Q

- Is SO a unilateral, or bilateral disease?
Is SO a unilateral, or bilateral disease?

It is a **bilateral** condition
Is SO a unilateral, or bilateral disease?

It is a **bilateral** condition

SO is a bilateral **general condition** following ocular injury or different event in one eye.
Is SO a unilateral, or bilateral disease?

It is a **bilateral** condition

SO is a bilateral **panuveitis** following ocular **injury** or **surgery** in one eye
● Is SO a unilateral, or bilateral disease? It is a bilateral condition.
● SO is a bilateral panuveitis following ocular injury or surgery.

Is it granulomatous, or nongranulomatous?
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease?
  It is a **bilateral** condition

- SO is a bilateral **panuveitis** following ocular injury or surgery.
Sympathetic Ophthalmia (SO): Wadda ya know?

SO: Granulomatous KP
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease? It is a **bilateral** condition.
- SO is a bilateral panuveitis following ocular **injury or surgery** in one eye.

Which is a more common cause: Injury, or surgery?
Is SO a unilateral, or bilateral disease? It is a **bilateral** condition.

SO is a bilateral **panuveitis** following ocular **injury** or **surgery** in one eye.

*Which is a more common cause: Injury, or surgery?*

Back in the day, it was injury by a mile.
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease? It is a **bilateral** condition.
- SO is a bilateral panuveitis following ocular **injury or surgery** in one eye.

*Which is a more common cause: Injury, or surgery?*
Back in the day, it was injury by a mile. However, refinements in managing ocular trauma have reduced the post-trauma SO rate such that it is now **below** that after surgery.
Q

- Is SO a unilateral, or bilateral disease? It is a **bilateral** condition.
- SO is a bilateral **panuveitis** following ocular **injury or surgery** in one eye.

Which is a more common cause: Injury, or surgery? Back in the day, it was injury by a mile. However, refinements in managing ocular trauma have reduced the post-trauma SO rate such that it is now **below** that after surgery.

What is the classic injury-related scenario associated with SO; ie, what would be seen at the slit-lamp?
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease? It is a **bilateral** condition.
- SO is a bilateral panuveitis following ocular **injury or surgery** in one eye.

Which is a more common cause: Injury, or surgery? Back in the day, it was injury by a mile. However, refinements in managing ocular trauma have reduced the post-trauma SO rate such that it is now below that after surgery.

What is the classic injury-related scenario associated with SO; ie, what would be seen at the slit-lamp? tissue incarcerated in the wound.
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease? It is a **bilateral** condition.
- SO is a bilateral **panuveitis** following ocular **injury** or **surgery** in one eye.

Which is a more common cause: Injury, or surgery? Back in the day, it was injury by a mile. However, refinements in managing ocular trauma have reduced the post-trauma SO rate such that it is now **below** that after surgery.

What is the classic injury-related scenario associated with SO; *ie, what would be seen at the slit-lamp?* Uveal tissue incarcerated in the wound.
Q

Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease? It is a **bilateral** condition.
- SO is a bilateral panuveitis following ocular **injury** or surgery in one eye.

You know that perforating/penetrating injury can result in SO, but what about a contusion?
● Is SO a unilateral, or bilateral disease? It is a **bilateral** condition

● SO is a bilateral **panuveitis** following ocular **injury** or surgery in one eye

*You know that perforating/penetrating injury can result in SO, but what about a contusion? Yes, globe contusion has resulted in SO (although this is **exceedingly** rare)*
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease? It is a **bilateral** condition.
- SO is a bilateral *panuveitis* following ocular injury or **surgery** in one eye.

Which of these surgeries has been associated with SO--
---PPV?
---Cataract surgery?
---Trabeculectomy?
---Cyclocryoablation?
---Cyclophotocoagulation?
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease?
  It is a **bilateral** condition.
- SO is a bilateral panuveitis following ocular injury or surgery.

Which of these surgeries has been associated with SO—
- PPV!
- Cataract surgery!
- Trabeculectomy!
- Cyclocryoablation!
- Cyclophotocoagulation!

All have been associated with SO!
Q

- Is SO a unilateral, or bilateral disease?
  It is a bilateral condition.

- SO is a bilateral panuveitis following ocular injury or surgery.

Which of these surgeries has been associated with SO--
- PPV?
- Cataract surgery?
- Trabeculectomy?
- Cyclocryoablation?
- Cyclophotocoagulation?

Which surgery carries the highest risk of SO?
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease?
  - It is a **bilateral** condition.

- SO is a bilateral panuveitis following ocular injury or surgery in one eye.

Which of these surgeries has been associated with SO--

- PPV!
- Cataract surgery
- Trabeculectomy
- Cyclocryoablation
- Cyclophotocoagulation

Which surgery carries the highest risk of SO?

**Vitrectomy**
Q

- Is SO a unilateral, or bilateral disease? It is a **bilateral** condition.
- SO is a bilateral panuveitis following ocular injury or surgery.

**Sympathetic Ophthalmia (SO): Wadda ya know?**

- Which of these surgeries has been associated with SO--
  --PPV!

**Which incidence is higher: Post-PPV endophthalmitis, or post-PPV SO?**

--Cyclophotocoagulation
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease? It is a **bilateral** condition.
- SO is a bilateral panuveitis following ocular injury or surgery.

Which of these surgeries has been associated with SO--

--PPV!

Which incidence is higher: Post-PPV endophthalmitis, or post-PPV SO?

Post-PPV SO

--Cyclophotocoagulation
Is SO a unilateral, or bilateral disease? It is a **bilateral** condition

SO is a bilateral **panuveitis** following ocular injury or **surgery** in one eye

- Previously injured/operated eye is called the **inciting eye**
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease?
  - It is a **bilateral** condition

- SO is a bilateral **panuveitis** following ocular **injury** or **surgery** in one eye
  - Previously injured/operated eye is called the **exciting** eye
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease?
  It is a **bilateral** condition

- SO is a bilateral **panuveitis** following ocular **injury** or **surgery** in one eye
  -Previously injured/operated eye is called the **exciting** eye
  -Previously normal eye is called the **sympathizing** eye
Is SO a unilateral, or bilateral disease?

It is a **bilateral** condition.

SO is a bilateral **panuveitis** following ocular **injury** or **surgery** in one eye.

- Previously injured/operated eye is called the **exciting** eye.
- Previously normal eye is called the **sympathizing** eye.

Sympathetic Ophthalmia (SO): Wadda ya know?
Is SO a unilateral, or bilateral disease?

It is a **bilateral** condition

SO is a bilateral **panuveitis** following ocular **injury** or **surgery** in one eye

- Previously injured/operated eye is called the **exciting** eye
- Previously normal eye is called the **sympathizing** eye

What is the cause of SO?
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease? **It is a bilateral** condition.
- SO is a bilateral **panuveitis** following ocular **injury** or **surgery** in one eye:
  - Previously injured/operated eye is called the **exciting** eye.
  - Previously normal eye is called the **sympathizing** eye.
- What is the cause of SO? **Unknown**.
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease? It is bilateral.
- SO is a bilateral panuveitis following ocular injury or surgery in one eye.
- Previously injured/operated eye is called the exciting eye.
- Previously normal eye is called the sympathizing eye.
- What is the cause of SO? Unknown

That said, we are not completely in the dark vis a vis etiology, so…

Is it infectious, or noninfectious?

Most experts are convinced it is noninfectious.

Ok, so it's immune-related. Is it T-cell, or B-cell mediated?

This one we know—T-cells are the culprit.

To what antigens are the T cells responding? This is less certain, but it seems uveal antigens—specifically, melanin-associated?—play a central role.
Is SO a unilateral, or bilateral disease?

It is a **bilateral** condition.

SO is a bilateral panuveitis following ocular injury or surgery in one eye.

Previously injured/operated eye is called the **exciting eye**.

Previously normal eye is called the **sympathizing eye**.

What is the cause of SO? **Unknown**

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  It is a bilateral condition.

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  Previously injured/operated eye is called the exciting eye.
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Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral or bilateral disease? It is bilateral.
- SO is a bilateral panuveitis following ocular injury or surgery in one eye.
- Previously injured/operated eye is called the exciting eye.
- Previously normal eye is called the sympathizing eye.
- What is the cause of SO? Unknown

That said, we are not completely in the dark vis a vis etiology, so...

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- Ok, so it’s immune-related. Is it T-cell, or B-cell mediated? This one we know—T-cells are the culprit.
- To what antigens are the T cells responding?
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease? It is a bilateral condition.
- SO is a bilateral panuveitis following ocular injury or surgery in one eye. Previously injured/operated eye is called the exciting eye. Previously normal eye is called the sympathizing eye.
- What is the cause of SO? Unknown

That said, we are not completely in the dark vis a vis etiology, so…

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To what antigens are the T cells responding?
This is less certain, but it seems uveal antigens—specifically melanin-associated—play a central role.
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease?
  It is a **bilateral** condition

- SO is a bilateral **panuveitis** following ocular **injury** or **surgery** in one eye
  - Previously injured/operated eye is called the **exciting** eye
  - Previously normal eye is called the **sympathizing** eye

- What is the cause of SO? **Unknown**

- What is the classic presenting complaint?
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease?  
  It is a **bilateral** condition

- SO is a bilateral **panuveitis** following ocular **injury** or **surgery** in one eye
  - Previously injured/operated eye is called the **exciting** eye
  - Previously normal eye is called the **sympathizing** eye

- What is the cause of SO? **Unknown**

- What is the classic presenting complaint?  
  Impaired near vision (ie, loss of accommodation) in the previously normal eye
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease? It is a **bilateral** condition.
- SO is a bilateral **panuveitis** following ocular **injury** or **surgery** in one eye.
  - Previously injured/operated eye is called the **exciting** eye.
  - Previously normal eye is called the **sympathizing** eye.
- What is the cause of SO? Unknown.
- What is the **classic presenting complaint**? Impaired near vision (ie, **loss of accommodation**).

*Take note of this!* IMHO, it would make a great Orals question—a pt with a remote hx of ocular trauma presenting with what sounds like early-onset presbyopia.
Sympathetic Ophthalmia (SO): Wadda ya know?

- Is SO a unilateral, or bilateral disease?
  It is a **bilateral** condition

- SO is a bilateral **panuveitis** following ocular **injury** or **surgery** in one eye
  - Previously injured/operated eye is called the **exciting** eye
  - Previously normal eye is called the **sympathizing** eye

- What is the cause of SO? Unknown

- What is **the classic presenting complaint**?
  Impaired near vision (ie, **loss of accommodation**)

*Take note of this!* IMHO, it would make a great Orals question—a pt with a remote hx of ocular trauma presenting with what sounds like early-onset presbyopia. It would be all too easy to send them out with OTC readers, thereby consigning this hypothetical pt to profound vision loss—and yourself to repeating the Boards.
SO: Treatment/course/prognosis

- In a nutshell, treat like any other
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
Sympathetic Ophthalmia (SO): Wadda ya know?

- **SO**: Treatment/course/prognosis
  - In a nutshell, treat like any other panuveitis
    - Local
Sympathetic Ophthalmia (SO): Wadda ya know?

- SO: Treatment/course/prognosis
  - In a nutshell, treat like any other panuveitis
    - Local steroids
Sympathetic Ophthalmia (SO): Wadda ya know?

SO: Treatment/course/prognosis

- In a nutshell, treat like any other *panuveitis*
  - Local **steroids**

*Is SO steroid responsive?*
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local **steroids**

*Is SO steroid responsive?*
Yes, reliably and significantly
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - for comfort
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort

Sympathetic Ophthalmia (SO): Wadda ya know?
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
SO: Treatment/course/prognosis

In a nutshell, treat like any other panuveitis

- Local steroids
- Cycloplegia for comfort
- +/- systemic steroids
- May need systemic (two) related/words
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression
  - Should the exciting eye be removed?

Sympathetic Ophthalmia (SO): Wadda ya know?
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression
  - Should the exciting eye be removed? Not if it has any potential for useful vision
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression
  - Should the exciting eye be removed? Not if it has any potential for useful vision

Can the risk of SO be reduced by prophylactic enucleation?
Q/A

Sympathetic Ophthalmia (SO): Wadda ya know?

SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression
- Should the exciting eye be removed? Not if it has any potential for useful vision

Can the risk of SO be reduced by prophylactic enucleation?
Yes, if it’s done within about 2 weeks of injury occurrence
**Sympathetic Ophthalmia (SO): Wadda ya know?**

- **SO: Treatment/course/prognosis**
  - In a nutshell, treat like any other panuveitis
    - Local steroids
    - Cycloplegia for comfort
    - +/- systemic steroids
    - May need systemic immunomodulation/suppression
  - Should the exciting eye be removed? **Not if it has any potential for useful vision**

---

*Can the risk of SO be reduced by prophylactic enucleation?*

Yes, if it’s done within about 2 weeks of injury occurrence
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression
- Should the exciting eye be removed? Not if it has any potential for useful vision

Can the risk of SO be reduced by prophylactic enucleation? Yes, if it’s done within about 2 weeks of injury occurrence

Once the process commences, can the course (severity; duration, etc) be mitigated by enucleating the exciting eye?
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression
- Should the exciting eye be removed? Not if it has any potential for useful vision

Can the risk of SO be reduced by prophylactic enucleation?
Yes, if it’s done within about 2 weeks of injury occurrence

Once the process commences, can the course (severity, duration, etc) be mitigated by enucleating the exciting eye?
No
**Sympathetic Ophthalmia (SO): Wadda ya know?**

- **SO: Treatment/course/prognosis**
  - In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression
  - Should the exciting eye be removed? Not if it has any potential for useful vision

**Can the risk of SO be reduced by prophylactic enucleation?**
- Yes, if it's done within about 2 weeks of injury occurrence.

**If the injured eye is not salvageable, is evisc a reasonable option?**
- No
SO: Treatment/course/prognosis

- In a nutshell, treat like any other *panuveitis*
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression
  - Should the exciting eye be removed? Not if it has any potential for useful vision

Can the risk of SO be reduced by prophylactic enucleation?
Yes, if it’s done within about 2 weeks of injury occurrence.

Once the process commences, can the course (severity, duration, etc) be mitigated by enucleating the exciting eye?
No

*If the injured eye is not salvageable, is evisc a reasonable option?*
Tough call, but probably not. Evisc incurs a risk of leaving small amounts of uveal tissue, and thus does not completely eliminate the risk of inciting SO.

Sympathetic Ophthalmia (SO): Wadda ya know?
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression
  - Should the exciting eye be removed? Not if it has any potential for useful vision

- What is the course? chronic vs a one-time acute event
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression
  - Should the exciting eye be removed? Not if it has any potential for useful vision

- What is the course? Chronic--waxing and waning
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression
  - Should the exciting eye be removed? Not if it has any potential for useful vision

- What is the course? Chronic--waxing and waning
- What is the prognosis?
SO: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression
  - Should the exciting eye be removed? Not if it has any potential for useful vision

- What is the course? Chronic--waxing and waning

- What is the prognosis? Far better than it used to be—with modern steroids/immuno drugs, probability of maintaining useful vision is excellent
Fill in the blanks regarding the time course of post-trauma SO:

- The onset of SO is very rare before \[\text{[length of time since trauma]}\].
Fill in the blanks regarding the time course of post-trauma SO:

- The onset of SO is very rare before **2 weeks**.
Fill in the blanks regarding the time course of post-trauma SO:

- The onset of SO is very rare before _____ 2 weeks. 
- 80% declare by [length of time since trauma], and 90% by [length of time since trauma].

Sympathetic Ophthalmia (SO): Wadda ya know?
**Sympathetic Ophthalmia (SO): Wadda ya know?**

- **Fill in the blanks regarding the time course of post-trauma SO:**
  - The onset of SO is very rare before **2 weeks**.
  - 80% declare by **3 months**, and 90% by **1 year**.
Fill in the blanks regarding the time course of post-trauma SO:

- The onset of SO is very rare before **2 weeks**.
- 80% declare by **3 months**, and 90% by **1 year**.
- The shortest documented time to onset was **[length of time since trauma]**; the longest, **[length of time since trauma]**.
**Fill in the blanks regarding the time course of post-trauma SO:**

- The onset of SO is very rare before **2 weeks**.
- 80% declare by **3 months**, and 90% by **1 year**.
- The shortest documented time to onset was **5 days**; the longest, **66 years**.
Now we will turn our attention to VKH.
Now we will turn our attention to VKH. If during this section you find yourself experiencing a strong sense of déjà vu, relax—it’s real, not a glitch in the Matrix.
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

- Is VKH a unilateral, or bilateral disease?
Is VKH a unilateral, or bilateral disease?

It is a **bilateral** condition
Is VKH a unilateral, or bilateral disease?

It is a **bilateral** condition

VKH is a bilateral **absent** ocular history or
• Is VKH a unilateral, or bilateral disease?
  It is a **bilateral** condition

• VKH is a bilateral **panuveitis** **absent** ocular **injury** or **surgery** history
Is VKH a unilateral, or bilateral disease?

It is a **bilateral** condition

VKH is a bilateral **panuveitis** absent ocular injury or surgery history

*Is it granulomatous, or nongranulomatous?*
Is VKH a unilateral, or bilateral disease? It is a **bilateral** condition.

VKH is a bilateral **panuveitis** absent ocular injury or surgery history.

*Is it granulomatous, or nongranulomatous?*

**Granulomatous**
Is VKH a unilateral, or bilateral disease? It is a **bilateral** condition.

VKH is a bilateral **panuveitis** **absent** ocular **injury** or **surgery** history.

What is the cause of VKH?
Is VKH a unilateral, or bilateral disease? 
It is a **bilateral** condition

VKH is a bilateral **panuveitis** absent ocular **injury** or **surgery** history

What is the cause of VKH? **Unknown**
Is VKH a unilateral, or bilateral disease? It is a \textit{bilateral} condition.

VKH is a bilateral \textit{panuveitis} \textit{absent} ocular injury or \textit{surgery} history.

What is \textit{the cause of VKH}? \textit{Unknown}

That said, we are not completely in the dark vis a vis etiology, so…

\textit{Is it infectious, or noninfectious?}
Is VKH a unilateral, or bilateral disease? It is a **bilateral** condition.

VKH is a bilateral **panuveitis** **absent** ocular injury or **surgery** history.

What is **the cause of VKH?** **Unknown**

That said, we are not completely in the dark vis a vis etiology, so…

*Is it infectious, or noninfectious?*

Most experts are convinced it is noninfectious.
Is VKH a unilateral, or bilateral disease? It is a **bilateral** condition.

VKH is a bilateral panuveitis **absent** ocular injury or **surgery** history.

What is the cause of VKH? **Unknown**

That said, we are not completely in the dark vis a vis etiology, so…

*Is it infectious, or noninfectious?*
Most experts are convinced it is noninfectious.

*Ok, so it’s immune-related. Is it T-cell, or B-cell mediated?*
Is VKH a unilateral, or bilateral disease? It is a **bilateral** condition.

VKH is a bilateral panuveitis **absent** ocular injury or surgery history.

What is the cause of VKH? **Unknown**

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This one we know—T-cells are the culprit.
Q

Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

- Is VKH a unilateral, or bilateral disease? It is a bilateral condition.
- VKH is a bilateral panuveitis absent ocular injury or surgery history.
- What is the cause of VKH? Unknown

That said, we are not completely in the dark vis a vis etiology, so...

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This one we know—T-cells are the culprit

*To what antigens are the T cells responding?*
Is VKH a unilateral, or bilateral disease?
It is a bilateral condition

VKH is a bilateral panuveitis absent ocular injury or surgery history

What is the cause of VKH? Unknown

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Ok, so it’s immune-related. Is it T-cell, or B-cell mediated?
This one we know—T-cells are the culprit

To what antigens are the T cells responding?
The experimental evidence strongly suggests that the antigens in question are associated with type of cell
Is VKH a unilateral, or bilateral disease? It is a **bilateral** condition.

VKH is a bilateral **panuveitis** **absent** ocular injury or **surgery** history.

What is the cause of VKH? **Unknown**

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*Ok, so it’s immune-related. Is it T-cell, or B-cell mediated?*
This one we know—T-cells are the culprit.

*To what antigens are the T cells responding?*
The experimental evidence strongly suggests that the antigens in question are associated with melanocytes.
Is VKH a unilateral, or bilateral disease? It is a **bilateral** condition.

VKH is a bilateral panuveitis **absent** ocular injury or surgery history.

What is **the cause of VKH?** **Unknown**

That said, we are not completely in the dark vis a vis etiology, so…

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Most experts are convinced it is noninfectious

*Ok, so it’s immune related. Is it T-cell, or B-cell mediated?*

As a prominent AAO source puts it, “**both [SO and VKH] represent an autoimmune response to tissue pigment**”

To what antigens are the T cells responding?
The experimental evidence strongly suggests that **the antigens in question are associated with melanocytes**
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

- VKH: Treatment/course/prognosis
  - In a nutshell, treat like any other
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

- VKH: Treatment/course/prognosis
  - In a nutshell, treat like any other panuveitis
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

- VKH: Treatment/course/prognosis
  - In a nutshell, treat like any other panuveitis
    - Local
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

- VKH: Treatment/course/prognosis
  - In a nutshell, treat like any other panuveitis
    - Local steroids
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

VKH: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - for comfort
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

- VKH: Treatment/course/prognosis
  - In a nutshell, treat like any other panuveitis
    - Local steroids
    - Cycloplegia for comfort
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

- **VKH: Treatment/course/prognosis**
  - In a nutshell, treat like any other **panuveitis**
  - Local **steroids**
  - **Cycloplegia** for comfort
  - +/- systemic
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

**VKH: Treatment/course/prognosis**

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

**VKH: Treatment/course/prognosis**

- In a nutshell, treat like any other **panuveitis**
  - Local **steroids**
  - **Cycloplegia** for comfort
  - +/- systemic **steroids**
  - May need systemic **immunomodulation/suppression**
VKH: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

**VKH: Treatment/course/prognosis**

- In a nutshell, treat like any other panuveitis
  - Local **steroids**
  - **Cycloplegia** for comfort
  - +/- systemic **steroids**
  - May need systemic **immunomodulation/suppression**
- What is the course?
  - chronic vs a one-time acute event
**Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?**

- **VKH: Treatment/course/prognosis**
  - In a nutshell, treat like any other **panuveitis**
    - Local **steroids**
    - **Cycloplegia** for comfort
    - +/- systemic **steroids**
    - May need systemic **immunomodulation/suppression**
  - What is the course? **Chronic--waxing and waning**
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

**VKH: Treatment/course/prognosis**
- In a nutshell, treat like any other panuveitis
  - Local **steroids**
  - **Cycloplegia** for comfort
  - +/- systemic **steroids**
  - May need systemic **immunomodulation/suppression**
- What is the course? **Chronic--waxing and waning**
- What is the prognosis?
VKH: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression

- What is the course? Chronic--waxing and waning

- What is the prognosis? Far better than it used to be—with modern steroids/immuno drugs, probability of maintaining useful vision is good.
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

- **VKH: Treatment/course/prognosis**
  - In a nutshell, treat like any other panuveitis
    - Local steroids
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression

What is the course? Chronic--waxing and waning

What is the prognosis? Far better than it used to be—with modern steroids/immuno drugs, probability of maintaining useful vision is good.

What factors tend to limit the prognosis in VKH?
VKH: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression

What is the course? Chronic--waxing and waning

What is the prognosis? Far better than it used to be—with modern steroids/immuno drugs, probability of maintaining useful vision is good.

What factors tend to limit the prognosis in VKH?
The sequelae of the severe intraocular inflammation that characterizes the disease
VKH: Treatment/course/prognosis

- In a nutshell, treat like any other panuveitis
  - Local steroids
  - Cycloplegia for comfort
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression

What is the course? Chronic—waxing and waning

What is the prognosis? Far better than it used to be—
with modern steroids/immuno drugs, **probability of maintaining useful vision is good.**
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

- **VKH: Treatment/course/prognosis**
  - In a nutshell, treat like any other panuveitis
    - Local steroids
  - +/- systemic steroids
  - May need systemic immunomodulation/suppression

What factors tend to limit the prognosis in VKH?
The sequelae of the severe intraocular inflammation that characterizes the disease

What are some of these sight-threatening sequelae?
- Secondary angle-closure glaucoma
- Cataracts that are difficult to manage successfully due to intra- and/or post-op complications
- Retinal neovascularization
- Phthisis

With modern steroids/immuno drugs, **probability of maintaining useful vision is good.**
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

- VKH is a **bilateral** condition
- VKH is a **granulomatous panuveitis**
- VKH is an **autoimmune response to tissue pigment**
- VKH is **steroid responsive**

Note the similarities…

Sympathetic Ophthalmia (SO): Wadda ya know?

- SO is a **bilateral** condition
- SO is a **granulomatous panuveitis**
- SO is an **autoimmune response to tissue pigment**
- SO is **steroid responsive**
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

- VKH is a **bilateral** condition
- VKH is a **granulomatous panuveitis** *absent* ocular injury/surgery history
- VKH is an **autoimmune response to tissue pigment**
- VKH is **steroid responsive**

**Note the similarities...And the key difference**

Sympathetic Ophthalmia (SO): Wadda ya know?

- SO is a **bilateral** condition
- SO is a **granulomatous panuveitis** *following* ocular injury/surgery
- SO is an **autoimmune response to tissue pigment**
- SO is **steroid responsive**
As the *Uveitis* book puts it, “The numerous clinical and pathological similarities between SO and VKH syndrome suggest that they share a similar immunopathogenesis.” Given this, it likely won’t surprise you that:

**Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?**

**Sympathetic Ophthalmia (SO): Wadda ya know?**
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

As the *Uveitis* book puts it, “The numerous clinical and pathological similarities between SO and VKH syndrome suggest that they share a similar immunopathogenesis.” Given this, it likely won’t surprise you that:

**Number one on the DDx for VKH: SO.**

**Number one on the DDx for SO: VKH.**

Sympathetic Ophthalmia (SO): Wadda ya know?
Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

As the *Uveitis* book puts it, “The numerous clinical and pathological similarities between SO and VKH syndrome suggest that they share a similar immunopathogenesis.” Given this, it likely won’t surprise you that:

*Number one on the DDx for VKH: SO.*
*Number one on the DDx for SO: VKH.*

**So let’s compare and contrast them!**

Sympathetic Ophthalmia (SO): Wadda ya know?
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50:
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites:
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common:
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20–50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH

How common are skin (and hair) findings in VKH?

Vitiligo is a common skin finding in VKH, characterized by depigmentation of the skin.
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH

How common are skin (and hair) findings in VKH? They appear in about 1/3 of patients
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH

**How common are skin (and hair) findings in VKH?**
They appear in about 1/3 of patients

**What is the classic skin finding?**
Depigmentation of the skin
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH

**SO vs VKH**

*How common are skin (and hair) findings in VKH?*
They appear in about 1/3 of patients

*What is the classic skin finding?*
Vitiligo
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH), or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH

**Concurrent skin findings common: VKH**

**SO vs VKH**

*How common are skin (and hair) findings in VKH?*
They appear in about 1/3 of patients

*What is the classic skin finding?*
Vitiligo

*What is vitiligo?*
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH), or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH

**SO vs VKH**

**How common are skin (and hair) findings in VKH?**
They appear in about 1/3 of patients

**What is the classic skin finding?**
Vitiligo

**What is vitiligo?**
Depigmentation of the skin
A VKH pt early in the dz course

Same pt late in the dz course (and despite aggressive immunosuppressive therapy)
SO vs VKH

VKH: Vitiligo
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH

**How common are skin (and hair) findings in VKH?**
They appear in about 1/3 of patients

**What is the classic skin finding?**
Vitiligo

**What is vitiligo?**
Depigmentation of the skin

Vitiligo is not limited to the skin--a classic eye location is the perilimbal region.
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**

**How common are skin (and hair) findings in VKH?**
They appear in about 1/3 of patients

**What is the classic skin finding?**
Vitiligo

**What is vitiligo?**
Depigmentation of the skin

*Vitiligo is not limited to the skin--a classic eye location is the perilimbal region.*
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**

**Q**

How common are skin (and hair) findings in VKH? They appear in about 1/3 of patients.

What is the classic skin finding? **Vitiligo**

What is vitiligo? Depigmentation of the skin

Vitiligo is not limited to the skin--a classic eye location is the perilimbal region. What is the eponymous name for this sign?
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH

**SO vs VKH**

*How common are skin (and hair) findings in VKH?*
They appear in about 1/3 of patients

*What is the classic skin finding?*
Vitiligo

*What is vitiligo?*
Depigmentation of the skin

*Vitiligo is not limited to the skin--a classic eye location is the perilimbal region.*

*What is the eponymous name for this sign?*
Sugiura’s sign
Perilimbal vitiligo

SUGUIRA'S SIGN

Sugiura’s sign
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**

**How common are skin (and hair) findings in VKH?**
They appear in about 1/3 of patients

**What is the classic skin finding?**
Vitiligo

**What is vitiligo?**
Depigmentation of the skin

**Vitiligo is not limited to the skin--a classic eye location is the perilimbal region.**

**What is the eponymous name for this sign?**
Sugiura's sign

**In which pt population is it common?**
Almost never
- For each of the following questions, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.
  - Predilection for adults age 20 – 50: **VKH**
  - More common in whites: **SO**
  - Concurrent skin findings common: **VKH**

**SO vs VKH**

How common are skin (and hair) findings in VKH? They appear in about 1/3 of patients.

What is the classic skin finding? Vitiligo

What is vitiligo? Depigmentation of the skin

Vitiligo is not limited to the skin--a classic eye location is the perilimbal region. What is the eponymous name for this sign? Sugiura’s sign

In which pt population is it common? Pts of Japanese ancestry--almost all of them will manifest this finding.
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50:
  - VKH

- More common in whites:
  - SO

- Concurrent skin findings common: **VKH**

  Vitiligo is not limited to the skin--a classic eye location is the perilimbal region. What is the eponymous name for this sign?
  - Sugiura's sign

  In which pt population is it common?
  - Pts of Japanese ancestry--almost all of them will manifest this finding

  Does it occur in Caucasian pts?

How common are skin (and hair) findings in VKH?
- They appear in about 1/3 of patients

What is the classic skin finding?
- Vitiligo

What is vitiligo?
- Depigmentation of the skin
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH

**SO vs VKH**

- How common are skin (and hair) findings in VKH?
  - They appear in about 1/3 of patients

- What is the classic skin finding?
  - Vitiligo

- What is vitiligo?
  - Depigmentation of the skin

Vitiligo is not limited to the skin--a classic eye location is the perilimbal region.

- What is the eponymous name for this sign?
  - Sugiura’s sign

- In which pt population is it common?
  - Pts of Japanese ancestry--almost all of them will manifest this finding

- Does it occur in Caucasian pts?
  - Almost never
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH), or both:

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**

How common are skin (and hair) findings in VKH? They appear in about 1/3 of patients.

What is the classic skin finding? Vitiligo

What is vitiligo? Depigmentation of the skin

Vitiligo is not limited to the skin—A classic eye location is the perilimbal region. What is the eponymous name for this sign? Sugiura’s sign

In which pt population is it common? Pts of Japanese ancestry—almost all of them will manifest this finding.

Does it occur in Caucasian pts? Almost never

A ‘perilimbal adjacent’ structure also becomes depigmented. Which one? The trabecular meshwork. What is the eponymous name for TM depigmentation in VKH? Ohno’s sign.
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20–50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**

**How common are skin (and hair) findings in VKH?**
They appear in about 1/3 of patients

**What is the classic skin finding?**
Vitiligo

**What is vitiligo?**
Depigmentation of the skin

Vitiligo is not limited to the skin—a classic eye location is the **perilimbal region**.

What is the eponymous name for this sign? **Sugiura's sign**

**In which pt population is it common?**
Pts of Japanese ancestry—almost all of them will manifest this finding

Does it occur in Caucasian pts? **Almost never**

A ‘**perilimbal adjacent**’ structure also becomes depigmented. Which one? **The trabecular meshwork**
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH vs SO

How common are skin (and hair) findings in VKH? They appear in about 1/3 of patients.

What is the classic skin finding? Vitiligo

What is vitiligo? Depigmentation of the skin

Vitiligo is not limited to the skin--a classic eye location is the perilimbal region. The eponymous name for this sign is Sugiura’s sign.

In which pt population is it common? Pts of Japanese ancestry--almost all of them will manifest this finding.

Does it occur in Caucasian pts? Almost never.

A ‘perilimbal adjacent’ structure also becomes depigmented. Which one? The trabecular meshwork.

What is the eponymous name for TM depigmentation in VKH?
For each of the following statements, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**

**How common are skin (and hair) findings in VKH?**
They appear in about 1/3 of patients.

**What is the classic skin finding?**
Vitiligo

**What is vitiligo?**
Depigmentation of the skin

Vitiligo is not limited to the skin—a classic eye location is the perilimbal region.

**What is the eponymous name for this sign?**
Sugiura’s sign

**In which pt population is it common?**
Pts of Japanese ancestry—almost all of them will manifest this finding

**Does it occur in Caucasian pts?**
Almost never

A ‘perilimbal adjacent’ structure also becomes depigmented. Which one?
The trabecular meshwork

**What is the eponymous name for TM depigmentation in VKH?**
Ohno’s sign
Ohno sign. (a, b) Appearance of TM at 1 month after disease onset. (c, d) Five months after disease onset, TM pigmentation was noticeably reduced.
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH

How common are skin (and hair) findings in VKH? They appear in about 1/3 of patients.

What is the classic skin finding? Vitiligo

What are the classic hair findings? Alopecia and poliosis

Alopecia: Loss of hair
Poliosis: Loss of hair pigmentation
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**

How common are skin (and hair) findings in VKH? They appear in about 1/3 of patients.

What is the classic skin finding? **Vitiligo**

What are the classic hair findings? **Alopecia and poliosis**
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- **Predilection for adults age 20 – 50:** VKH
- **More common in whites:** SO
- **Concurrent skin findings common:** VKH

**How common are skin (and hair) findings in VKH?**

How common are skin (and hair) findings in VKH? They appear in about 1/3 of patients.

**What is the classic skin finding?**

Vitiligo

**What are the classic hair findings?**

Alopecia and poliosis

**What do these terms mean?**

- **Alopecia:** Loss of hair
- **Poliosis:** Loss of hair pigmentation
Q/A

For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH), or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH

How common are skin (and hair) findings in VKH? They appear in about 1/3 of patients.

What is the classic skin finding? Vitiligo

What are the classic hair findings? Alopecia and poliosis

What do these terms mean? Alopecia: Loss of hair Poliosis:
For each of the following conditions, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH

How common are skin (and hair) findings in VKH? They appear in about 1/3 of patients.

What is the classic skin finding? Vitiligo

What are the classic hair findings? Alopecia and poliosis

What do these terms mean? Alopecia: Loss of hair Poliosis:
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH

How common are skin (and hair) findings in VKH? They appear in about 1/3 of patients.

What is the classic skin finding? Vitiligo

What are the classic hair findings? Alopecia and poliosis

What do these terms mean?
- Alopecia: Loss of hair
- Poliosis: Loss of hair pigmentation
For each of the following traits, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**

How common are skin (and hair) findings in VKH? They appear in about 1/3 of patients.

What is the classic skin finding? Vitiligo

What is vitiligo? Depigmentation

Do the skin and hair findings precede, coincide with, or follow the onset of eye inflammation in VKH?
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings: VKH

How common are skin (and hair) findings in VKH? They appear in about 1/3 of patients.

What is the classic skin finding? Vitiligo

Do the skin and hair findings precede, coincide with, or follow the onset of eye inflammation in VKH? The skin/hair changes generally follow the onset of eye inflammation by a period of weeks.
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH

How common are skin (and hair) findings in VKH? They appear in about 1/3 of patients.

What is the classic skin finding? Vitiligo

What is vitiligo? Depigmentation

Do the skin and hair findings precede, coincide with, or follow the onset of eye inflammation in VKH? The skin/hair changes generally follow the onset of eye inflammation by a period of weeks.

Remember the pattern:

First: Neurologic
Second: Eye
Third: Integument
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH, SO?

Do skin findings occur in SO as well?
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH, SO**!

*Do skin findings occur in SO as well? Yes, but they are much less common*
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**
- CNS involvement rare:
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**
- CNS involvement rare: **SO**
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**
- CNS involvement rare: **SO**? Yes!

To be clear: Can CNS involvement occur in SO?
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**
- CNS involvement rare: **SO**? Yes!

*To be clear: Can CNS involvement occur in SO? Yes, it’s just much less common*
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**
- **CNS involvement rare: in VKH**

What is the classic sign/symptoms of CNS involvement in VKH?
Q/A

- For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.
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  - More common in whites: **SO**
  - Concurrent skin findings common: **VKH**
  - **CNS involvement rare:** in **VKH**

What is the classic sign/symptoms of CNS involvement in VKH?
Auditory issues, particularly **tinnitus** and **dysacusis**
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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**In what other ways can CNS involvement manifest?**

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**What is the classic sign/symptoms of CNS involvement in VKH?**
Auditory issues, particularly tinnitus and dysacusis

**In what other ways can CNS involvement manifest?**
--Meningeal signs/symptoms (eg, nuchal rigidity)
--Headache
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- Predilection for adults age 20 – 50: **VKH**
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- **CNS involvement rare:** in **VKH**

Take special note of this, as prominent AAO sources emphasize the presence of meningeal manifestations in both VKH and SO!

In what other ways can CNS involvement manifest?

- **Meningeal signs/symptoms**
  - Headache
  - Meningeal signs (e.g., nuchal rigidity)
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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- **More common in whites:** SO
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In what other ways can CNS involvement manifest?
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These same sources also emphasize a key difference in the temporal relationship between meningeal S/S in VKH vs in SO—what is that difference?
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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**Q/A**

**SO vs VKH**

In what other ways can CNS involvement manifest?

- **Meningeal signs/symptoms**
  - Meningeal signs/symptoms (e.g., nuchal rigidity)
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These same sources also emphasize a key difference in the temporal relationship between meningeal S/S in VKH vs in SO—what is that difference?

It is this: Meningeal S/S tend to *precede* ocular inflammation in VKH, but *follow* it in SO.
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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- **Meningeal signs/symptoms**
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Auditory issues, particularly tinnitus and dysacusis

In what other ways can CNS involvement manifest?
--Meningeal signs/symptoms (eg, nuchal rigidity)
--Headache

Do focal neurologic signs/symptoms occur?
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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**Do focal neurologic signs/symptoms occur?**
They can, but are rare
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**Can VKH cause an optic neuropathy?**
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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**What is the classic sign/symptoms of CNS involvement in VKH?**
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**In what other ways can CNS involvement manifest?**
--Meningeal signs/symptoms (eg, nuchal rigidity)
--Headache

**Do focal neurologic signs/symptoms occur?**
They can, but are rare

**Can VKH cause an optic neuropathy?**
Yes
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**
- CNS involvement rare: **SO**
- Dalen-Fuchs nodules present:
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
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- CNS involvement rare: **SO**
- Dalen-Fuchs nodules present: **Both**
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- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**
- CNS involvement rare: **SO**
- **Dalen-Fuchs nodules present:** **Both**

What are Dalen-Fuchs nodules?
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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- More common in whites: **SO**
- Concurrent skin findings common: **VKH**
- CNS involvement rare: **SO**
- **Dalen-Fuchs nodules present:** **Both**

*What are Dalen-Fuchs nodules?*
Focal collections of inflammatory cells between Bruch’s membrane and the RPE
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**What are Dalen-Fuchs nodules?**
Focal collections of inflammatory cells between Bruch’s membrane and the RPE

The classic test-association for Dalen-Fuchs nodules is SO/VKH. However, there is another condition, vastly more common, in which they are seen as well. So, whereas during an exam your first response to the term Dalen-Fuchs nodule should be SO/VKH, what condition should come to mind first if you encounter them in the clinic?
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
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Sarcoid
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH
- CNS involvement rare: SO
- Dalen-Fuchs nodules present: Both
- Choriocapillaris is spared:
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**
- CNS involvement rare: **SO**
- Dalen-Fuchs nodules present: **Both**
- Choriocapillaris is spared: **SO**
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH
- CNS involvement rare: SO
- Dalen-Fuchs nodules present: Both

**Choriocapillaris is spared:** SO

*What is the choriocapillaris?*
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH
- CNS involvement rare: SO
- Dalen-Fuchs nodules present: Both
- **Choriocapillaris is spared:** SO

What is the choriocapillaris?
The innermost portion of the choroid; it is a layer of highly-fenestrated capillaries.
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

• Predilection for adults age 20 – 50: **VKH**
• More common in whites: **SO**
• Concurrent skin findings common: **VKH**
• CNS involvement rare: **SO**
• Dalen-Fuchs nodules present: **Both**
• **Choriocapillaris is spared: SO**

A word of clarification is in order. Much is made about the presence/absence of choriocapillaris involvement as a feature distinguishing between SO and VKH. And it is true: The choriocapillaris **is** spared in SO, and it **is** affected in VKH.
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
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- Dalen-Fuchs nodules present: Both
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For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH
- CNS involvement rare: SO
- Dalen-Fuchs nodules present: Both

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A word of clarification is in order. Much is made about the presence/absence of choriocapillaris involvement as a feature distinguishing between SO and VKH. And it is true: The choriocapillaris is spared in SO, and it is affected in VKH. But note that the choriocapillaris is spared during the Acute Uveitic stage of VKH—it’s only later, during the Chronic Recurrent stage, that it becomes involved. Thus, choriocapillaris status does not distinguish between SO and VKH so much as it distinguishes between the different stages of VKH. (We’ll drill down on the stages of VKH shortly.)
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**
- CNS involvement rare: **SO**
- Dalen-Fuchs nodules present: **Both**
- Choriocapillaris is spared: **SO**
- More common in Hispanics, Asians: **SO**
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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- Dalen-Fuchs nodules present: **Both**
- Choriocapillaris is spared: **SO**
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- Dalen-Fuchs nodules present: Both
- Choriocapillaris is spared: SO
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What other ethnic groups are frequently affected?
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH
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What other ethnic groups are frequently affected?
Native-Americans; Middle Easterners
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What other ethnic groups are frequently affected?
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Hispanics, Asians, Native-Americans, Middle Easterners—what is the common thread?
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What other ethnic groups are frequently affected?
Native-Americans; Middle Easterners

Hispanics, Asians, Native-Americans, Middle Easterners—what is the common thread?
A relatively high level of skin pigmentation
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
- Concurrent skin findings common: **VKH**
- CNS involvement rare: **SO**
- Dalen-Fuchs nodules present: **Both**
- Choriocapillaris is spared: **SO**
- More common in **Hispanics, Asians**, and **Africans**?

*Given this, it must follow that sub-Saharan Africans are at high risk, yes?*
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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- CNS involvement rare: SO
- Dalen-Fuchs nodules present: Both
- Choriocapillaris is spared: SO
- More common in Hispanics, Asians; **but not Africans**

Given this, it must follow that sub-Saharan Africans are at high risk, yes? You’d think so, but no--their relative risk is quite low

What is the common thread? A relatively **high level of skin pigmentation**
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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Given this, it must follow that sub-Saharan Africans are at high risk, yes? You’d think so, but no--their relative risk is quite low

What does indicate about the disease process? What is the common thread? A relatively **high level of skin pigmentation**
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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**Given this, it must follow that sub-Saharan Africans are at high risk, yes?**
You’d think so, but no--their relative risk is quite low.

**What does indicate about the disease process?**
It indicates that pigmentation is not the sole contributor to the disease process, what is the common thread? A relatively **high level of skin pigmentation**.
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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- More common in Hispanics, Asians: **VKH**

What other ethnic groups are frequently affected? Native-Americans; Middle Easterners

Hispanics, Asians, Native-Americans, Middle Easterners—what is the common thread? A relatively high level of skin pigmentation

Speaking of contributing to the disease process...Is there a genetic predisposition to VKH? Very much so—strong HLA associations exist. All are of the HLA-DR* type—HLA-DR4 in Japanese pts; DR1 and DR4 among Hispanics; DRB among others.

Can these HLA types be used to differentiate between VKH and SO? Alas no, because SO has virtually identical HLA associations.
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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**Speaking of contributing to the dz process…** Is there a genetic predisposition to VKH? Very much so—strong HLA associations exist. All are of the **HLA-DR* type—HLA-DR4 in Japanese pts; DR1 and DR4 among Hispanics; DRB among others.**

**What does indicate about the disease process?**
It indicates that pigmentation is not the sole contributor to the dz process. A relatively high level of skin pigmentation is the common thread.
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
- More common in whites: **SO**
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Very much so—strong HLA associations exist. All are of the HLA-DR* type—HLA-DR4 in Japanese pts; DR1 and DR4 among Hispanics; DRB among others.

**Can these HLA types be used to differentiate between VKH and SO?**

**Is the common thread?**

A relatively high level of skin pigmentation
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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A relatively high level of skin pigmentation is the common thread.
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- Dalen-Fuchs nodules present: **Both**
- Choriocapillaris is spared: **SO**
- More common in Hispanics, Asians: **VKH**
- No gender predilection:
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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- Dalen-Fuchs nodules present: **Both**
- Choriocapillaris is spared: **SO**
- More common in Hispanics, Asians: **VKH**
- No gender predilection: **Depends…**
  - **VKH**: M=F
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: **VKH**
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- CNS involvement rare: **SO**
- Dalen-Fuchs nodules present: **Both**
- Choriocapillaris is spared: **SO**
- More common in Hispanics, Asians: **VKH**
- No gender predilection: **Depends…**
  - **VKH:** M < F
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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- More common in whites: **SO**
- Concurrent skin findings common: **VKH**
- CNS involvement rare: **SO**
- Dalen-Fuchs nodules present: **Both**
- Choriocapillaris is spared: **SO**
- More common in Hispanics, Asians: **VKH**
- No gender predilection: **Depends…**
  - VKH: M < F
  - SO after surgery: M = F
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

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- Dalen-Fuchs nodules present: **Both**
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- CNS involvement rare: **SO**
- Dalen-Fuchs nodules present: **Both**
- Choriocapillaris is spared: **SO**
- More common in Hispanics, Asians: **VKH**
- No gender predilection: **Depends…**
  - VKH: M < F
  - SO after surgery: M = F
  - SO after trauma: M \( \gg \) F
For each of the following, state whether it is associated with sympathetic ophthalmia (SO), Vogt-Koyanagi-Harada (VKH) disease, or both.

- Predilection for adults age 20 – 50: VKH
- More common in whites: SO
- Concurrent skin findings common: VKH
- CNS involvement rare: SO
- Dalen-Fuchs nodules present: Both
- Choriocapillaris is spared: SO
- More common in Hispanics, Asians: VKH
- No gender predilection: Depends…
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Vogt-Koyanagi-Harada (VKH) Syndrome: Wadda ya know?

Recall this slide from earlier in the set. As stated then, tops on the DDx for VKH is SO. That said, in the Masquerade Syndromes chapter of the Uveitis book, one condition is mentioned as masquerading for VKH. What is it?

Number one on the DDx for VKH: SO.
Number one on the DDx for SO: VKH.

Sympathetic Ophthalmia (SO): Wadda ya know?
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**Bilateral diffuse uveal melanocytic proliferation (BDUMP)**

Number one on the DDx for VKH: **SO**.
Number one on the DDx for SO: **VKH**.

Sympathetic Ophthalmia (SO): Wadda ya know?
In a word, what sort of condition is BDUMP?
A paraneoplastic syndrome

Wadda ya know?
Number one on the DDx for VKH: SO.
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So let's compare and contrast them!

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In a word, what sort of condition is BDUMP? A paraneoplastic syndrome

Very rare

An adult 50+
No
Gynecologic in women; lung and pancreatic in men
Bilateral rapid vision loss
Bilateral serous/exudative RDs
Bilateral…
--rapid cataract progression
--multiple large 'nevi' of the posterior choroid

What is the prognosis? Poor, in terms of both vision and life expectancy
In a word, what sort of condition is BDUMP?
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Is BDUMP common, or rare?
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Finally, let’s drill down on the stages of VKH
**VKH tends to present stepwise, in three stages. What are they?**

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*(If you’re thinking ‘But VKH has four stages!’…We’ll get to that momentarily.)*
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**Q/A**

What is the most common neurologic manifestation at this stage? Auditory difficulties, especially...
### Stage | ‘Phase Phrase’ | Signs/Symptoms
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**Prodromal** (a couple of days) | ‘Meningo-encephalitic’ | Flu-like symptoms plus multiple and varied neurologic findings
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**Convalescent** | ‘Depigmentation’ | Gradual depigmentation of the skin, hair, and choroid
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What is the classic retinal manifestation at this stage?
### SO vs VKH

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**What is the classic retinal manifestation at this stage?**
Multifocal serous retinal detachments
VKH: Bilateral multifocal serous RDs

**SO vs VKH**
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What is the classic retinal manifestation at this stage?  
Multifocal serous retinal detachments

Can these coalesce to form a substantial exudative retinal detachment?
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Multifocal serous retinal detachments

Can these coalesce to form a substantial exudative retinal detachment?
Yes
VKH: Big coalesced serous RDs
## Stage

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**What is the classic retinal manifestation at this stage?**
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**Optic nerve edema--common, or uncommon in this phase?**
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What is the classic **retinal manifestation at this stage**?
Multifocal serous retinal detachments

Can these coalesce to form a substantial exudative retinal detachment?
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**Optic nerve edema**--common, or uncommon in this phase?
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VKH: ONH edema
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**What is the classic retinal manifestation at this stage?**

- **Multifocal serous retinal detachments**

**How does this appear on FA?**

- Early, as multiple scattered pinpoint leakages; late, as pooling within the serous-RD spaces

**Optic nerve edema--common, or uncommon in this phase?**

- Very common
VKH FA: Pinpoint leakage (and serous RD pooling)
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Multifocal serous retinal detachments

**How does this appear on FA?**

Early, as multiple scattered pinpoint leakages; late, as pooling within the serous RD spaces

**By what colorful monikers is this appearance known?**

It is called ‘starry night sign’ or ‘Milky Way sign’
### Stages of VKH Disease

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**Prodromal** (a couple of days)

- Flu-like symptoms plus multiple and varied neurologic findings

**Acute Uveitic** (a couple of weeks)

- Multifocal serous retinal detachments
  - How does this appear on FA? Early, as multiple scattered pinpoint leakages; late, as pooling within the serous-RD spaces
  - By what colorful monikers is this appearance known? It is called ‘starry night sign’ or ‘Milky Way sign’

**Convalescent**

- Gradual depigmentation of the skin, hair, and choroid

**Chronic/Recurrent**

- Occurs when VKH undertreated

What is the classic retinal manifestation at this stage?

Multifocal serous retinal detachments

Can SO present with multifocal serous RD and a ‘starry night’ FA?

Yes
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Depigmentation of the choroid leads to a characteristic orange-red color change of the posterior pole. What is the classic term used in describing this finding?
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Depigmentation of the choroid leads to a characteristic orange-red color change of the posterior pole. What is the classic term used in describing this finding? ‘Sunset glow fundus’
VKH: Sunset glow fundus
As should be apparent by now, VKH has three broad sorts of manifestations: Neurologic, Ocular and Integumentary (i.e., skin and hair). These categories provide the basis for defining three “forms” of VKH.

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**If a pt presents with ocular signs/symptoms only, s/he has…Probable VKH**
**If s/he presents with ocular plus neuro or skin/hair changes, s/he has…**

(‘or’ here indicates ‘not both’)
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*If a pt presents with ocular signs/symptoms only, s/he has…Probable VKH*

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*If s/he presents with all three, s/he has…*
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### Stage vs Phase Phrase Signs/Symptoms

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**Q**

VKH can have a fourth phase. What is it, and why does it occur?
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<td>Occurs when VKH is undertreated</td>
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**VKH can have a fourth phase. What is it, and why does it occur?**
**Stage** | ‘Phase Phrase’ | **Signs/Symptoms**
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(a couple of days) |  |  
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(a couple of weeks) |  |  
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**VKH can have a fourth phase. What is it, and why does it occur?**

**What specific signs/symptoms characterize this stage?**
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What specific signs/symptoms characterize this stage?