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

Red
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
-- Degrade color vision

What signs will such pts likely manifest?
--?
--?
--?
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?

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

What sort of VF defect is expected?
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

What signs will such pts likely manifest?
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---Impaired color vision
---A visual field defect

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

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--Impaired color vision
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What about a relative afferent pupillary defect--will one be present?
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--Decreased visual acuity
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What signs will such pts likely manifest?
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What about a relative afferent pupillary defect--will one be present?
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Why not?
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?
-- Decreased BCVA
-- 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.
Pts with acquired optic neuropathy secondary to systemic drug toxicity will likely present with one (or both) of the following: decreased visual acuity and/or degraded color vision.

What signs will such pts likely manifest?

--Decreased BCVA
--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.
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Systemic drugs and ocular toxicity:
Acquired optic neuropathy--The ‘Big 8’

Hints forthcoming…
Systemic drugs and ocular toxicity: 
**Acquired optic neuropathy--The ‘Big 8’**

- These four are used primarily to treat TB
  - Ethambutol
  - Rifampin
  - Isoniazid
  - Streptomycin

- These two are ‘big gun’ antibiotics
  - Linezolid
  - Chloramphenicol

- This is a ‘big gun’ acne med
  - Isotretinoin

- This is an immunosuppressivem
Ethambutol
- These four are used primarily to treat TB

Rifampin

Isoniazid

Streptomycin

Linezolid

Chloramphenicol

Isotretinoin
- These two are ‘big gun’ antibiotics

Cyclosporine
- This is a ‘big gun’ acne med

- This is an immunosuppressive

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
These two are ‘big gun’ antibiotics
This is a ‘big gun’ acne med
This is an immunosuppressive

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

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

Rifampin

Isoniazid

Streptomycin

Linezolid

Chloramphenicol

Isotretinoin

Cyclosporine

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

These are all antibiotics

As you consider this list, what factoid jumps off the screen at you?
Most of the offending agents are antibiotics
Systemic drugs and ocular toxicity:

**Acquired optic neuropathy--The ‘Big 8’**

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

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

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

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- 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. 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.)

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

**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?**

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.
Systemic drugs and ocular toxicity: 

Acquired optic neuropathy--The ‘Big 8’

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

Does nutrition status play a role in optic neuropathy secondary to drug toxicity?
Systemic drugs and ocular toxicity: Acquired optic neuropathy--The ‘Big 8’

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

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

- Ethambutol
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- Isoniazid
- Streptomycin
- Linezolid
- Chloramphenicol
- Isotretinoin
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Which dietary components are thought to be especially critical in this regard?
Q/A

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

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

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*Which dietary components are thought to be especially critical in this regard?*
The B vitamins, especially B12 and folate.
Systemic drugs and ocular toxicity: Acquired optic neuropathy--The ‘Big 8’

- Ethambutol
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Isotretinoin

Cyclosporine

Systemic drugs and ocular toxicity:

Acquired optic neuropathy--The ‘Big 8’

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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.

What dietary habits place a pt at risk?

--?

--?

--?

(There are plenty of others, of course)

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

The B vitamins (especially B12) and folate
Systemic drugs and ocular toxicity:

**Acquired optic neuropathy--The ‘Big 8’**

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

**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.

**What dietary habits place a pt at risk?**

- Strict veganism
- Fad diets
- Eating disorders
- (There are plenty of others, of course)
Systemic drugs and ocular toxicity: Acquired optic neuropathy--The ‘Big 8’

- Ethambutol
- Rifampin
- Isoniazid
- Streptomycin
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What GI history places a pt at risk?
- --?
- --?
- --?
--(There are plenty of others, of course)
Systemic drugs and ocular toxicity: Acquired optic neuropathy--The ‘Big 8’

- Ethambutol
- Rifampin
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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.

What GI history places a pt at risk?
--Gastric bypass surgery
--Short bowel syndrome
--Hyperemesis gravidarum
--(There are plenty of others, of course)
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?*
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.
**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?*
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)
Systemic drugs and ocular toxicity: 
**Acquired optic neuropathy--The ‘Big 8’**

- Ethambutol

In addition to treating TB (i.e., 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?
Systemic drugs and ocular toxicity:
**Acquired optic neuropathy--The ‘Big 8’**

- **Ethambutol**

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  **Mycobacterium avium complex** (MAC)

  Is ethambutol optic neuropathy dose-related?
  Yes
Ethambutol

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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

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

- 35 mg/kg/d:
- 25 mg/kg/d:
- 15 mg/kg/d:
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

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Is ethambutol optic neuropathy dose-related?
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What proportion of pts will develop optic neuropathy at the following doses?
- 35 mg/kg/d: 20%
- 25 mg/kg/d: 5%
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- Cyclosporine
Ethambutol

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Per the BCSC: At what dose is monthly screening exams warranted?
Systemic drugs and ocular toxicity: Acquired optic neuropathy--The ‘Big 8’

- Ethambutol

  In addition to treating TB (infection with Mycobacterium tuberculosis), infections with what related infectious agents are also commonly treated with ethambutol?
  - Mycobacterium avium
  - Mycobacterium intracellulare

  Because they are so closely associated, M avium and M intracellulare are collectively referred to by what term?
  - Mycobacterium avium complex (MAC)

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  - 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%

  Per the BCSC: At what dose is monthly screening exams warranted?
  - Greater than 15 mg/kg/d
**Systemic drugs and ocular toxicity: Acquired optic neuropathy--The ‘Big 8’**

**Ethambutol**

In addition to treating TB (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).

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Is ethambutol optic neuropathy dose-related?

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- 35 mg/kg/d: 20%
- 25 mg/kg/d: 5%
- 15 mg/kg/d: 1%

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

Greater than 15 mg/kg/d

What constitutes an appropriate baseline exam?

--DFE
--Amsler grid
--VA
--Color vision
--Formal VF testing
Ethambutol

In addition to treating TB (infection with Mycobacterium tuberculosis), infections with what related infectious agents are also commonly treated with ethambutol? Mycobacterium avium and its first cousin Mycobacterium intracellulare are collectively referred to by what term? Mycobacterium avium complex (MAC)

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Per the BCSC: At what dose is monthly screening exams warranted? Greater than 15 mg/kg/d
Systemic drugs and ocular toxicity: Acquired optic neuropathy--The ‘Big 8’

- Ethambutol
- Rifampin
- Isoniazid
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- Linezolid
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- Isotretinoin
- Cyclosporine

In addition to treating TB (infection with Mycobacterium tuberculosis), infections with what related infectious agents are also commonly treated with ethambutol? *Mycobacterium avium* and its first cousin *Mycobacterium intracellularare* are collectively referred to by what term? *Mycobacterium avium complex* (MAC)

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

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

- **Ethambutol**

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

*Mycobacterium avium* and its first cousin

Because they are so closely associated, *M avium* and *M intracellular* 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%
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*Per the BCSC:* At what dose is monthly screening exams warranted?

Greater than 15 mg/kg/d

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?

The dose must be reduced, or the drug stopped entirely.
Systemic drugs and ocular toxicity: Acquired optic neuropathy--The ‘Big 8’

- Ethambutol

In addition to treating TB (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 intracelula* re are collectively referred to by what term?

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Is ethambutol optic neuropathy dose-related?

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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

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

What constitutes an appropriate baseline exam?

- DFE
- Amsler grid
- VA
- Color vision
- Formal VF testing

Cyclosporine
Systemic drugs and ocular toxicity: Acquired optic neuropathy--The ‘Big 8’

Ethambutol

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Is ethambutol optic neuropathy dose-related?
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- 35 mg/kg/d: 20%
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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?
Systemic drugs and ocular toxicity: Acquired optic neuropathy--The ‘Big 8’

**Ethambutol**

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

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- 35 mg/kg/d: 20%
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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”
**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, 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%

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)
Systemic drugs and ocular toxicity: Acquired optic neuropathy--The ‘Big 8’

Ethambutol

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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. Because they are so closely associated, Mycobacterium avium and Mycobacterium intracellular 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%

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).
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- 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
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