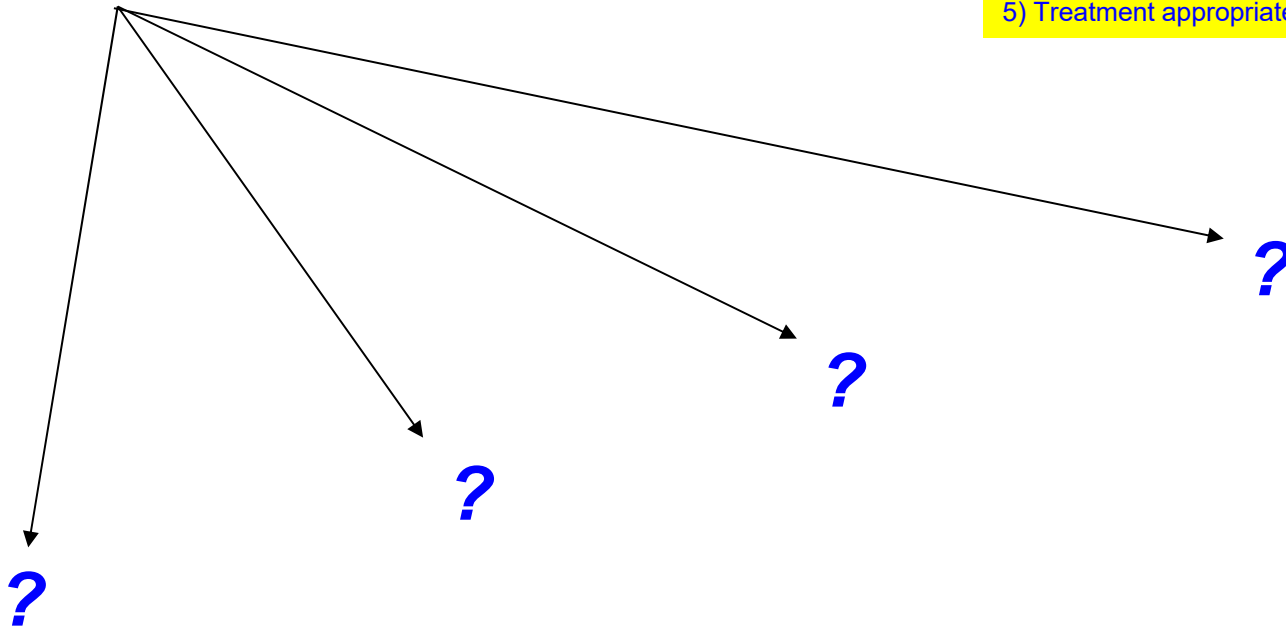


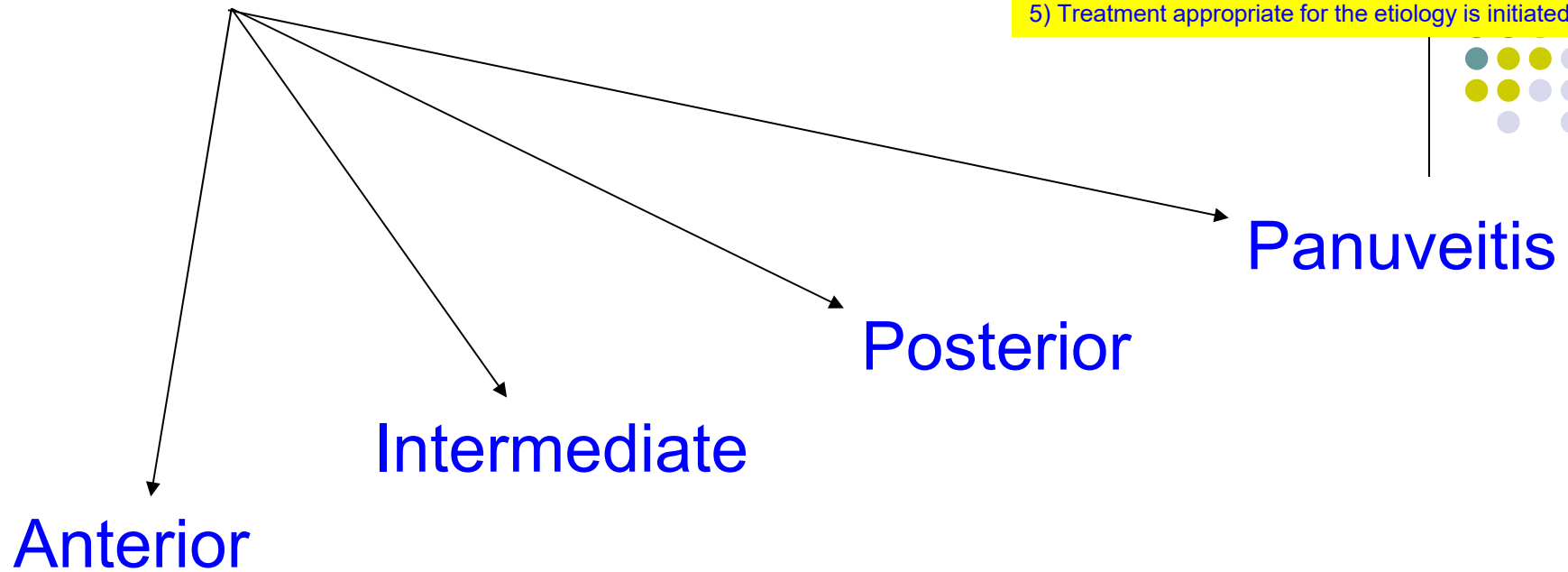
Uveitis

- 1) The uveitis is profiled
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What are the four basic anatomic locations for uveitis?

Uveitis



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Panuveitis

Anterior

Intermediate

Posterior

As this slide-set concerns leptospirosis and Whipple's, it should come as no surprise that both are on the panuveitis DDx. What are the other five panuveitic conditions the Uveitis book addresses?

— ?

— ?

— ?

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— ?

— Leptospirosis

— Whipple's

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Panuveitis

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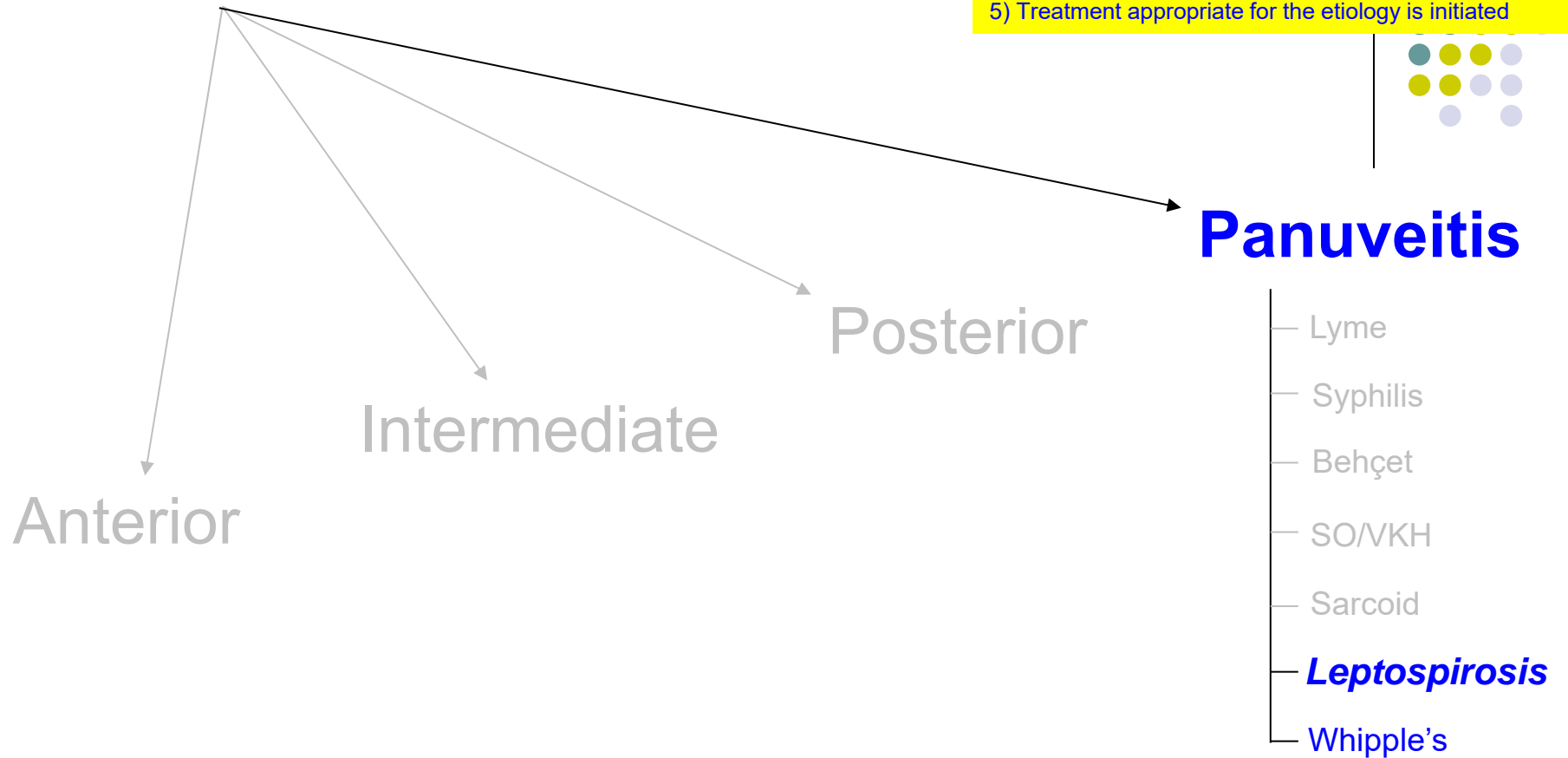
Posterior

As this slide-set concerns leptospirosis and Whipple's, it should come as no surprise that both are on the panuveitis DDx. What are the other five panuveitic conditions the Uveitis book addresses?

- Lyme
- Syphilis
- Behçet
- SO/VKH
- Sarcoid
- Leptospirosis
- Whipple's

Uveitis

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

Uveitis: *Leptospirosis*

Overview

Is leptospirosis a common cause of uveitis in the US?

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Uveitis: *Leptospirosis*

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No, it is distinctly uncommon, with only a couple hundred cases/year

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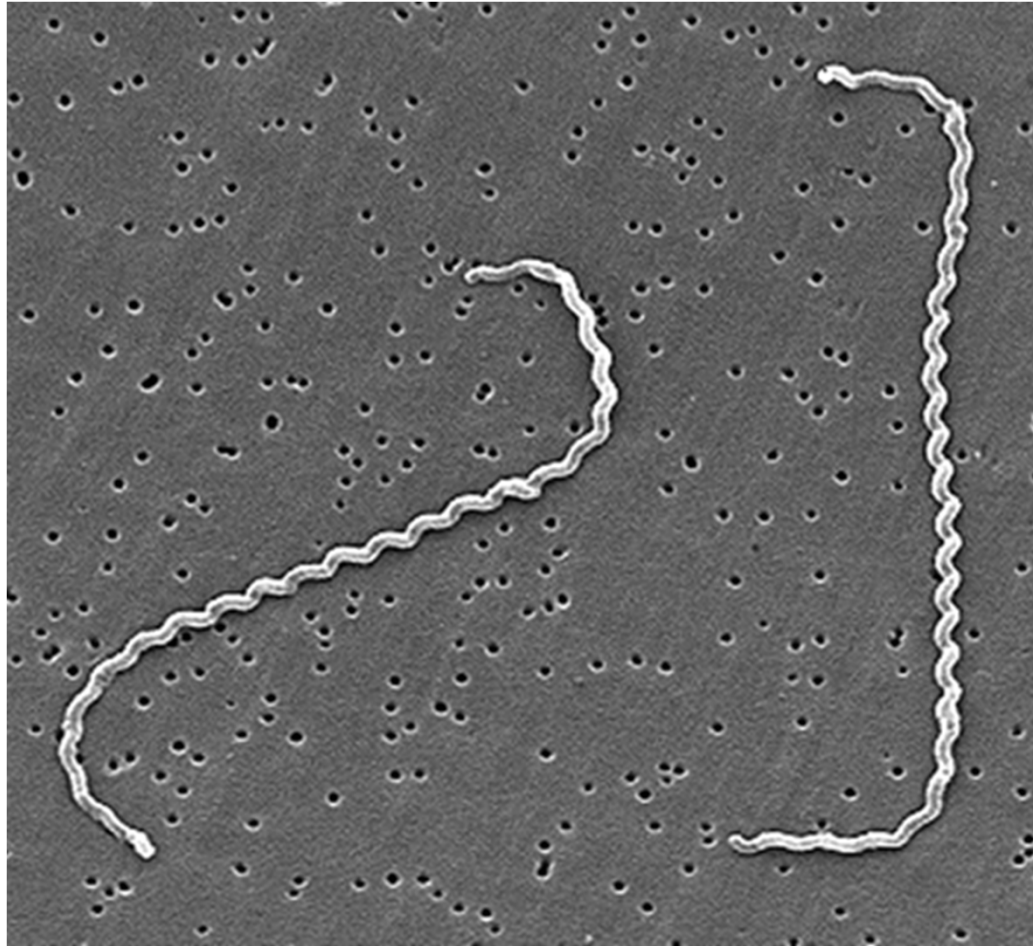
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Uveitis: *Leptospirosis*



Leptospira interrogans; electron micrograph
(bugs are bound to a 0.2-μm membrane filter)

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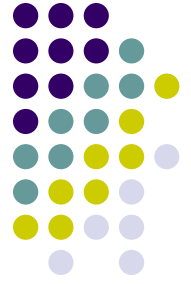
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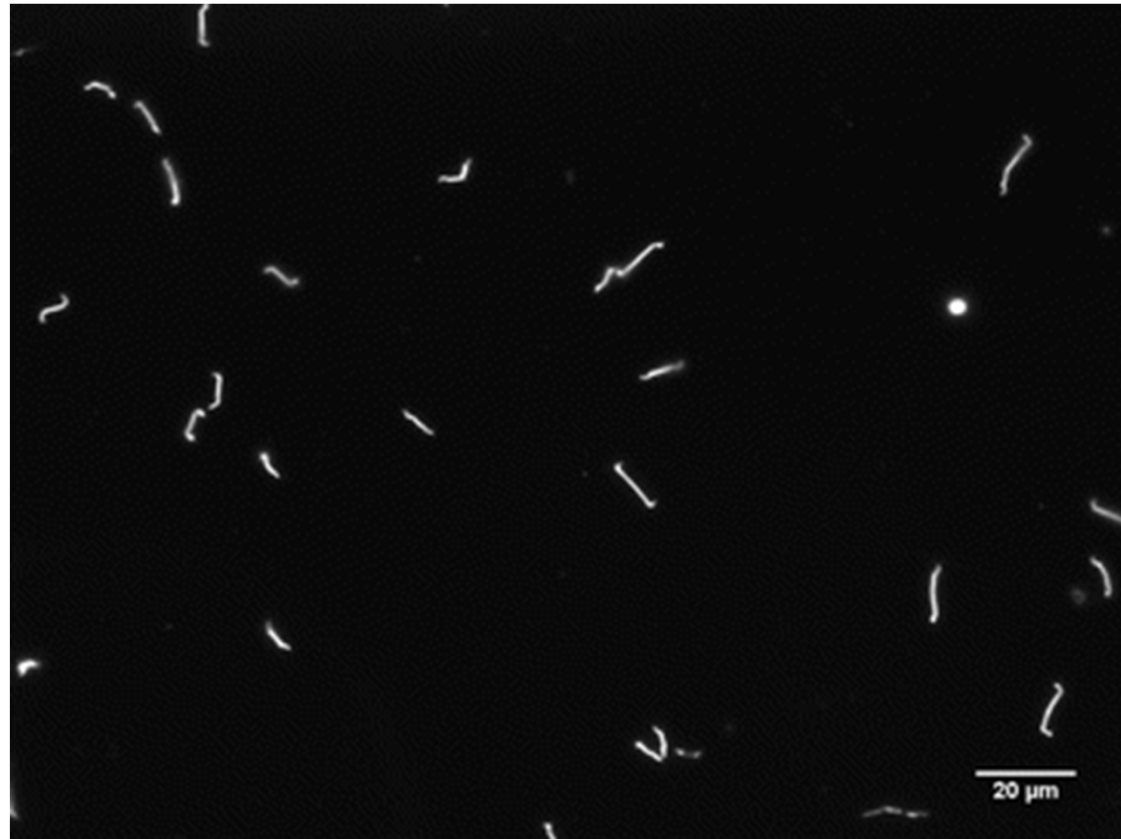
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Uveitis: *Leptospirosis*



Leptospira interrogans. Darkfield microscopy

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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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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?

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Uveitis: *Leptospirosis*

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How does leptospirosis present?

Leptospirosis presents in a biphasic fashion:

--First:

--Second:

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How does the leptospiremic phase present?

With systemic, constitutional findings: Fever, HA, myalgias, GI distress

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What is the time-of-onset after inoculation?

A few weeks, maybe a month

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At what point in this phase does the circumcorneal conj congestion appear?

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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

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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.**

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

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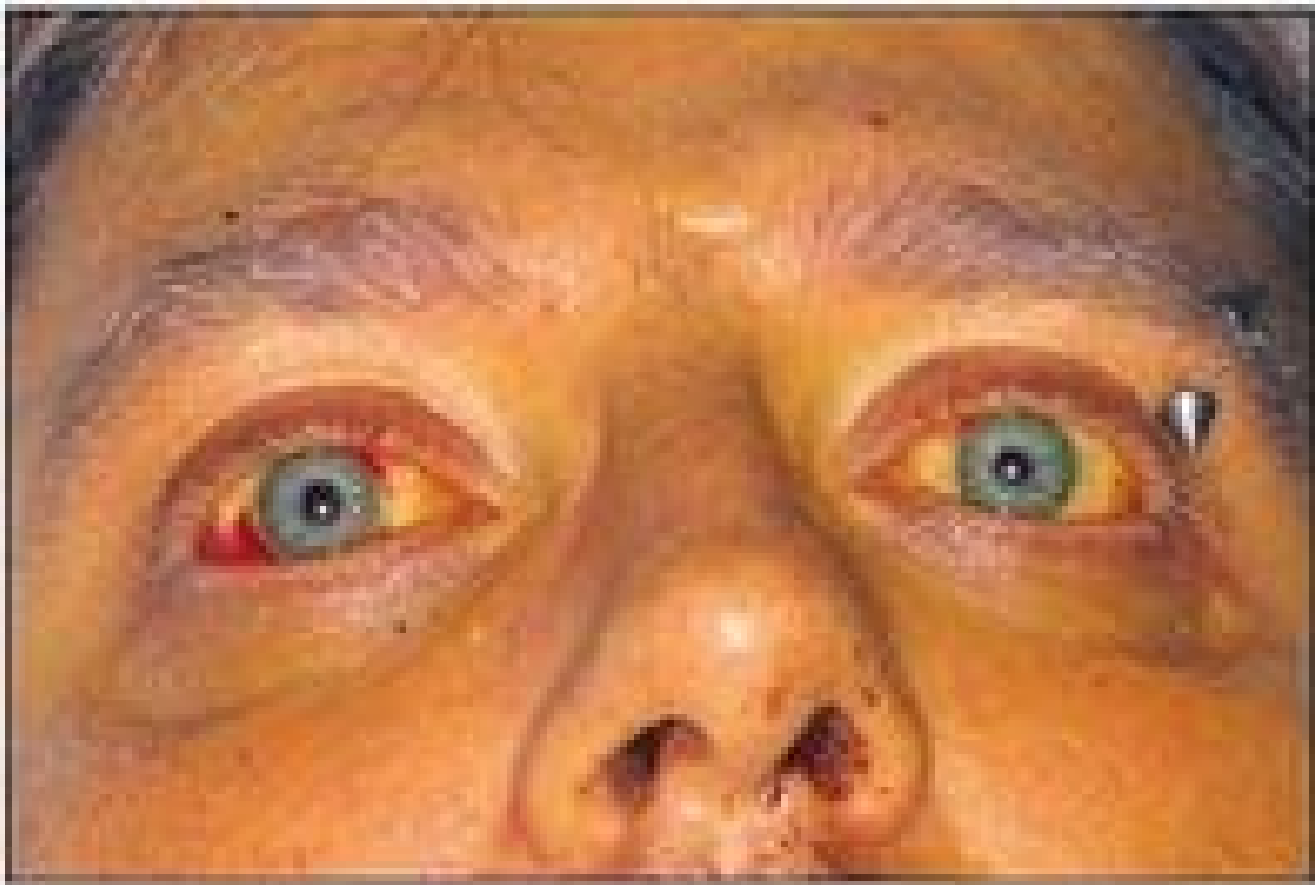
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Scleral icterus, which indicates the dz is particularly serious (associated mortality rate ~30%)

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Leptospirosis: Circumcorneal conj congestion with icterus

Uveitis: *Leptospirosis*

Presentation

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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**

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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 does the immune phase present?

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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 does the immune phase present?

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

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

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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.

- 1) The uveitis is profiled
- 2) The profiled case is meshed
- 3) A differential diagnosis list is generated
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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?

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How many leptospirosis pts go on to develop intraocular inflammation?

About half

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About half

Does ocular leptospirosis present unilaterally, or bilaterally?

It can do either, but **50:50 shot** is far more common

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--Second: The **immune phase**

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Does ocular lepto present unilaterally, or bilaterally?

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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*

Presentation

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

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 leptospirosis present?

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How does leptospirosis panuveitis present?

Anterior: Dense nongranulomatous inflammation (~ 50% will have a hypopyon)

Vitreous:

Retina:

ONH:

Uveitis: *Leptospirosis*

Presentation

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How does leptospirosis present?

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--Second: The **immune phase**

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How does lepto panuveitis present?

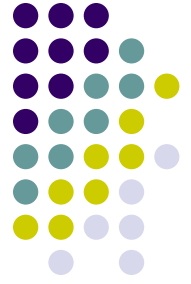
Anterior: Dense nongranulomatous inflammation (~10% will have a hypopyon)

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:

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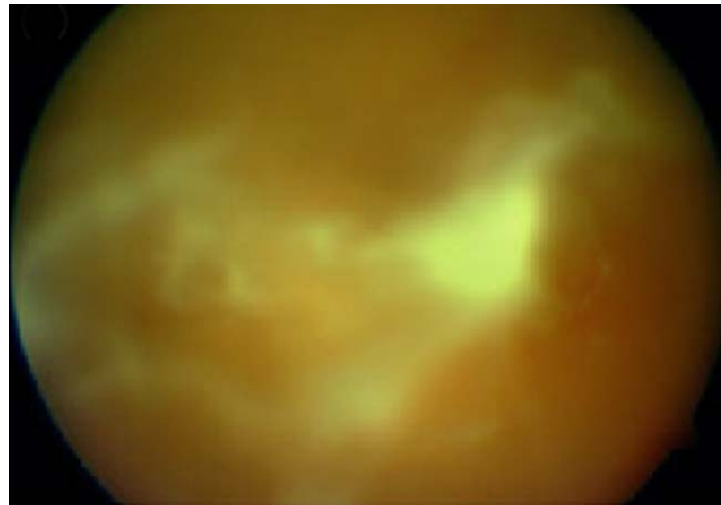
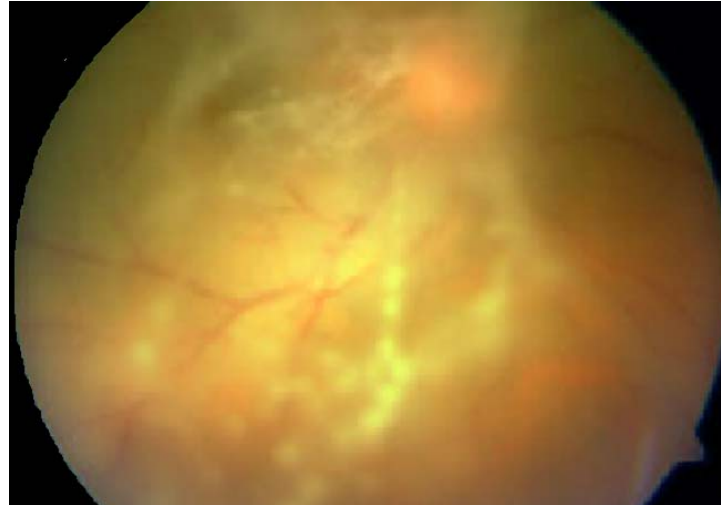
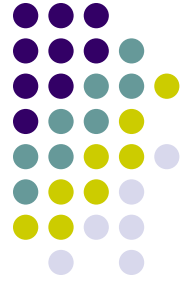
Anterior: Dense nongranulomatous inflammation (~10% will have a hypopyon)

Vitreous: Dense vitritis, which can coalesce into veils

Retina:

ONH:

Uveitis: *Leptospirosis*



Leptospirosis: Vitreous inflammation, veils

Uveitis: *Leptospirosis*

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abb.

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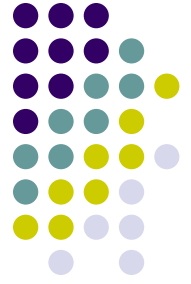
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Vitreous: Dense vitritis, which can coalesce into veils

Retina: Periphlebitis, but (usually) no CME

ONH:

Uveitis: *Leptospirosis*



Leptospirosis: Periphlebitis

Uveitis: *Leptospirosis*

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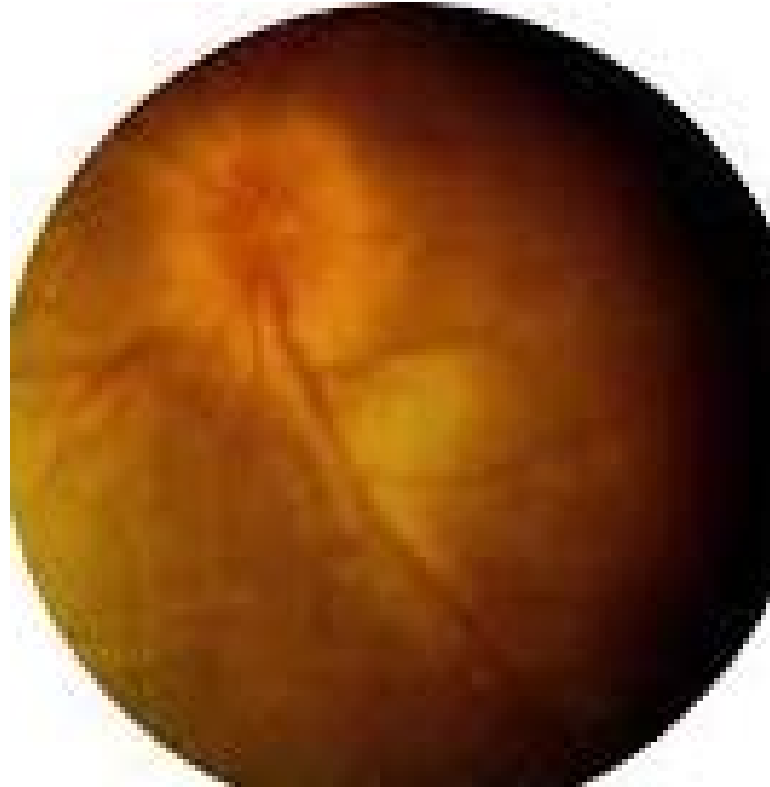
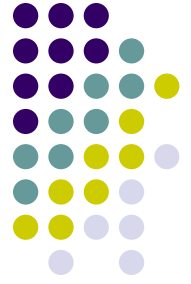
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ONH: Disc edema

Uveitis: *Leptospirosis*



Leptospirosis: disc edema

Uveitis: *Leptospirosis*

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Retina: Periphlebitis, but (usually) no CME

ONH: Disc edema

How do you know it's lepto, and not...

--HLA-B27 dz?

Uveitis: *Leptospirosis*

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ONH: Disc edema

How do you know it's lepto, and not...

--*HLA-B27 dz?* Lepto is bilateral, and has vitritis

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--Behçet?

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How do you know it's lepto, and not...

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--*Pars planitis?*

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--*Eales dz?*

Uveitis: *Leptospirosis*

Presentation

- 1) The uveitis is profiled
- 2) The profiled case is meshed
- 3) A differential diagnosis list is generated
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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: Disc edema

How do you know it's lepto, and not...

--*HLA-B27 dz?* Lepto is bilateral, and has vitritis

--*Behçet?* No occlusive vasculitis in leptospirosis

--*Pars planitis?* No CME

--*Eales dz?* No retinal peripheral neovascularization in lepto

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Because like *T pallidum*, *L interrogans* is a spirochete

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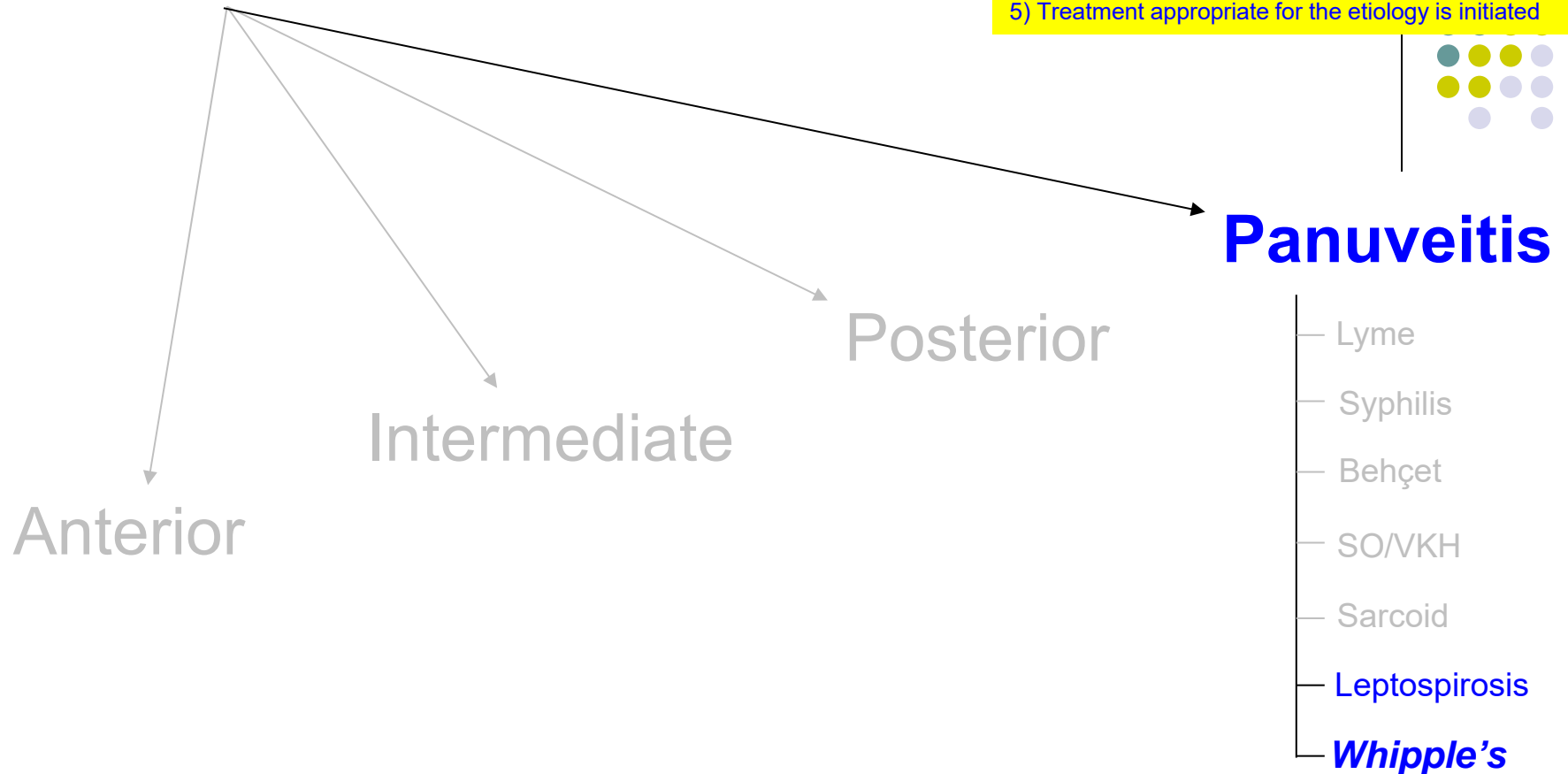
The ocular inflammation responds well to steroids--topical, periocular and/or systemic may all be needed.

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*Now let's turn our attention to **Whipple's dz***

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What speci
Whipple's p
weight loss

By what name is this simultaneous eye + masticatory movement pattern known?

What CNS findings are associated with Whipple's?

It can cause seizures, dementia, and even coma. Neuro-ophthalmic findings include cranial nerve palsies (including ophthalmoplegia) and **nystagmus**.

Uveitis: *Whipple's*

Overview

- 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



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

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

In addition
With a histo

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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?

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What is the prognosis for untreated Whipple's?

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What is the prognosis for untreated Whipple's?

It is uniformly fatal

Uveitis: *Whipple's*

Ocular

How does intraocular Whipple's disease present?

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Uveitis: *Whipple's*

Ocular

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

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Uveitis: *Whipple's*

Ocular

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What is the 'gold standard' method for diagnosing Whipple's disease?

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Uveitis: *Whipple's*

Ocular

How does intraocular Whipple's disease present?
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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

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Ocular

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What is the classic finding on small-intestine biopsy?

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Uveitis: *Whipple's*

Ocular

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As a bilateral panuveitis, including retinal vasculitis

Diagnosis

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What is the classic finding on small-intestine biopsy?

classic
descriptor

macrophages' containing PAS-positive bacilli within intestinal villi

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Uveitis: *Whipple's*

Ocular

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

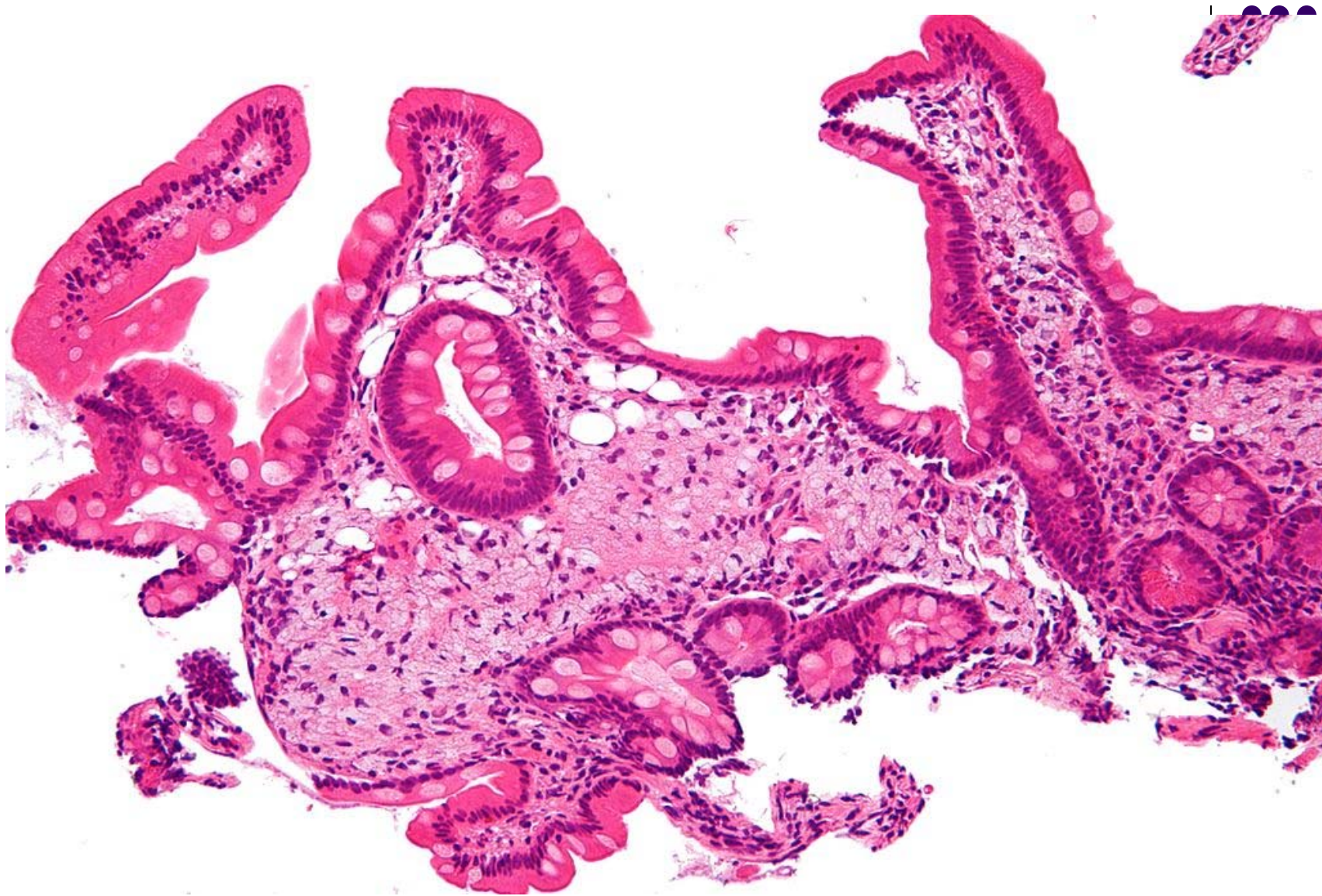
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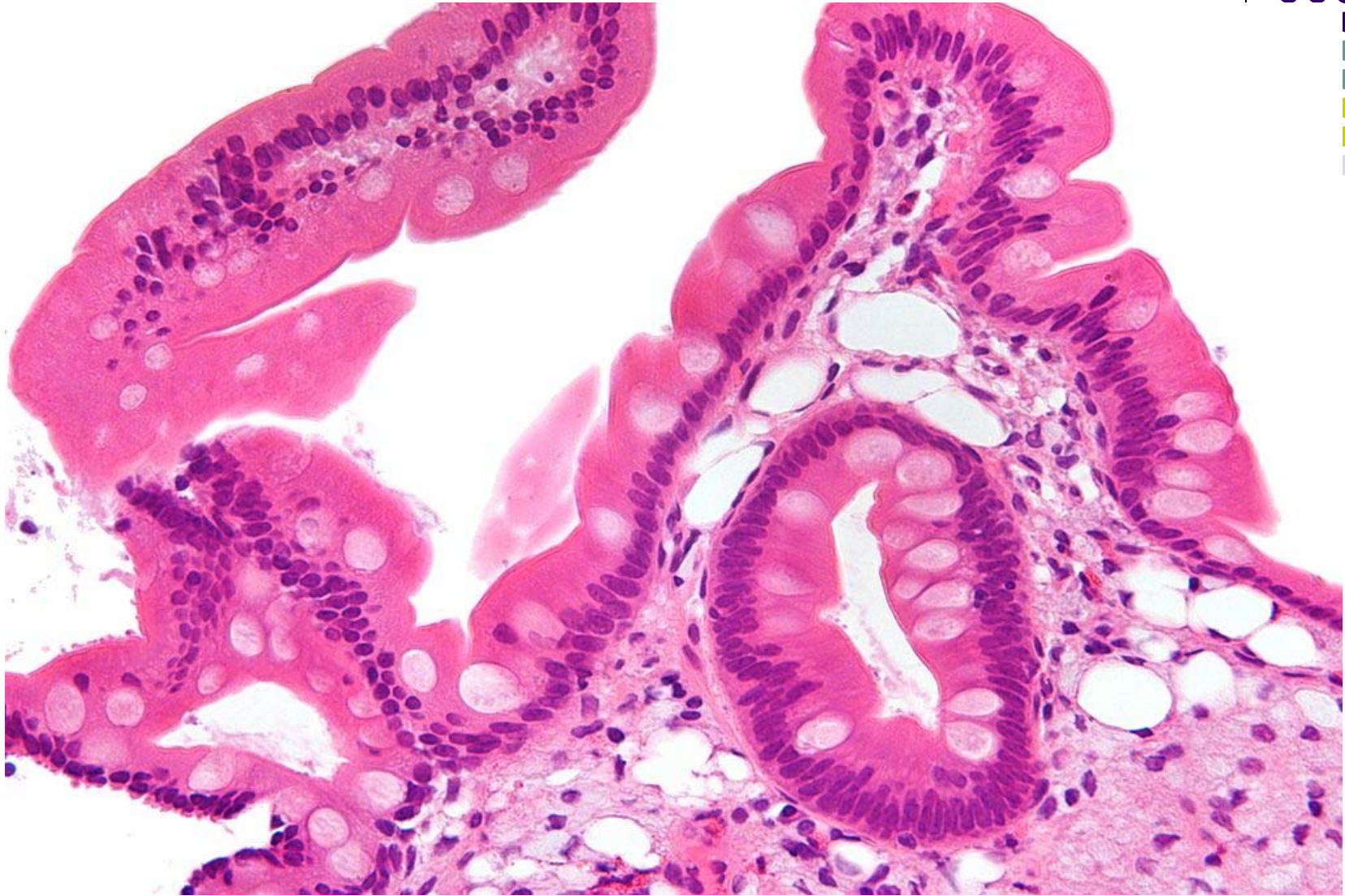
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'Foamy macrophages' containing PAS-positive bacilli within intestinal villi

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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

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?

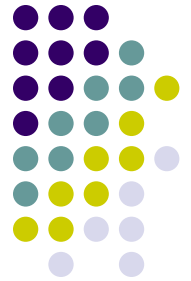
'Foamy macrophages' containing PAS-positive bacilli within intestinal villi

*Speaking of 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

- 1) The uveitis is profiled
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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?
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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:

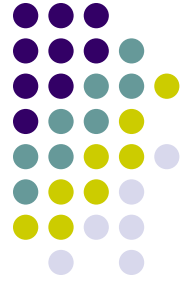
A very young child with unilateral pigmented iris nodules?

Who had heterochromia iridis 2ndry to those nodules?

← Second clue

- 1) The uveitis is profiled
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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

What is the 'gold standard' method for diagnosing Whipple's disease?
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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

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

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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'...

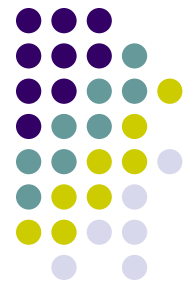
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A very young child with unilateral pigmented iris nodules?

Who had heterochromia iridis 2ndry to those nodules?

And a nontraumatic hyphema in the affected eye?

Associated with orangish skin papules? ← Last clue--the answer is next



Mystery condition clue #4: Orange skin nodules

Uveitis: *Whipple's*

Ocular

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

Diagnosis

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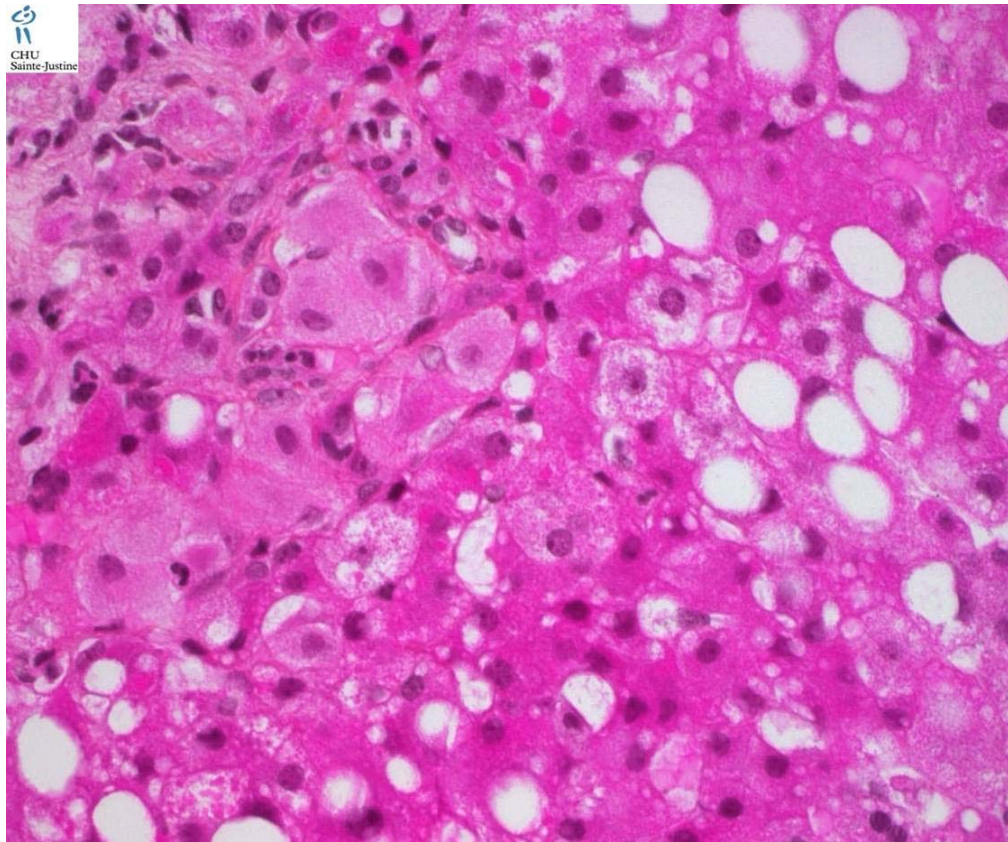
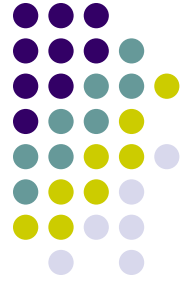
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A very young child with unilateral pigmented iris nodules?
Who had heterochromia iridis 2ndry to those nodules?
And a nontraumatic hyphema in the affected eye?
Associated with orangish skin papules?
Juvenile xanthogranuloma (JXG) ← Ding ding ding!



‘Foamy macrophages’ in JXG

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?
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Can Whipple's be diagnosed via serology?

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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

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A minimum of 1-3 months; however, many pts relapse, necessitating treatment for up to a year