What are the four basic anatomic locations for uveitis?
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Uveitis

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

Let's now take a look at these, starting with leptospirosis
Uveitis: Leptospirosis

Overview

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

Is leptospirosis a common cause of uveitis in the US?
No, it is distinctly uncommon, with only a couple hundred cases/year
Uveitis: *Leptospirosis*

**Overview**

*Is leptospirosis a common cause of uveitis in the US?*
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*What kind of bug is Leptospira?*
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*Leptospira interrogans*; electron micrograph (bugs are bound to a 0.2-μm membrane filter)
Uveitis: *Leptospirosis*

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*Leptospira interrogans*. Darkfield microscopy
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Who is at risk for leptospirosis uveitis?  
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Uveitis: Leptospirosis

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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)*
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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:
Uveitis: Leptospirosis Presentation

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**
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*How does the *leptospiremic phase* present?*
How does leptospirosis present?
Leptospirosis presents in a biphasic fashion:
--First: The leptospiremic phase
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*How does the leptospiremic phase present?*
With systemic, constitutional findings: Fever, HA, myalgias, GI distress
Uveitis: **Leptospirosis**

**Presentation**

*How does leptospirosis present?*

Leptospirosis presents in a biphasic fashion:

--**First: The leptospiremic phase**

--**Second:**

*How does the leptospiremic phase present?*

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*What is the time-of-onset after inoculation?*
Uveitis: **Leptospirosis**

**Presentation**

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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?*
Uveitis: **Leptospirosis**

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

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

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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
Uveitis: Leptospirosis

Presentation

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

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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

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.
How does leptospirosis present?

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At what point in this phase does the circumcorneal conj congestion appear?
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What other eye finding (present in only ~10% of leptospirosis pts) may be present?
How does leptospirosis present?
Leptospirosis presents in a biphasic fashion:
--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%)
Leptospirosis: Circomcorneal conj congestion with icterus
Uveitis: **Leptospirosis**

**Presentation**

*How does leptospirosis present?*

Leptospirosis presents in a biphasic fashion:

---First: The **leptospiremic phase**

---Second:
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?

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

The time-of-onset between the leptospiremic phase and the immune phase 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

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Uveitis: Leptospirosis

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Uveitis: Leptospirosis

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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*?
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

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*Does ocular lepto present unilaterally, or bilaterally?*
Uveitis: **Leptospirosis**

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It can do either, but **50:50 shot** is far more common
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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?
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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 (~10% will have a hypopyon)
Vitreous:
Retina:
ONH:
How does leptospirosis present?

Leptospirosis presents in a biphasic fashion:
--- First: The leptospiremic phase
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Vitreous:
Retina:
ONH:
Uveitis: *Leptospirosis*

Leptospirosis: Nongranulomatous uveitis with hypopyon
Uveitis: Leptospirosis

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How does lepto panuveitis present?
_Anterior:_ Dense nongranulomatous inflammation (~10% will have a hypopyon)  
_Vitreous:_ Dense vitritis, which can coalesce into

_Retina:_
_ONH:_
Uveitis: **Leptospirosis**

**Presentation**

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*How does lepto panuveitis present?*
**Anterior:** Dense nongranulomatous inflammation (~10% will have a hypopyon)
**Vitreous:** Dense vitritis, which can coalesce into veils
**Retina:**
**ONH:**
Uveitis: *Leptospirosis*

Leptospirosis: Vitreous inflammation, veils
How does leptospirosis present?
Leptospirosis presents in a biphasic fashion:
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Retina: ONH:
Uveitis: **Leptospirosis**

**Presentation**

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*How does lepto panuveitis present?*
*Anterior:* Dense nongranulomatous inflammation (~10% will have a hypopyon)
*Vitreous:* Dense vitritis, which can coalesce into veils
*Retina:* Periphlebitis, but (usually) no CME
*ONH:*
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, which can coalesce into veils

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

**ONH:**
Uveitis: **Leptospirosis**

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Uveitis: *Leptospirosis*

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--HLA-B27 dz?
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Leptospiroisis

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Uveitis: **Leptospirosis**

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 (eg, 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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Because like T pallidum, L interrogans is a spirochete.
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How is lepto treated?
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The bug itself is treated with IV Pen G q6 hr for a week. (Sound familiar?) Mild cases might respond to PO.
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The ocular inflammation responds well to steroids--topical, periocular and/or systemic may all be needed.
Now let’s turn our attention to Whipple’s dz
Uveitis: **Whipple’s**

**Overview**

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

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What sort of nystagmus (ie, direction; speed) occurs in Whipple’s dz?
A pendular vergence nystagmus; ie, the eyes slowly and rhythmically converge, then diverge
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
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What sort of nystagmus (ie, direction; speed) occurs in Whipple’s dz?
A pendular vergence nystagmus; ie, the eyes slowly and rhythmically converge, then diverge
Uveitis: Whipple’s

Overview

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. 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+?
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)

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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

Is OMM pathognomonic for Whipple’s?
Yes
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*What is the prognosis for untreated Whipple’s?*
It is uniformly fatal
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

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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**

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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

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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
Whipple’s disease: Duodenal biopsy, low mag. The image shows the characteristic feature of foamy macrophages in the lamina propria.
Whipple’s disease: Duodenal biopsy, high mag. The image shows the characteristic feature of foamy macrophages in the lamina propria.
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?
**Foamy macrophages** containing PAS-positive bacilli within intestinal villi

Speaking of dz associated with ‘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?

First of four clues
Mystery condition clue #1: Pigmented iris lesion
**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?*
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Speaking of dz associated with ‘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?*
*Who had heterochromia iridis 2ndry to those nodules?*

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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

---

Second clue
Mystery condition clue #2: Heterochromia iridis
Uveitis: **Whipple’s**

**Ocular**

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

**Diagnosis**

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Via biopsy of the mucosa of the small intestine

What is the classic finding on small-intestine biopsy?
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Speaking of dz associated with ‘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?
**Who had heterochromia iridis 2ndry to those nodules?**
And a nontraumatic hyphema in the affected eye?

Clue #3
Mystery condition clue #3: Spontaneous hyphema
Uveitis:  **Whipple’s**

**Ocular**

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**Diagnosis**

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Who had heterochromia iridis 2ndry to those nodules?
And a nontraumatic hyphema in the affected eye?
Associated with orangish skin papules?

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1) The uveitis is profiled
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Mystery condition clue #4: Orange skin nodules
Uveitis: **Whipple’s**

**Ocular**

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**Diagnosis**

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Who had heterochromia iridis 2ndry to those nodules?
And a nontraumatic hyphema in the affected eye?
Associated with orangish skin papules?
**Juvenile xanthogranuloma (JXG)**

Ding ding ding!
‘Foamy macrophages’ in JXG
Uveitis: **Whipple’s**

**Ocular**

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**Diagnosis**

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*Can Whipple’s be diagnosed via serology?*
Uveitis: Whipple’s

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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*

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**Treatment**

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

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

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

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**Treatment**

How is Whipple’s disease managed?
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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