating infection with *Mycobacterium tuberculosis*), infections with what related infectious agents are also commonly treated with ethambutol?
- *Mycobacterium avium* complex (MAC) is first considered in the differential diagnosis of what condition?
- Because they are so commonly associated, what term is used to describe the association between *Mycobacterium avium* complex (MAC) and optic neuropathy?
- Is ethambutol optic neuropathy dose-related?
- Yes
- What proportion of patients develop optic neuropathy at the following doses?
- 35 mg/kg/d: **20%**
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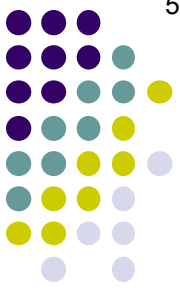
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Which must be checked monthly?

--VA  
--Color vision  
--Formal VF testing

If one of these is found to be diminished, what should be done?  
The dose must be reduced, or the drug stopped entirely

Per the BCSC: At what dose is monthly screening exams warranted?  
Greater than 15 mg/kg/d



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

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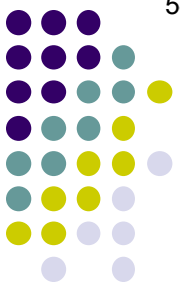
35 mg/kg/d: **20%**

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15 mg/kg/d: **1%**

Per the BCSC: At what dose is monthly screening exams warranted?  
Greater than 15 mg/kg/d

What is the recommended screening schedule for those taking 15 mg/kg/d or less?



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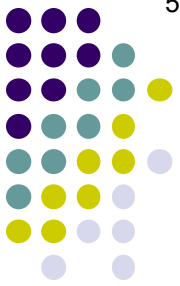
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Per the BCSC: At what dose is monthly screening exams warranted?  
Greater than 15 mg/kg/d

What is the recommended screening schedule for those taking 15 mg/kg/d or less?

This is not established—the BCSC just says to screen them “regularly”



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

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

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

● Be to My referred

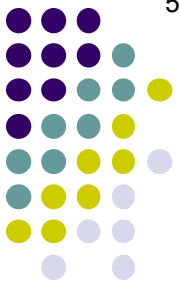
● to My

● Is Ye

● W

● 35 mg/kg/d: 5%  
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● Cyclosporine



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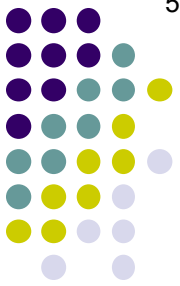
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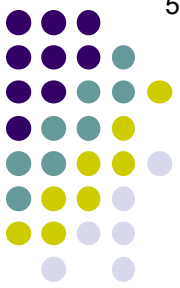
● How (ie, via what system) is ethambutol cleared by the body?

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

● Yes  
 ● No  
 ● W  
 ● 35  
 ● 25 mg/kg/d: 5%  
 ● 15 mg/kg/d: 1%

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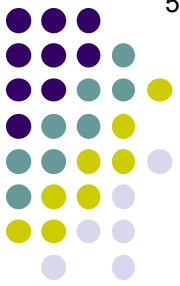
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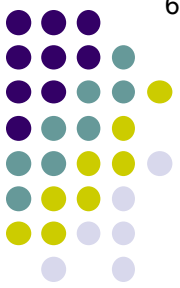
● Does impaired renal function increase the risk of ethambutol optic neuropathy?

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%



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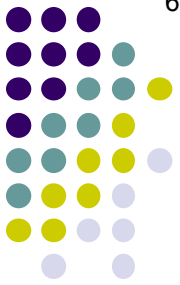
Yes

● 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%



# Q

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

- Ethambutol
- **Rifampin** *Rifampin has a benign-but-alarming (to the pt) side effect related to the tear film—what is it?*
- Isoniazid
- Streptomycin
- Linezolid
- Chloramphenicol
- Isotretinoin
- Cyclosporine

# A

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

- Ethambutol
- **Rifampin** *Rifampin has a benign-but-alarming (to the pt) side effect related to the tear film—what is it?*  
Pink-tinged tears
- Isoniazid
- Streptomycin
- Linezolid
- Chloramphenicol
- Isotretinoin
- Cyclosporine

