1) The uveitis is profiled
2) The profiled case is meshed
3) A differential diagnosis list is generated
4) Studies are obtained to identify the etiology
5) Treatment appropriate for the etiology is initiated

- Anterior
- Intermediate
- Posterior

Panuveitis
- Lyme
- Syphilis
- Behçet
- SO/VKH
- Sarcoid
- Leptospirosis
- Whipple’s
Uveitis: *Leptospirosis*

**Overview**

*Is leptospirosis a common cause of uveitis in the US?*
Uveitis: **Leptospirosis**

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No, it is distinctly uncommon, with only a couple hundred cases/year
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--Avocation: People who swim in open waters; eg triathletes

Does it have a climate preference?
Yes, it tends to occur in tropical/subtropical climes
**Uveitis: Leptospirosis**

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*At least half of all US cases are reported to occur in a single state--which one? (Hint: Consider lepto’s preferred climate, and that open-water swimming is a risk factor)*
**Uveitis: Leptospiroisis**

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*At least half of all US cases are reported to occur in a single state--which one? (Hint: Consider lepto’s preferred climate, and that open-water swimming is a risk factor)*
**Hawaii**, the tropical paradise where the Ironman Triathlon is held. (Coincidence? Probably, but it still might help with recalling this factoid)
Uveitis: Leptospirosis

Presentation

How does leptospirosis present?
Uveitis: *Leptospirosis*

*Presentation*

*How does leptospirosis present?*

Leptospirosis presents in a biphasic fashion:

--First:

--Second:
How does leptospirosis present?

Leptospirosis presents in a biphasic fashion:

--First: The **leptospiremic phase**
--Second:
How does leptospirosis present?
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--First: The **leptospiremic phase**
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**How does the leptospiremic phase present?**

How does leptospirosis present?
Leptospirosis presents in a biphasic fashion:
--First: The **leptospiremic phase**
--Second:
Uveitis: Leptospirosis

Presentation

How does leptospirosis present?
Leptospirosis presents in a biphasic fashion:
--First: The leptospiremic phase
--Second:

How does the leptospiremic phase present?
With systemic, constitutional findings: Fever, HA, myalgias, GI distress
Uveitis: Leptospirosis

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What is the time-of-onset after inoculation?
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What is the time-of-onset after inoculation?
A few weeks, maybe a month
Uveitis: Leptospirosis

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*There is an important eye finding to look for in this phase--what is it?*
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‘Circumcorneal conjunctival congestion’ (aka *ciliary flush*). Subconjunctival hemorrhage may be present as well.
Uveitis: **Leptospirosis**

Presentation

How does leptospirosis present?
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*At what point in this phase does the circumcorneal conj congestion appear?*
Uveitis: Leptospirosis

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‘Circumcorneal conjunctival congestion’ (aka ciliary flush). Subconjunctival hemorrhage may be present as well.

At what point in this phase does the circumcorneal conj congestion appear?
About 3-4 days after the onset of the systemic signs/symptoms
How does leptospirosis present?

Leptospirosis presents in a biphasic fashion:

--First: The leptospiremic phase

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_How does the leptospiremic phase present?_
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‘Circumcorneal conjunctival congestion’ (aka ciliary flush). Subconjunctival hemorrhage may be present as well.

_At what point in this phase does the circumcorneal conj congestion appear?_
About 3-4 days after the onset of the systemic signs/symptoms

If an OKAP pt has the right profile (vocational, avocational and/or geographic), and manifests the systemic symptoms described, **consider the presence of circumcorneal conj congestion pathognomonic for leptospirosis.**
Leptospirosis Presentation

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Leptospirosis presents in a biphasic fashion:
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*At what point in this phase does the circumcorneal conj congestion appear?*
About 3-4 days after the onset of the systemic signs/symptoms

*What other eye finding (present in only ~10% of leptospirosis pts) may be present?*
Uveitis: **Leptospirosis**

**Presentation**

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--First: The leptospiremic phase
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What other eye finding (present in only ~10% of leptospirosis pts) may be present? **Scleral icterus**, which indicates the dz is particularly serious (associated mortality rate ~30%)
How does leptospirosis present?
Leptospirosis presents in a biphasic fashion:
--First: The leptospiremic phase
--Second:
Uveitis: **Leptospirosis**

*Presentation*

*How does leptospirosis present?*
Leptospirosis presents in a biphasic fashion:
--First: The **leptospiremic phase**
--Second: The **immune phase**
Uveitis: *Leptospirosis*

Presentation

*How does leptospirosis present?*

Leptospirosis presents in a biphasic fashion:
--First: The *leptospiremic phase*
--Second: The *immune phase*

*How does the immune phase present?*
Uveitis: **Leptospirosis**

*Presentation*

*How does leptospirosis present?*
Leptospirosis presents in a biphasic fashion:
--First: The *leptospiremic phase*
--Second: The *immune phase*

*How does the immune phase present?*
Most commonly, with meningitis and leptospirosis. Other S/S include cranial nerve palsies, and of course intraocular inflammation.
Uveitis: **Leptospirosis**

**Presentation**

*How does leptospirosis present?*
Leptospirosis presents in a biphasic fashion:
--First: The **leptospiremic phase**
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*How does the immune phase present?*
Most commonly, with meningitis and leptospirosis. Other S/S include cranial nerve palsies, and of course intraocular inflammation.

*What is the time-of-onset between the leptospiremic phase and the immune phase?*
How does leptospirosis present?

Leptospirosis presents in a biphasic fashion:
--First: The leptospiremic phase
--Second: The immune phase

How does the immune phase present?

Most commonly, with meningitis and leptospiruria. Other S/S include cranial nerve palsies, and of course intraocular inflammation.

What is the time-of-onset between the leptospiremic phase and the immune phase?

It is highly variable--can be many months later. Thus, when taking a history with these pts, if you don’t ask specifically about leptospiremic-phase S/S that may have occurred months previously, you’ll miss it.
Uveitis: **Leptospirosis**

*Presentation*

*How does leptospirosis present?*
Leptospirosis presents in a biphasic fashion:
--First: The **leptospiremic phase**
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*How many leptospirosis pts go on to develop intraocular inflammation?*
Uveitis: **Leptospirosis**

*Presentation*

How does leptospirosis present?
Leptospirosis presents in a biphasic fashion:
--First: The *leptospiremic phase*
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How many leptospirosis pts go on to develop intraocular inflammation?
About half
Uveitis: Leptospirosis

Presentation

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--First: The leptospiremic phase
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How many leptospirosis pts go on to develop intraocular inflammation?
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Does ocular lepto present unilaterally, or bilaterally?
Uveitis: Leptospirosis

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Uveitis: **Leptospirosis**

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*When presenting as an isolated anterior uveitis, is it an acute and severe dz, or insidious and mild?*
Uveitis: **Leptospirosis**

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How does lepto panuveitis present?
Anterior:
Vitreous:
Retina:
ONH:
Uveitis: **Leptospirosis**

Presentation

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*How does lepto panuveitis present?*
**Anterior:** Dense nongranulomatous inflammation (70% will have a hypopyon)
**Vitreous:**
**Retina:**
**ONH:**
Uveitis: **Leptospirosis**

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Leptospirosis presents in a biphasic fashion:
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*How does lepto panuveitis present?*
**Anterior:** Dense nongranulomatous inflammation (~10% will have a hypopyon)
**Vitreous:**
**Retina:**
**ONH:**
Uveitis: **Leptospirosis**

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Leptospirosis presents in a biphasic fashion:
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*How does lepto panuveitis present?*
**Anterior:** Dense nongranulomatous inflammation (~10% will have a hypopyon)
**Vitreous:** Dense vitritis
**Retina:**
**ONH:**
How does leptospirosis present?
Leptospirosis presents in a biphasic fashion:
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How does lepto panuveitis present?
Anterior: Dense nongranulomatous inflammation (~10% will have a hypopyon)
Vitreous: Dense vitritis
Retina: Periphlebitis, but (usually) no CME
ONH:
How does leptospirosis present?
Leptospirosis presents in a biphasic fashion:
--First: The **leptospiremic phase**
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How does leptospirosis present?
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How do you know it’s lepto, and not…
--HLA-B27?
Uveitis: **Leptospirosis**

**Presentation**

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--First: The **leptospiremic phase**
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*Anterior*: Dense nongranulomatous inflammation (~10% will have a hypopyon)
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*Retina*: Periphlebitis, but (usually) no CME
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*How do you know it’s lepto, and not…*
--**HLA-B27**? Lepto is bilateral, and has vitritis
Uveitis: **Leptospirosis**

**Presentation**

*How does leptospirosis present?*

Leptospirosis presents in a biphasic fashion:

--First: The **leptospiremic phase**
--Second: The **immune phase**

*How many leptospirosis pts go on to develop intraocular inflammation?*

About half

*Does ocular lepto present unilaterally, or bilaterally?*

It can do either, but bilateral is far more common

*As leptospirosis is listed here as a panuveitis, is it safe to assume they all present in this manner?*

No, a small subset will present with an isolated anterior uveitis

*How does lepto panuveitis present?*

**Anterior:** Dense nongranulomatous inflammation (~10% will have a hypopyon)

**Vitreous:** Dense vitritis

**Retina:** Periphlebitis, but (usually) no CME

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Uveitis: **Leptospirosis**

**Diagnosis**

What is the ‘gold standard’ method for diagnosing lepto disease?
Uveitis: **Leptospirosis**

**Diagnosis**

*What is the ‘gold standard’ method for diagnosing lepto disease?*

Finding the organism on fluid samples (e.g., blood; CSF). That said, the bug is only recoverable for a short time during the leptospiremic phase, and thus is seldom found in actual practice.
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*Are other tests available?*
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*Why is this not surprising?*
Because like *T pallidum*, *L interrogans* is a spirochete
Uveitis: **Leptospirosis**

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*How is lepto treated?*
The bug itself is treated with IV Pen G q6 hr for a week. (Sound familiar?) Mild cases might respond to PO for short.
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*How is lepto treated?*

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The ocular inflammation responds well to steroids--topical, periocular and/or systemic may all be needed.
Uveitis: Whipple’s

1) The uveitis is profiled
2) The profiled case is meshed
3) A differential diagnosis list is generated
4) Studies are obtained to identify the etiology
5) Treatment appropriate for the etiology is initiated
Uveitis: **Whipple’s**

**Overview**

Is Whipple’s disease a common cause of uveitis in the US?

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Demographically speaking, who is the typical Whipple’s pt?
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Demographically speaking, who is the typical Whipple’s pt?
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Is it Gram+, or Gram-?
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The nystagmus in Whipple’s is accompanied by another set of movements--what are they?
The contraction of the muscles of mastication.

By what name is this simultaneous eye + masticatory movement pattern known?
Oculomasticatory myorhythmia (OMM).

Is OMM pathognomonic for Whipple’s?
Yes.
Is Whipple's disease a common cause of uveitis in the US?
No, it is very rare. Whipple’s disease itself is rare, and on top of that, less than 5% of pts manifest panuveitis. So Whipple’s panuveitis is a rare complication of a rare disease.

Demographically speaking, who is the typical Whipple’s pt?
A middle-aged white male

What is the causative organism in Whipple’s?
A bacterium called *Tropheryma whipplei*

Is it Gram+, or Gram-?
Technically considered G+, it does not take the stain well. It does take PAS well, however.

In addition to any eye signs/symptoms, how will a Whipple’s pt present?
With a history of chronic migratory arthritis and GI disturbances, and possible CNS findings

What specific 'GI disturbance,' and what are its sequelae?
Whipple’s pts have a malabsorption diarrhea. Of note, their inability to absorb protein leads to weight loss, and pitting edema (secondary to hypoalbuminemia).

What CNS findings are associated with Whipple’s?
It can cause seizures, dementia, and even coma. Neuro-ophthalmic findings include cranial nerve palsies (up to and including ophthalmoplegia) and nystagmus.

**Overview**

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Uveitis: **Whipple’s**

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Uveitis: **Whipple’s**

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*What is the prognosis for untreated Whipple’s?*
Uveitis: **Whipple’s**

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*What is the prognosis for untreated Whipple’s?*
It is uniformly fatal
Uveitis: Whipple’s

How does intraocular Whipple’s disease present?
Uveitis: Whipple’s

Ocular

How does intraocular Whipple’s disease present?
As a bilateral panuveitis, including retinal vasculitis
Uveitis: Whipple’s

Ocular

How does intraocular Whipple’s disease present?
As a bilateral panuveitis, including retinal vasculitis

Diagnosis

What is the ‘gold standard’ method for diagnosing Whipple’s disease?
Uveitis: **Whipple’s**

**Ocular**

*How does intraocular Whipple’s disease present?*
As a bilateral panuveitis, including retinal vasculitis

**Diagnosis**

*What is the ‘gold standard’ method for diagnosing Whipple’s disease?*
Via biopsy of the mucosa of the small intestine
Uveitis: *Whipple’s*

**Ocular**

How does *intraocular* Whipple’s disease present?  
As a bilateral panuveitis, including retinal vasculitis

**Diagnosis**

What is the ‘gold standard’ method for diagnosing Whipple’s disease?  
Via biopsy of the mucosa of the small intestine

What is the classic finding on small-intestine biopsy?
Uveitis: Whipple’s

Ocular

How does intraocular Whipple’s disease present?
As a bilateral panuveitis, including retinal vasculitis

Diagnosis

What is the ‘gold standard’ method for diagnosing Whipple’s disease?
Via biopsy of the mucosa of the small intestine

What is the classic finding on small-intestine biopsy?
Macrophages’ containing PAS-positive bacilli within intestinal villi
Uveitis: Whipple’s

Ocular

How does intraocular Whipple’s disease present?
As a bilateral panuveitis, including retinal vasculitis

Diagnosis

What is the ‘gold standard’ method for diagnosing Whipple’s disease?
Via biopsy of the mucosa of the small intestine

What is the classic finding on small-intestine biopsy?
‘Foamy macrophages’ containing PAS-positive bacilli within intestinal villi
Uveitis: Whipple’s

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Diagnosis

What is the ‘gold standard’ method for diagnosing Whipple’s disease?
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What is the classic finding on small-intestine biopsy?

‘Foamy macrophages’ containing PAS-positive bacilli within intestinal villi

Speaking of ‘foamy macrophages’…
What dz comes to mind if, instead of a middle-aged white guy with bilateral panuveitis, the pt in question was a very young child with unilateral pigmented iris nodules?
Uveitis: Whipple’s

Ocular

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Diagnosis

What is the ‘gold standard’ method for diagnosing Whipple’s disease?
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What is the classic finding on small-intestine biopsy?
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Speaking of ‘foamy macrophages’…
What dz comes to mind if, instead of a middle-aged white guy with bilateral panuveitis, the pt in question was a very young child with unilateral pigmented iris nodules?
And heterochromia iridis 2ndry to those nodules? Second clue
Uveitis: *Whipple’s*

How does intraocular Whipple’s disease present? As a bilateral panuveitis, including retinal vasculitis

**Diagnosis**

What is the ‘gold standard’ method for diagnosing Whipple’s disease? Via biopsy of the mucosa of the small intestine

What is the classic finding on small-intestine biopsy? *Foamy macrophages* containing PAS-positive bacilli within intestinal villi

Speaking of ‘foamy macrophages’…

*What dz comes to mind if, instead of a middle-aged white guy with bilateral panuveitis, the pt in question was a very young child with unilateral pigmented iris nodules? And heterochromia iridis 2ndry to those nodules? Along with a nontraumatic hyphema in the affected eye?*
Uveitis: **Whipple’s**

**Ocular**
How does intraocular Whipple’s disease present? As a bilateral panuveitis, including retinal vasculitis

**Diagnosis**
What is the ‘gold standard’ method for diagnosing Whipple’s disease? Via biopsy of the mucosa of the small intestine

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Speaking of ‘foamy macrophages’…
What dz comes to mind if, instead of a middle-aged white guy with bilateral panuveitis, the pt in question was a very young child with unilateral pigmented iris nodules? And heterochromia iridis 2ndry to those nodules? Along with a nontraumatic hyphema in the affected eye? Associated with orangish skin papules? Last clue--the answer is next
Uveitis: Whipple’s

Ocular

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As a bilateral panuveitis, including retinal vasculitis

Diagnosis

What is the ‘gold standard’ method for diagnosing Whipple’s disease?
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What dz comes to mind if, instead of a middle-aged white guy with bilateral panuveitis, the pt in question was a very young child with unilateral pigmented iris nodules?
And heterochromia iridis 2ndry to those nodules?
Along with a nontraumatic hyphema in the affected eye?
Associated with orangish skin papules?
Juvenile xanthogranuloma (JXG) ← Ding ding ding!
Uveitis: **Whipple’s**

**Ocular**

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**Diagnosis**

*What is the ‘gold standard’ method for diagnosing Whipple’s disease?*
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*Can Whipple’s be diagnosed via serology?*
Ocular

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Diagnosis

What is the ‘gold standard’ method for diagnosing Whipple’s disease?
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What is the classic finding on small-intestine biopsy?
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Can Whipple’s be diagnosed via serology?
Yes, PCR on blood and/or vitreous samples may reveal the presence of *T. whipplei* DNA
Uveitis: *Whipple’s*

### Ocular

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## Diagnosis

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## Treatment

*How is Whipple’s disease managed?*
Uveitis: *Whipple’s* Ocular

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**Treatment**

How is Whipple’s disease managed?  
With long-term systemic trimethoprim-sulfamethoxazole
Uveitis: **Whipple’s**

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As a bilateral panuveitis, including retinal vasculitis

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How ‘long term’ are we talking about here?
Uveitis: **Whipple’s**

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### Diagnosis

*What is the ‘gold standard’ method for diagnosing Whipple’s disease?*
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### Treatment

*How is Whipple’s disease managed?*
With long-term systemic trimethoprim-sulfamethoxazole

*How ‘long term’ are we talking about here?*
A minimum of 1-3 months; however, many pts relapse, necessitating treatment for up to a year