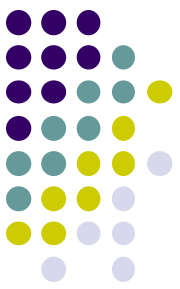


DDx for an RP-like Fundus



In my teaching experience, this is one of the more challenging topics in ophthalmology. (The corneal dystrophies are up there too.) While I won't say this set makes learning the material easy—there's simply too much esoterica for that—I do think it makes it **easier**. My point here is not to toot my own horn, but rather to give hope and encouragement—you can master this topic!

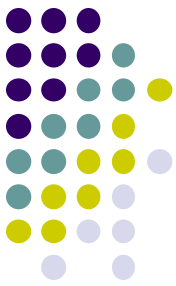
My advice: In prepping for the OKAP, try to run through this slide-set once or twice a month. When you reach the final, frantic few weeks of cramming, don't wade through the whole thing—just do the *tl;dr* at the end (it starts around slide 364).

Finally: This is a big topic, and big topics beget big slide-sets. There's a natural break around slide 236; I placed a *Break time!* slide at that point to mark it.

Now, let's get* this bread!

**Bake* this bread? *Make* this bread? I can never remember.

DDx for an RP-like Fundus



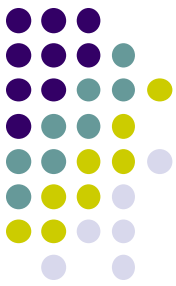
*First things first. An RP-like fundus has three characteristic attributes.
What are they?*

--?

--?

--?

DDx for an RP-like Fundus



First things first. An RP-like fundus has three characteristic attributes.

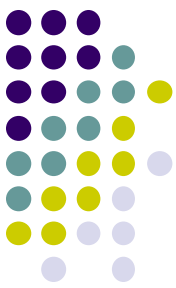
What are they?

-- spicules

-- disc pallor

--Arteriolar

DDx for an RP-like Fundus

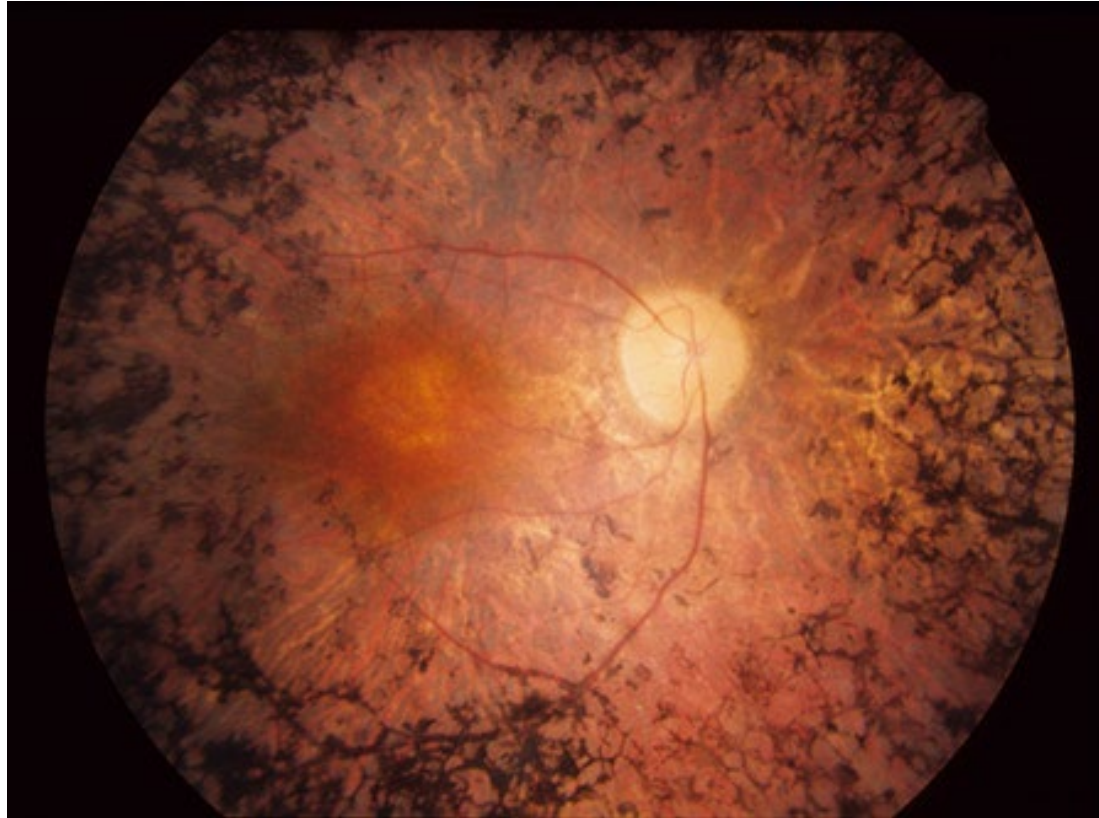


First things first. An RP-like fundus has three characteristic attributes.

What are they?

- Bone spicules
- Waxy disc pallor
- Arteriolar narrowing

DDx for an RP-like Fundus



RP-like fundus: Bone spicules, waxy disc pallor, arteriolar narrowing

DDx for an RP-like Fundus



First things first. An RP-like fundus has three characteristic attributes.

What are they?

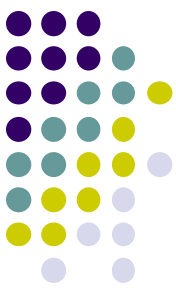
- Bone spicules
- Waxy disc pallor
- Arteriolar narrowing

What two vision issues are the defining characteristics of RP?

--?

--?

DDx for an RP-like Fundus



First things first. An RP-like fundus has three characteristic attributes.

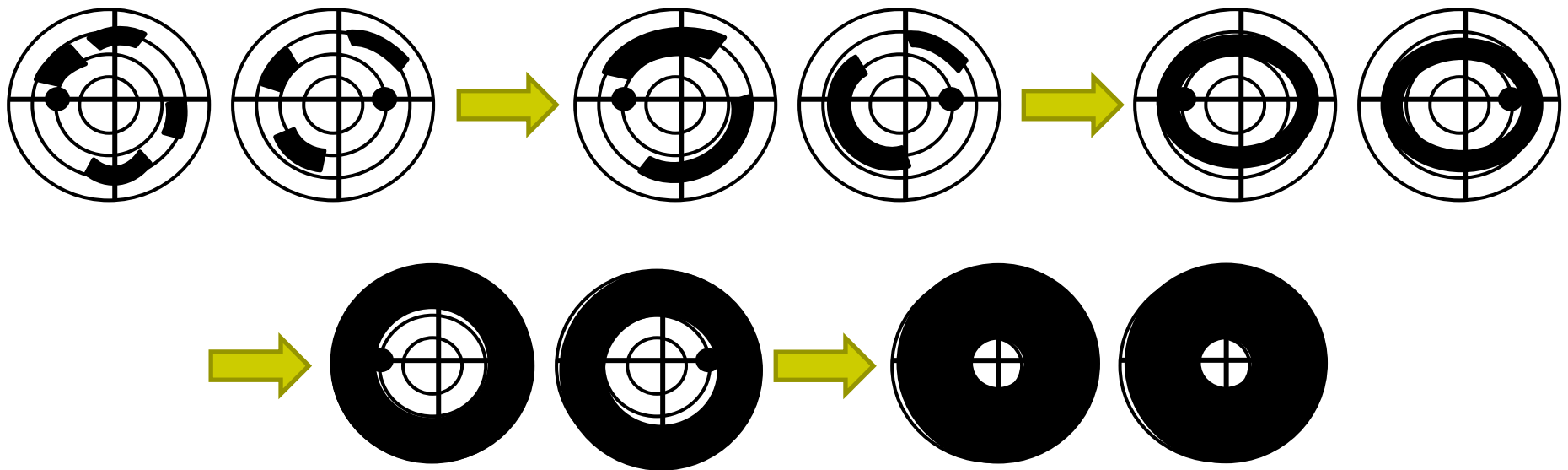
What are they?

- Bone spicules
- Waxy disc pallor
- Arteriolar narrowing

What two vision issues are the defining characteristics of RP?

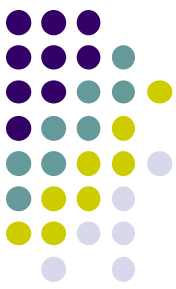
- Nyctalopia
- Visual field loss

DDx for an RP-like Fundus



Typical pattern of VF loss in RP: Mid-peripheral scotomata → coalesce into *partial* rings → coalesce into *complete* ring → expand rapidly *outward* → expand slowly *inward*

DDx for an RP-like Fundus



First things first. An RP-like fundus has three characteristic attributes.

What are they?

- Bone spicules
- Waxy disc pallor
- Arteriolar narrowing

What two vision issues are the defining characteristics of RP?

- Nyctalopia
- Visual field loss

Results of what specialized testing modality are always abnormal in RP?

DDx for an RP-like Fundus



First things first. An RP-like fundus has three characteristic attributes.

What are they?

- Bone spicules
- Waxy disc pallor
- Arteriolar narrowing

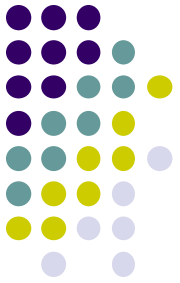
What two vision issues are the defining characteristics of RP?

- Nyctalopia
- Visual field loss

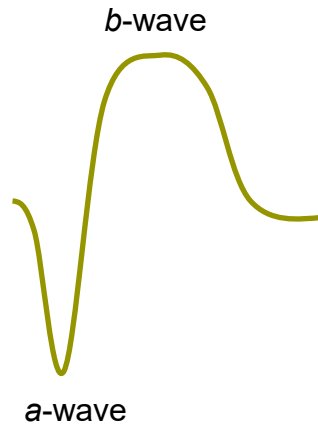
Results of what specialized testing modality are always abnormal in RP?

Electroretinogram (ERG)

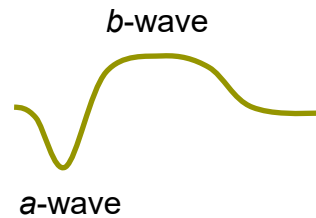
DDx for an RP-like Fundus



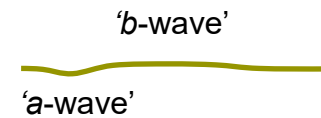
Normal ERG



Early RP



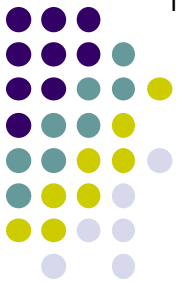
Late RP



Characteristic ERG changes in RP:

--**Early**: Reduced *a* and *b* waves

--**Late**: Undetectable



DDx for an RP-like Fundus

First things first. An RP-like fundus has three characteristic attributes.

What are they?

- Bone spicules
- Waxy disc pallor
- Arteriolar narrowing

What two vision issues are the defining characteristics?

- Nyctalopia
- Visual field loss

*These are the defining
features of RP*

Results of what specialized testing modality are always abnormal in RP?

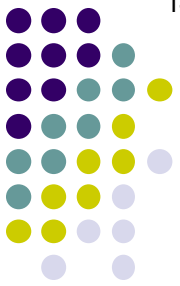
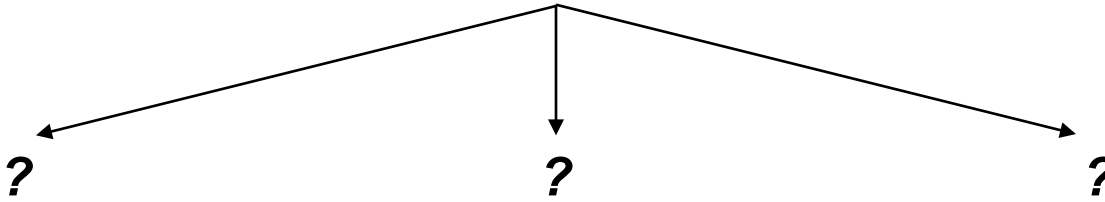
Electroretinogram (ERG)

DDx for an RP-like Fundus



These next few slides lay out the overall way you should think about an RP-like fundus (especially on the OKAP/Boards)

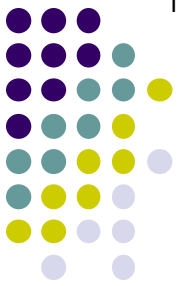
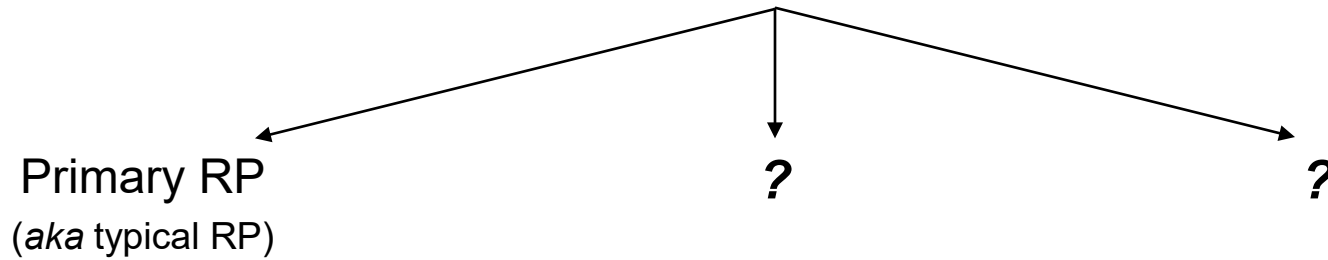
DDx for an RP-like Fundus



When a pt's fundi have an RP-like appearance, one of three things is going on:

- 1) ?
- 2) ?
- 3) ?

DDx for an RP-like Fundus

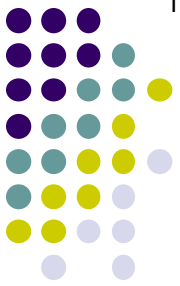


When a pt's fundi have an RP-like appearance, one of three things is going on:

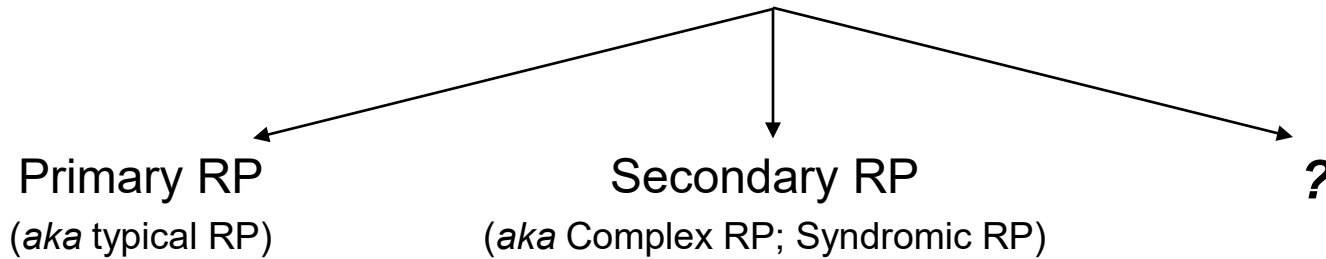
1) The pt has RP (duh)

2) ?

3) ?

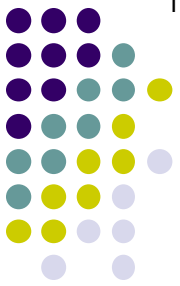
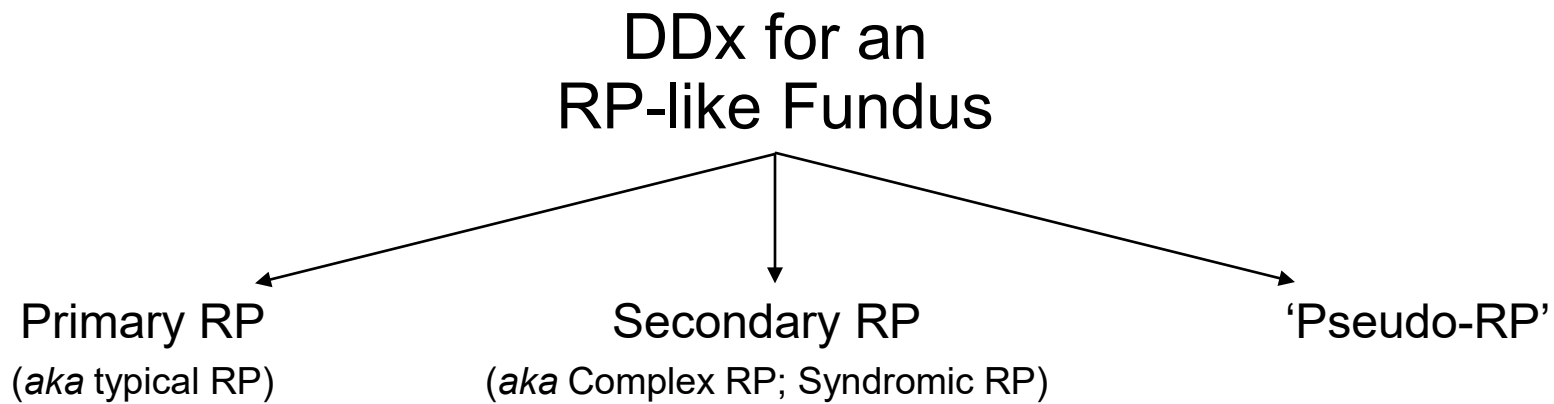


DDx for an RP-like Fundus



When a pt's fundi have an RP-like appearance, one of three things is going on:

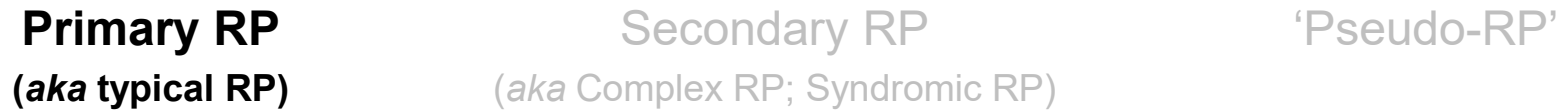
- 1) The pt has RP; **or**
- 2) s/he has a systemic condition in which retinal manifestations c/w RP occur
- 3) ?



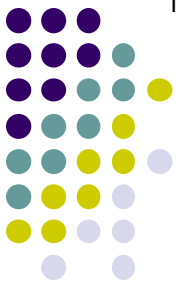
When a pt's fundi have an RP-like appearance, one of three things is going on:

- 1) The pt has RP; **or**
- 2) s/he has a systemic condition in which retinal manifestations c/w RP occur; **or**
- 3) s/he has a condition that has nothing to do with RP—it just happens to have a similar appearance

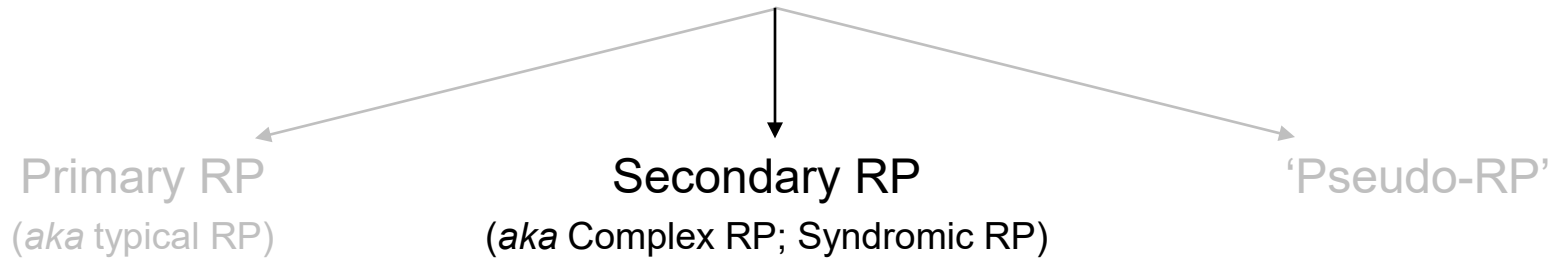
DDx for an RP-like Fundus



*For more on RP itself,
see slide-set R38*



DDx for an RP-like Fundus



• ?

• ?

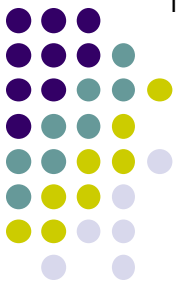
• ?

• ?

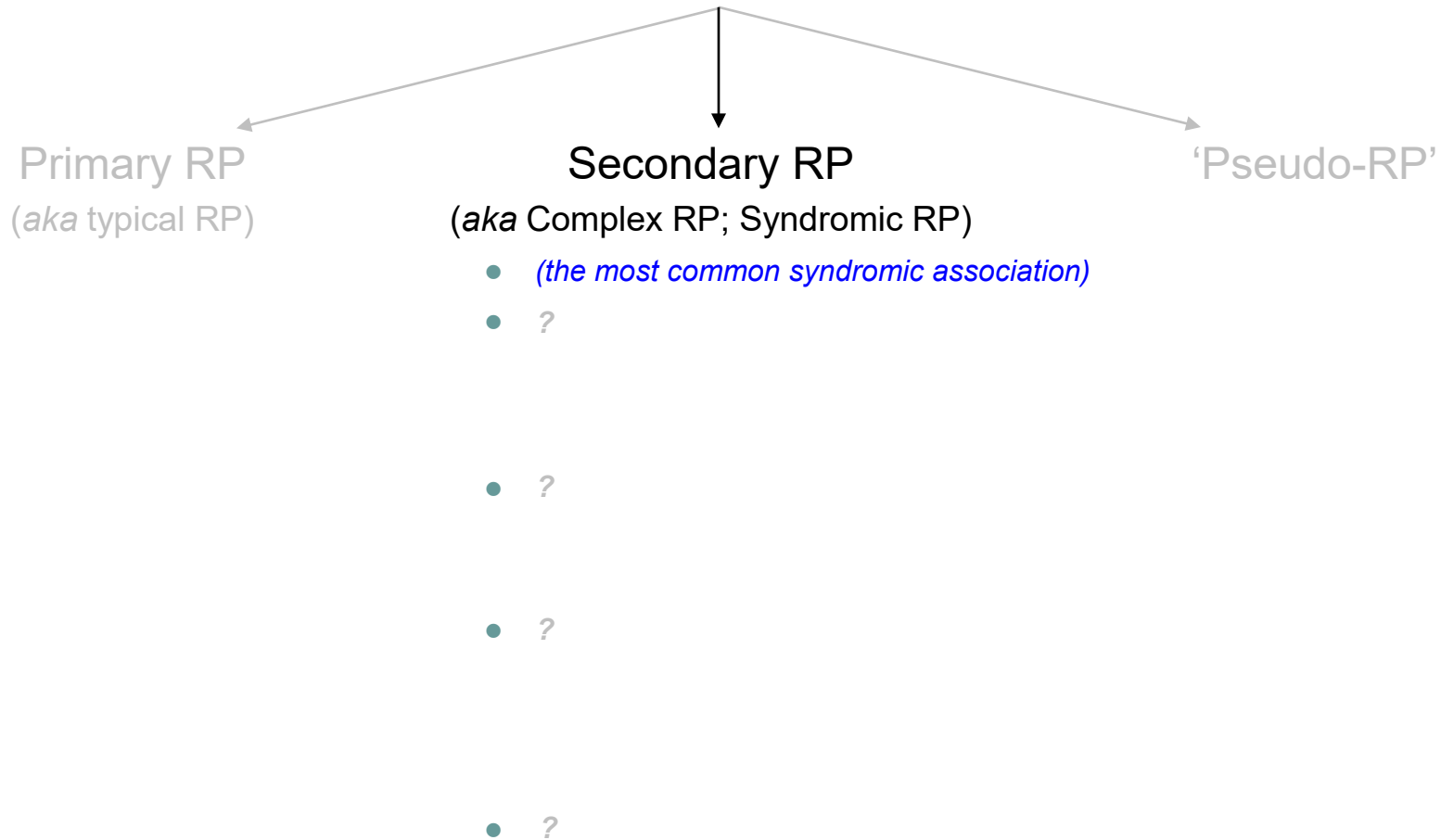
• ?

(Hints forthcoming on the next slide)

The 2ndry/syndromic RP conditions are can be grouped into five categories based on the underlying issue—what are these categories?

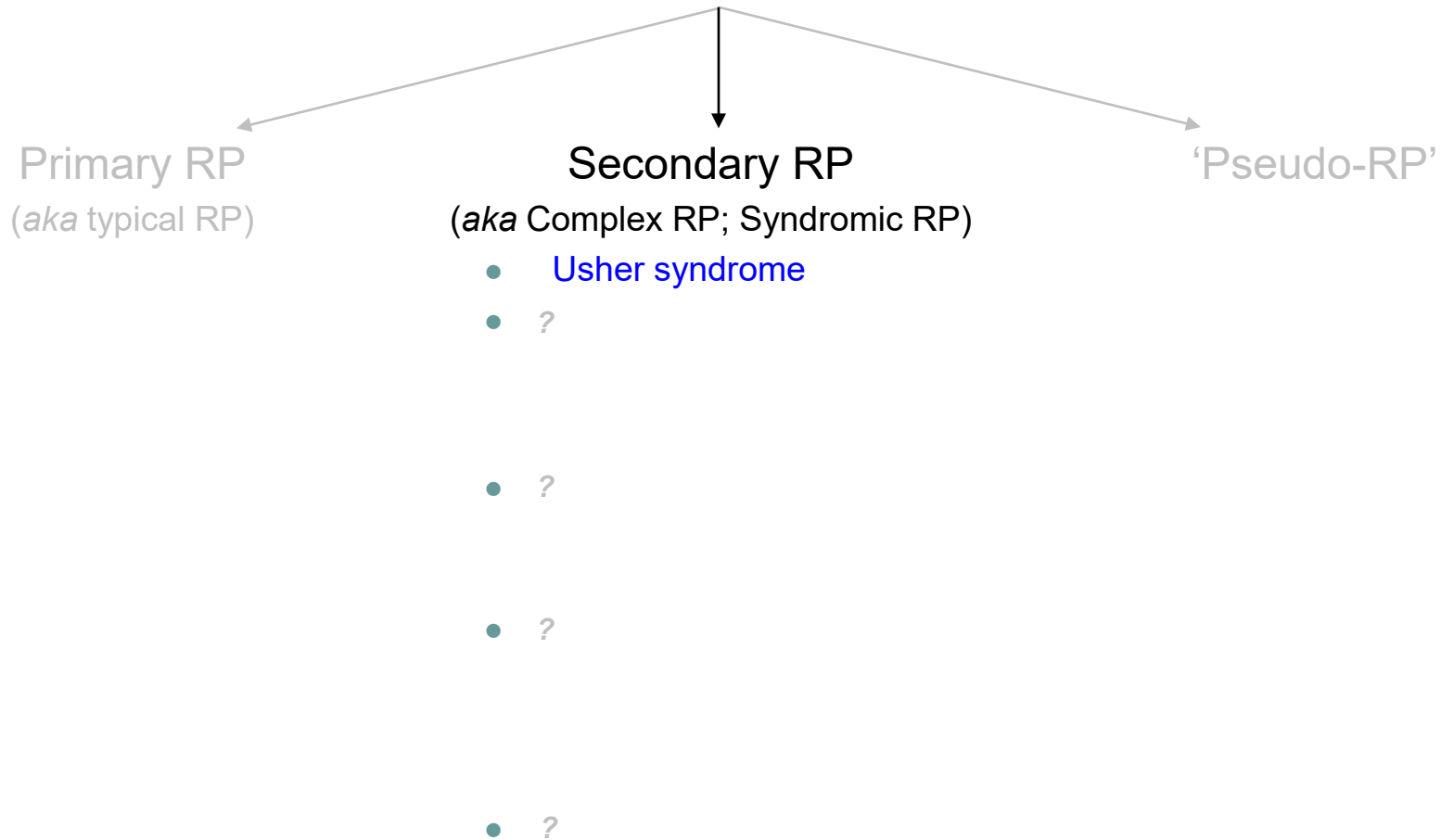


DDx for an RP-like Fundus



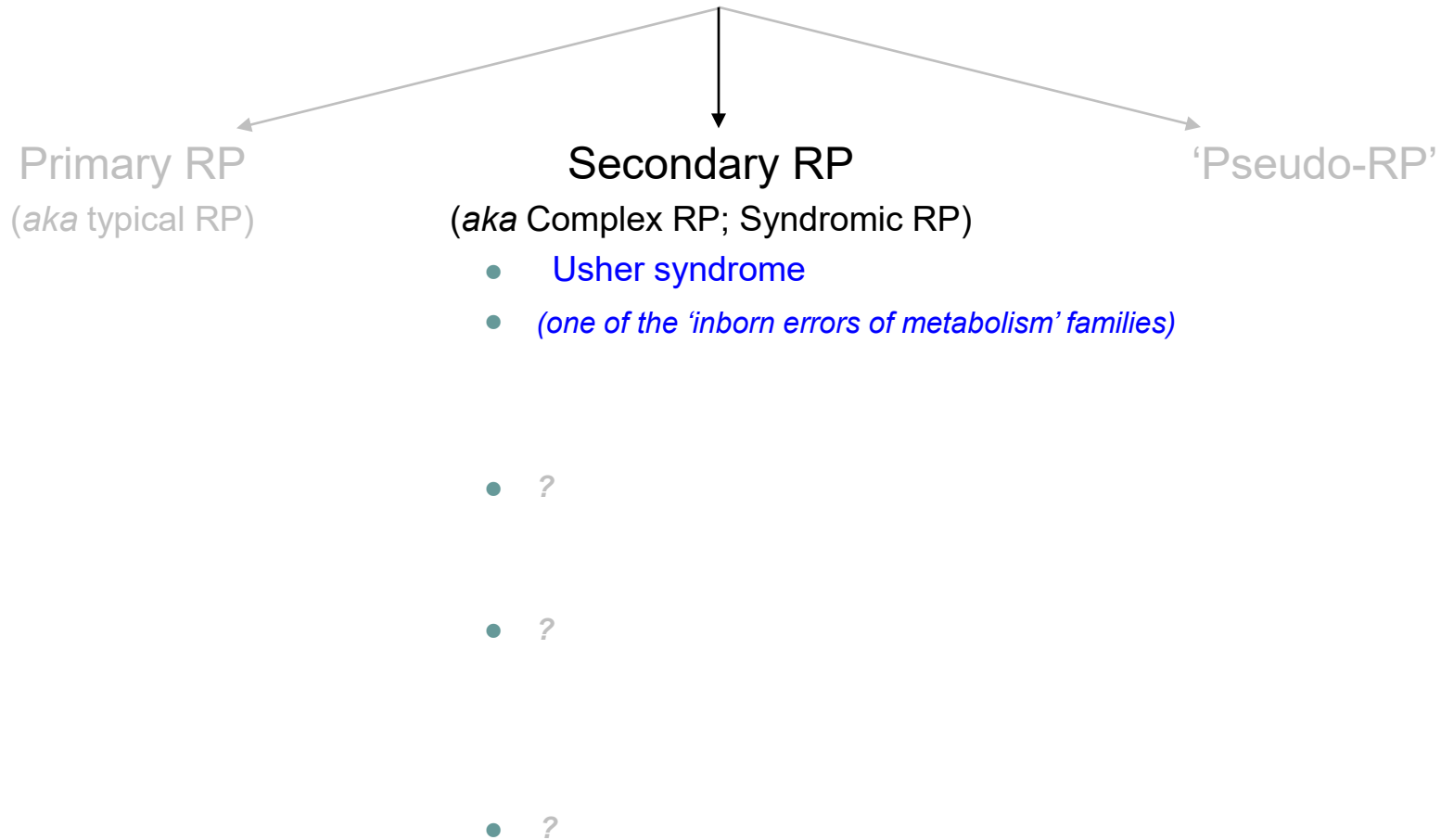
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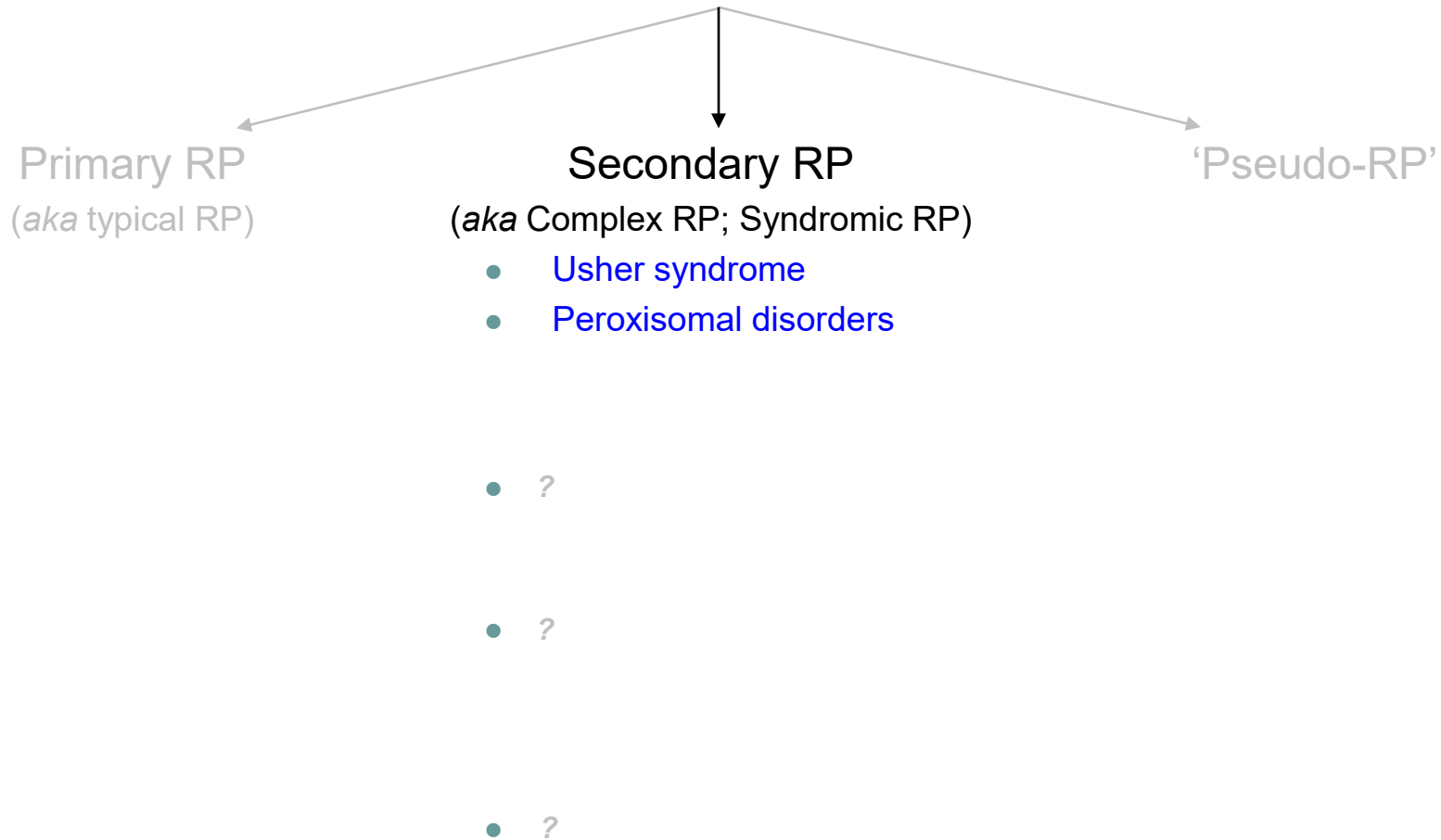
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DDx for an RP-like Fundus



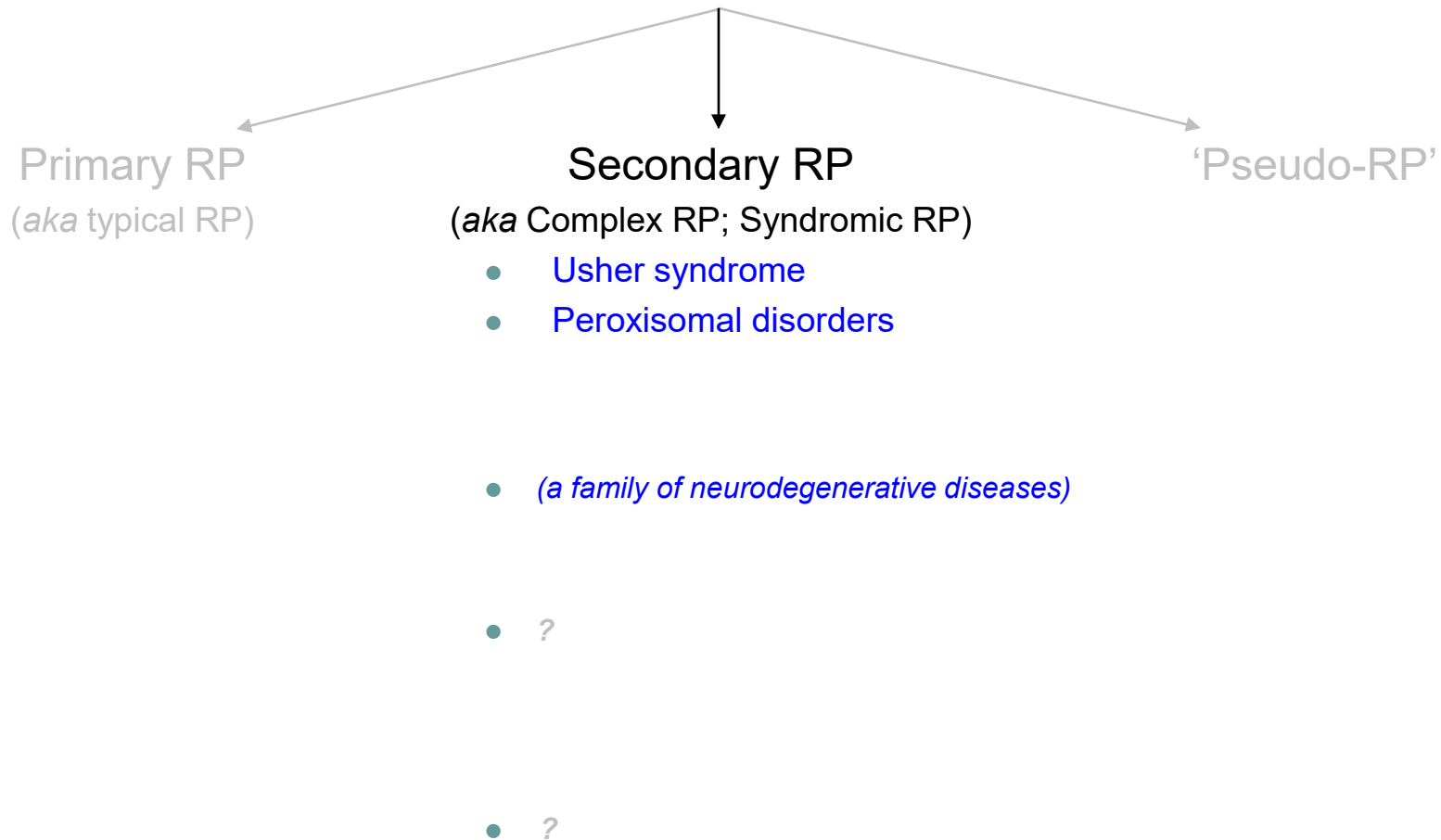
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DDx for an RP-like Fundus



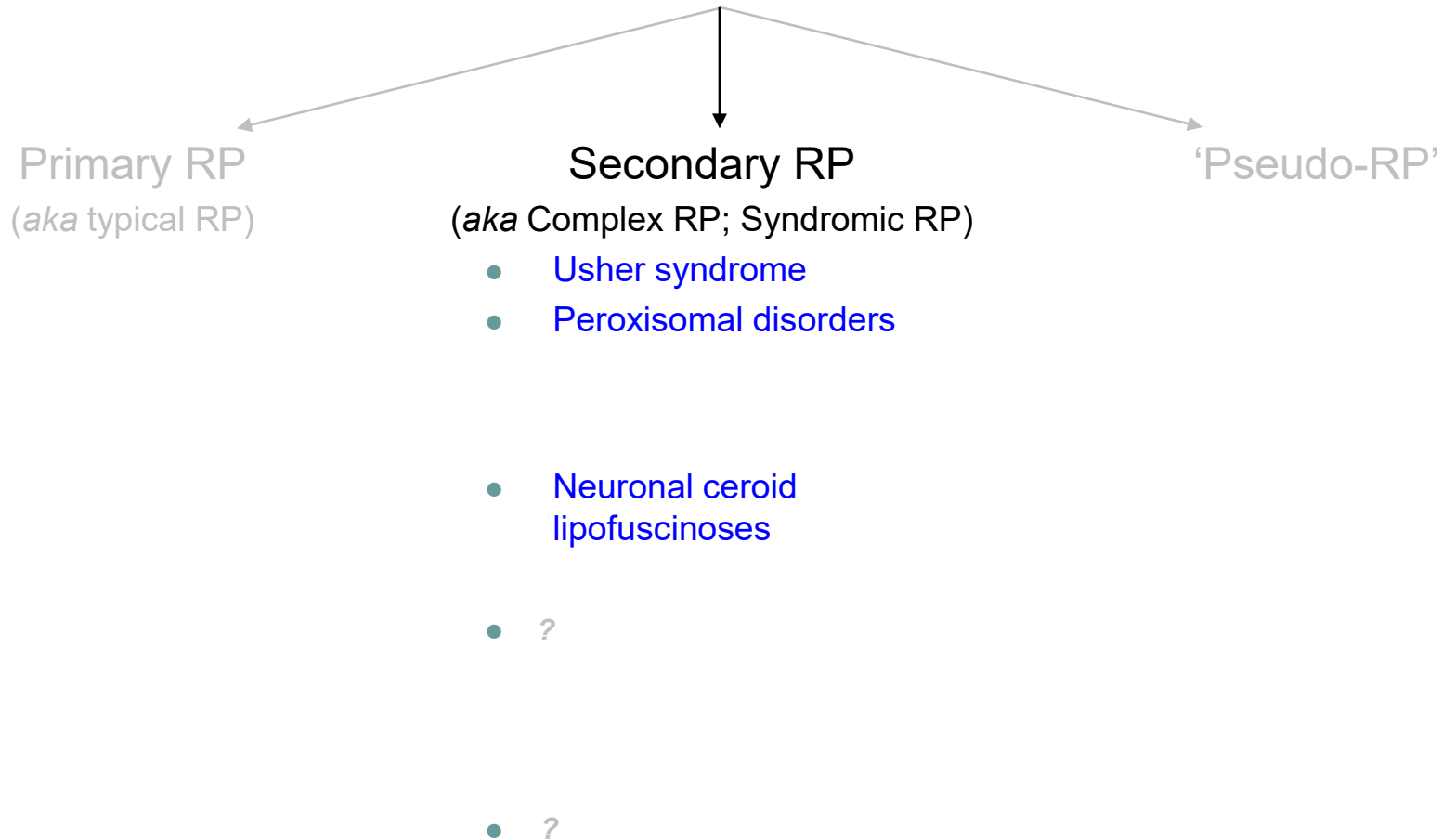
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DDx for an RP-like Fundus



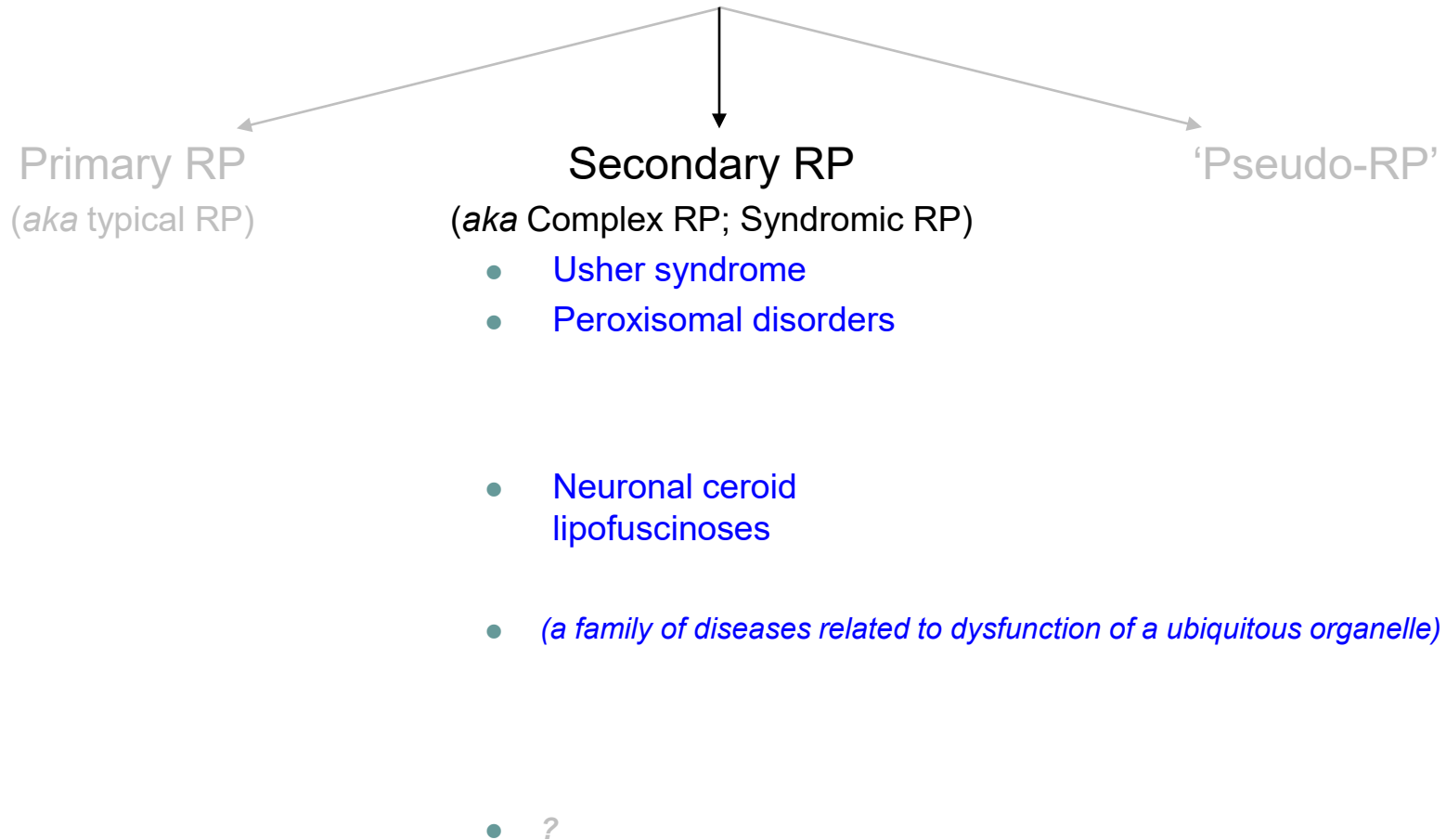
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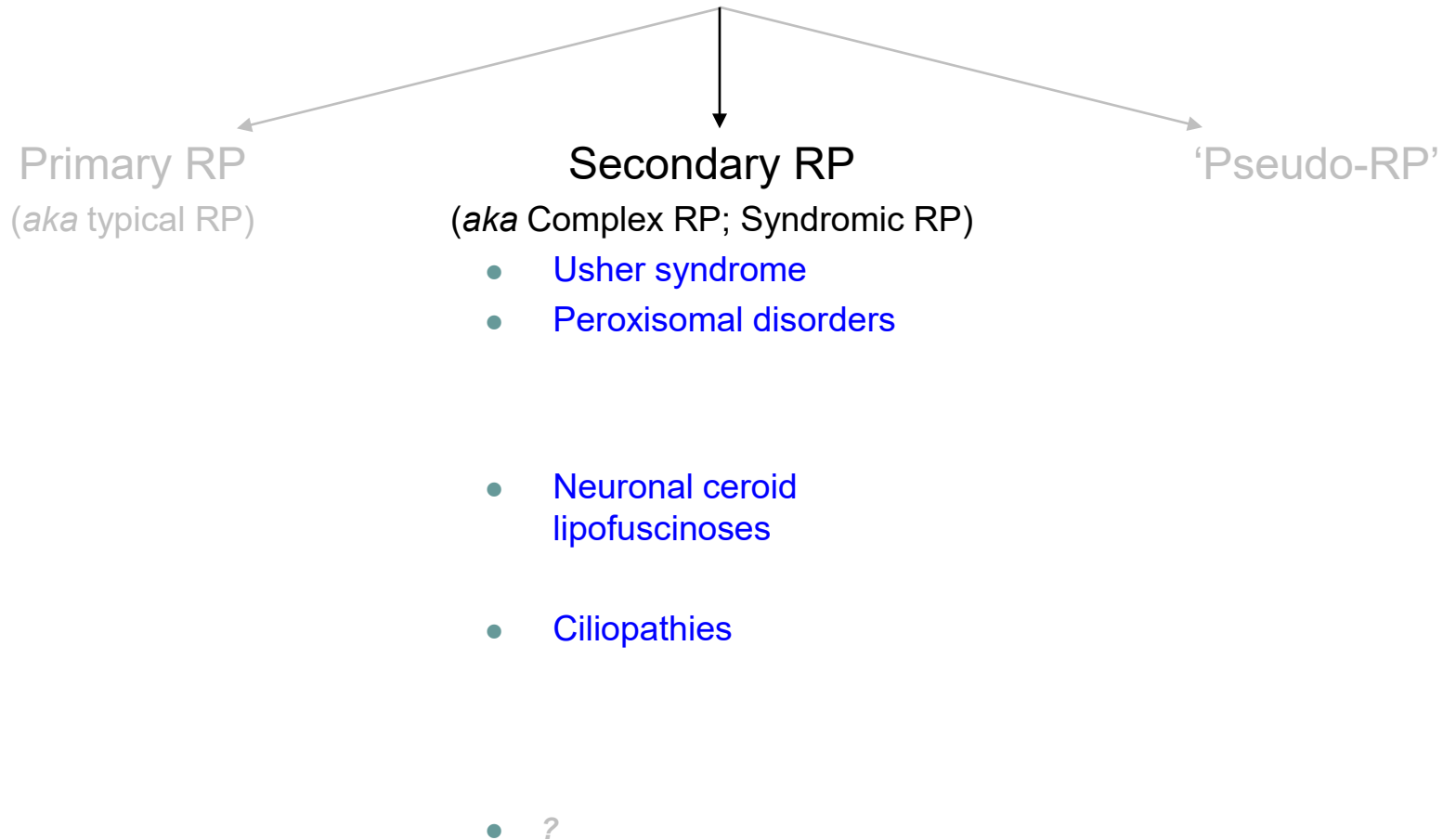
The 2ndry/syndromic RP conditions are can be grouped into five categories based on the underlying issue—what are these categories?

DDx for an RP-like Fundus



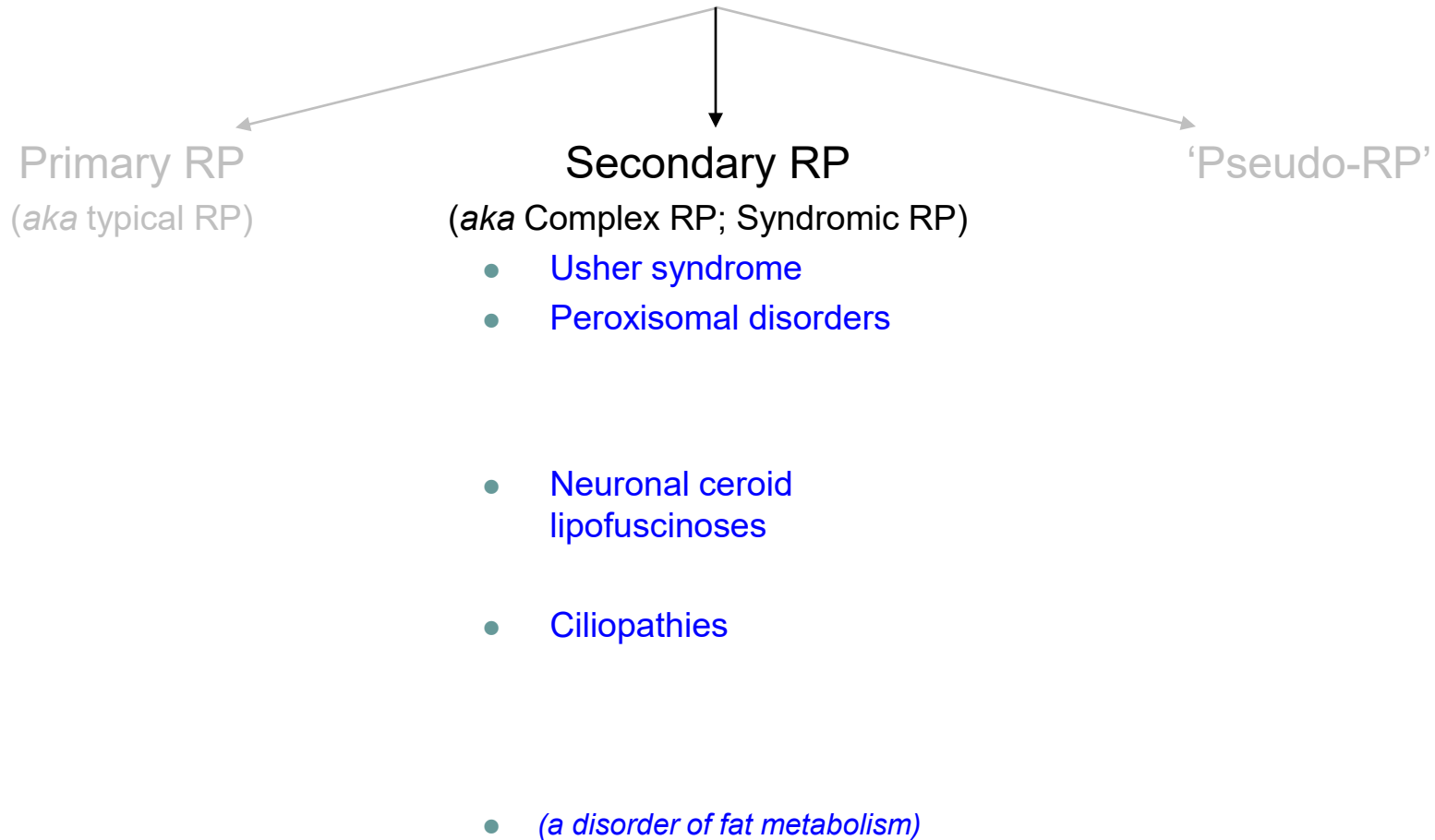
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DDx for an RP-like Fundus

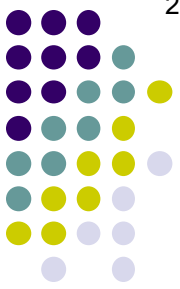


The 2ndry/syndromic RP conditions are can be grouped into five categories based on the underlying issue—what are these categories?

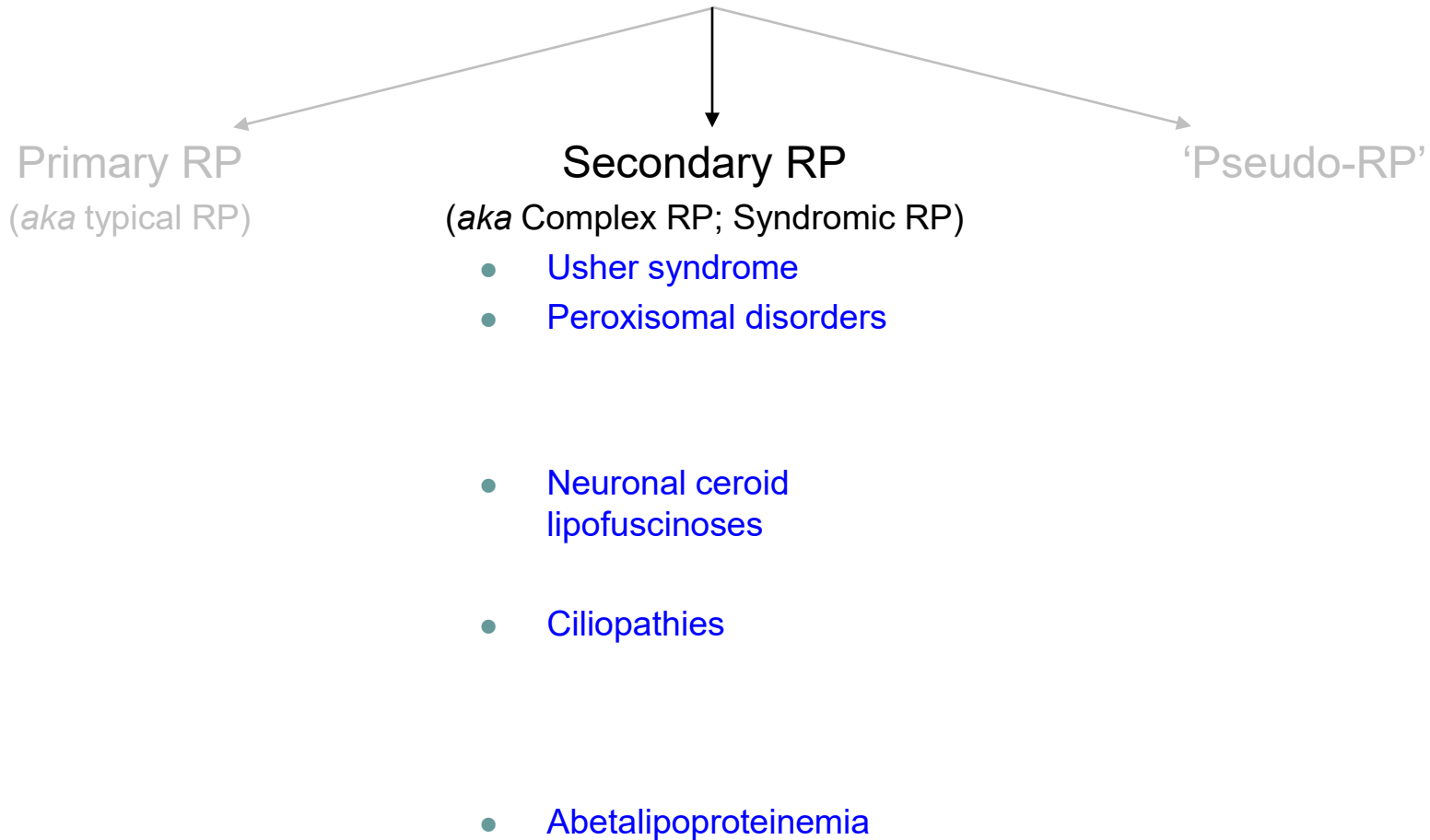
DDx for an RP-like Fundus



The 2ndry/syndromic RP conditions are can be grouped into five categories based on the underlying issue—what are these categories?

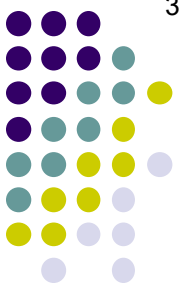
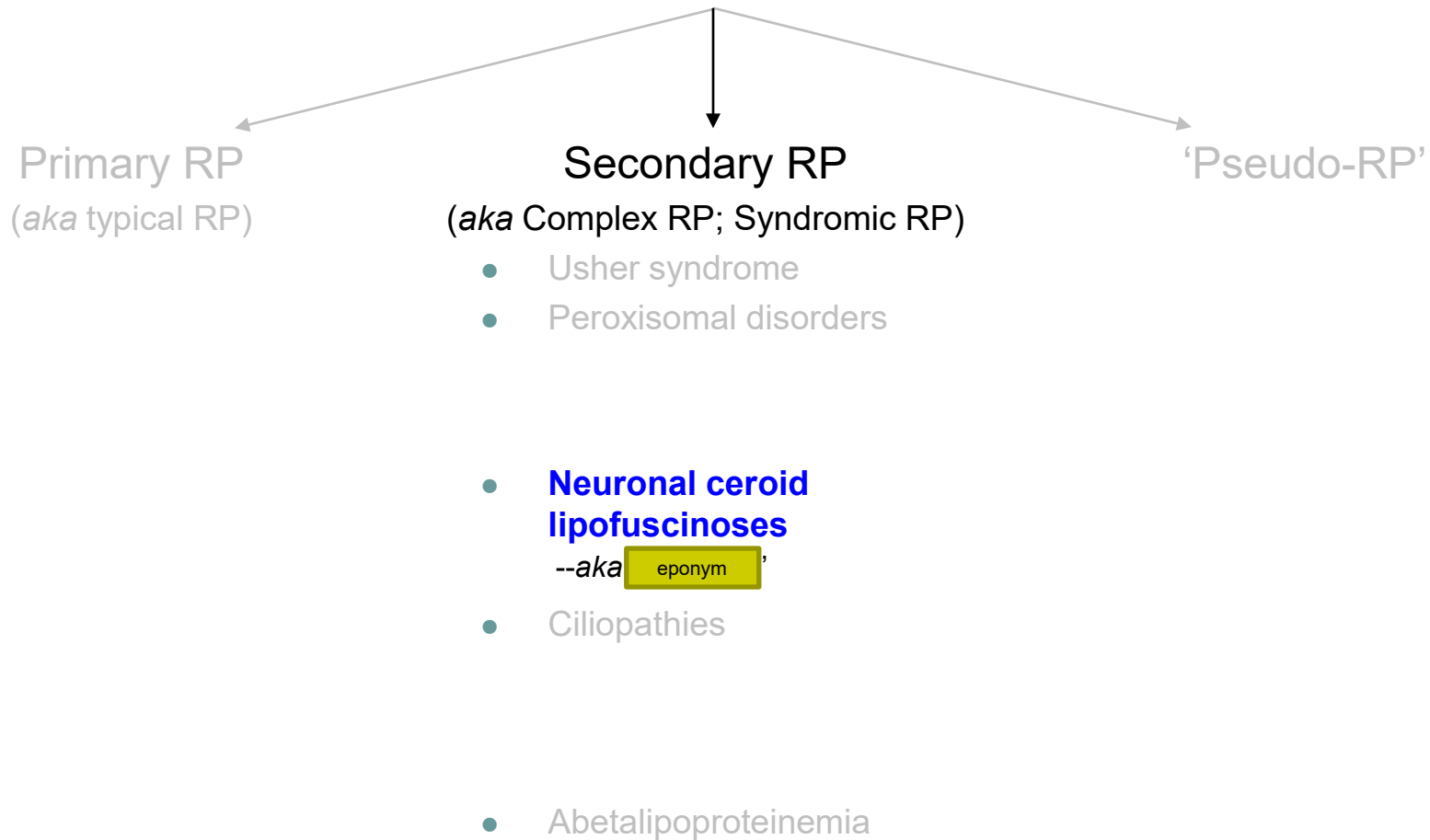


DDx for an RP-like Fundus

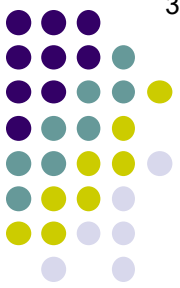
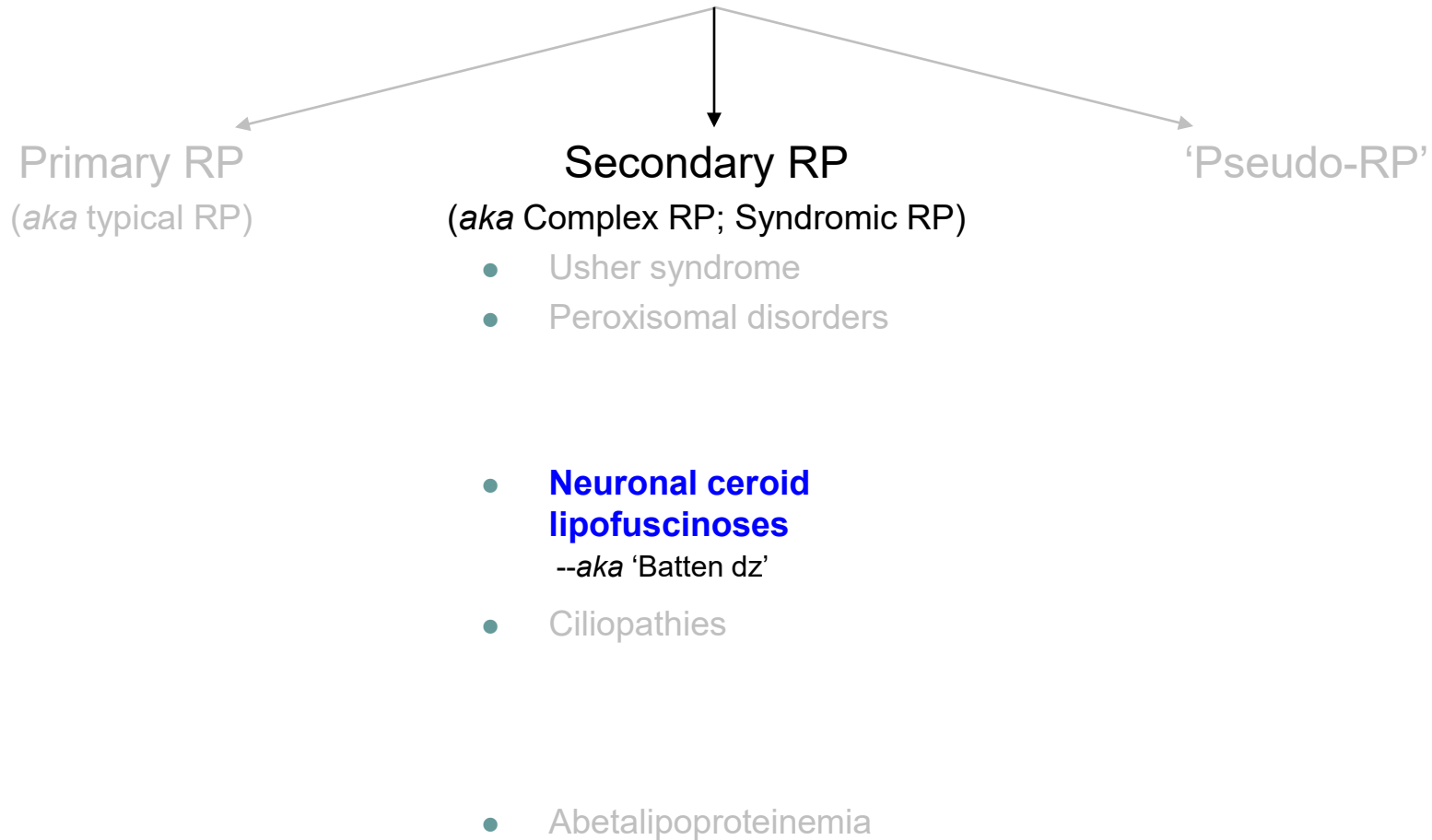


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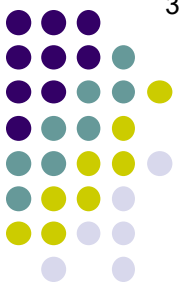
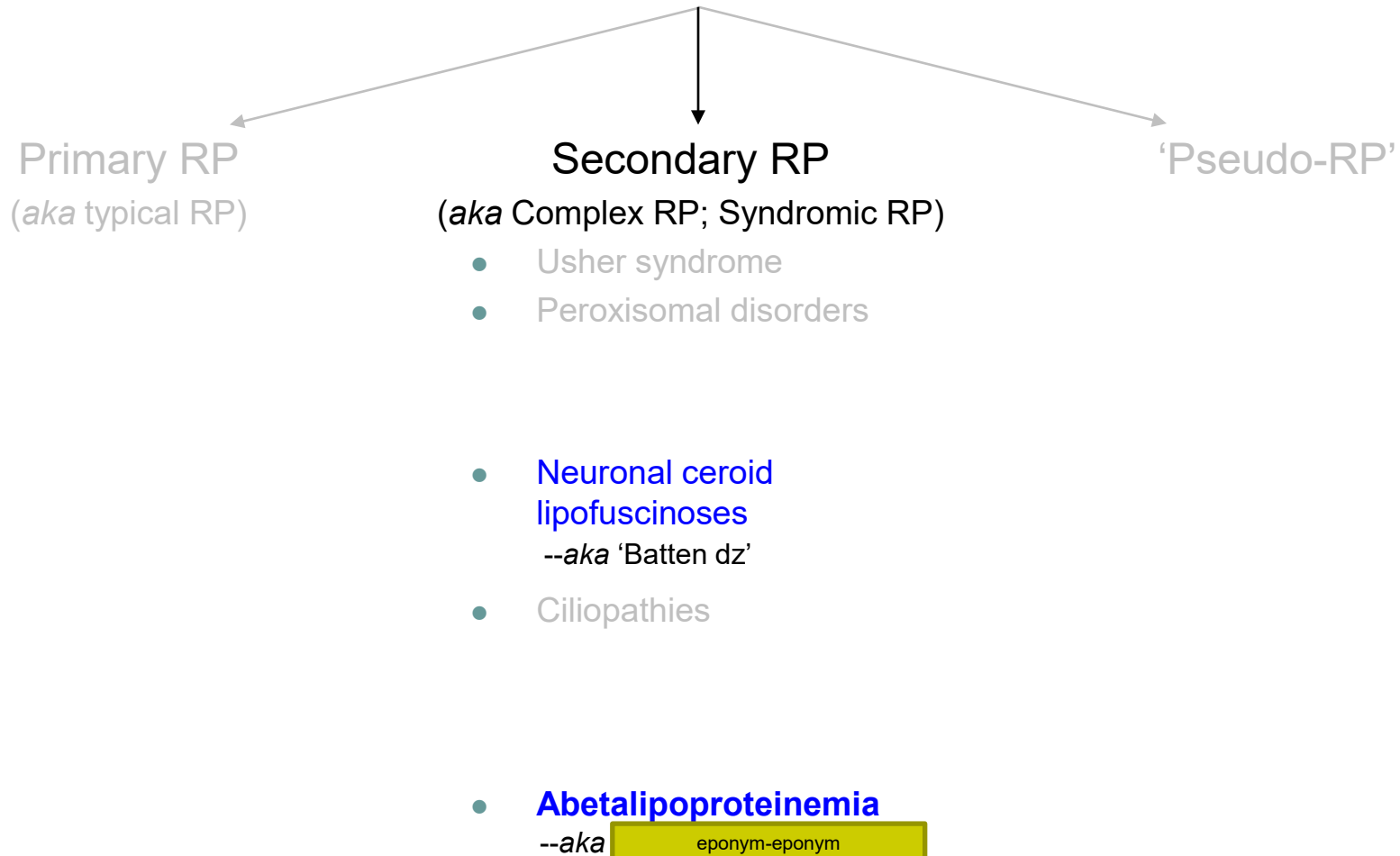
DDx for an RP-like Fundus



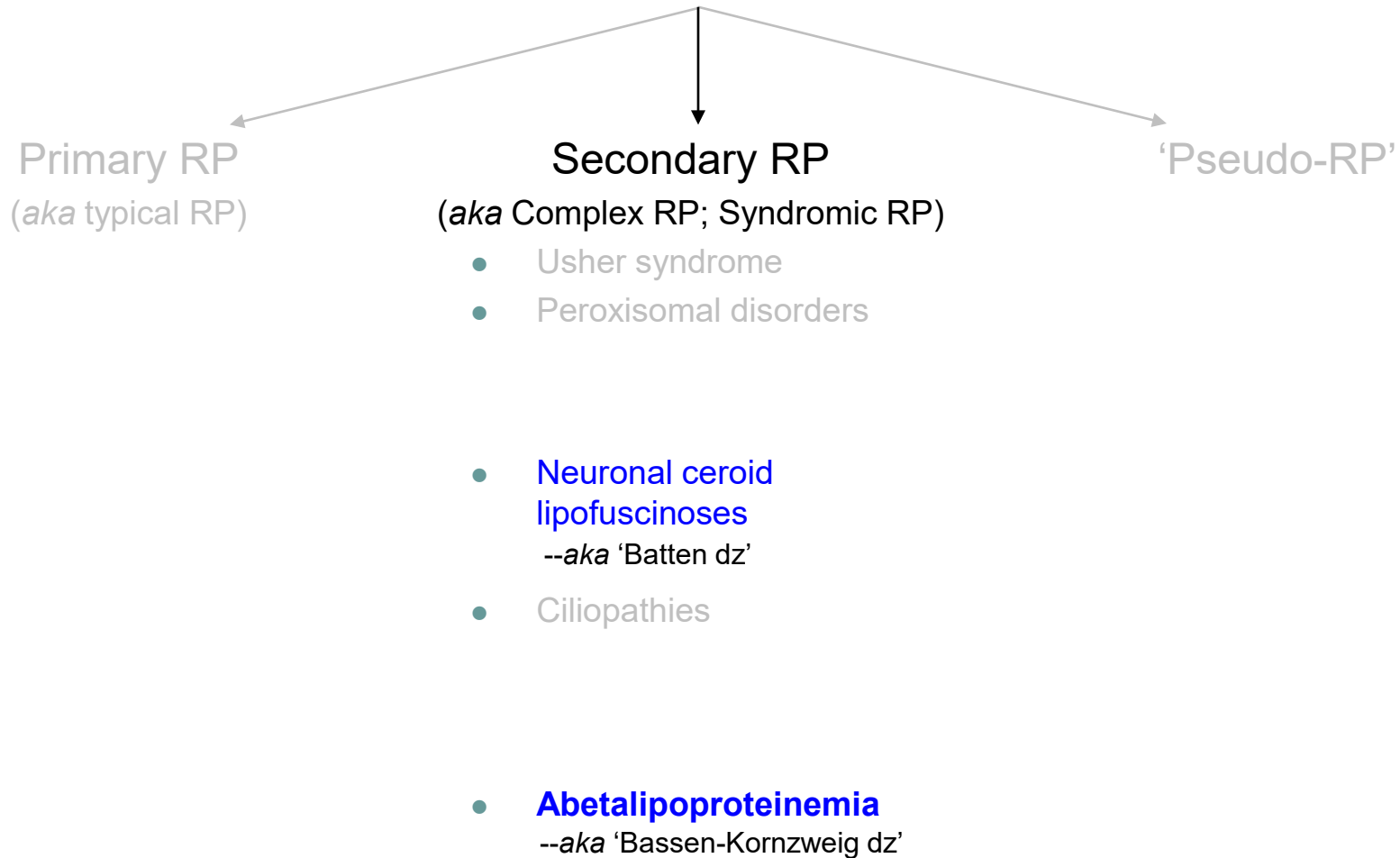
DDx for an RP-like Fundus

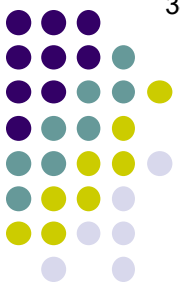


DDx for an RP-like Fundus

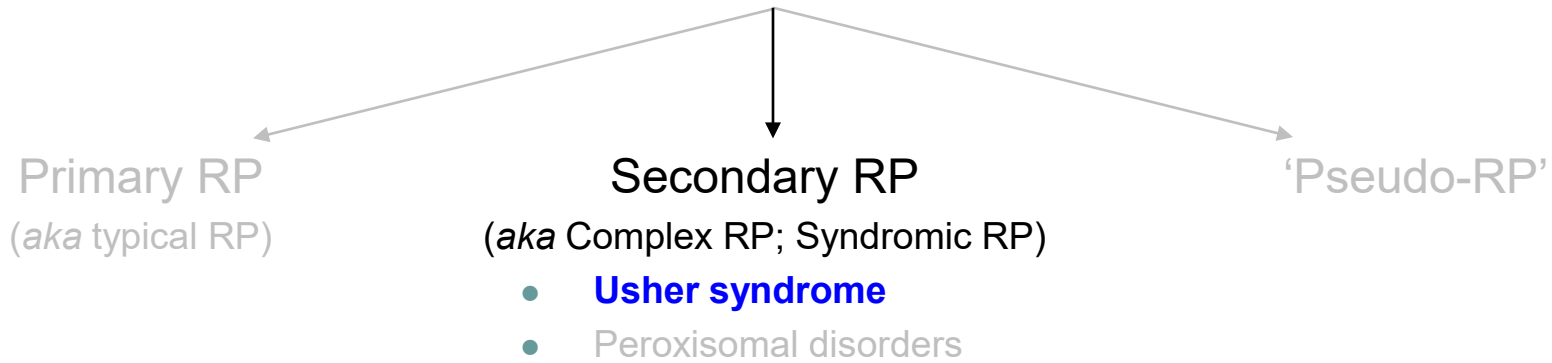


DDx for an RP-like Fundus





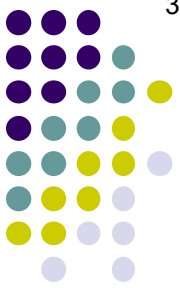
DDx for an RP-like Fundus



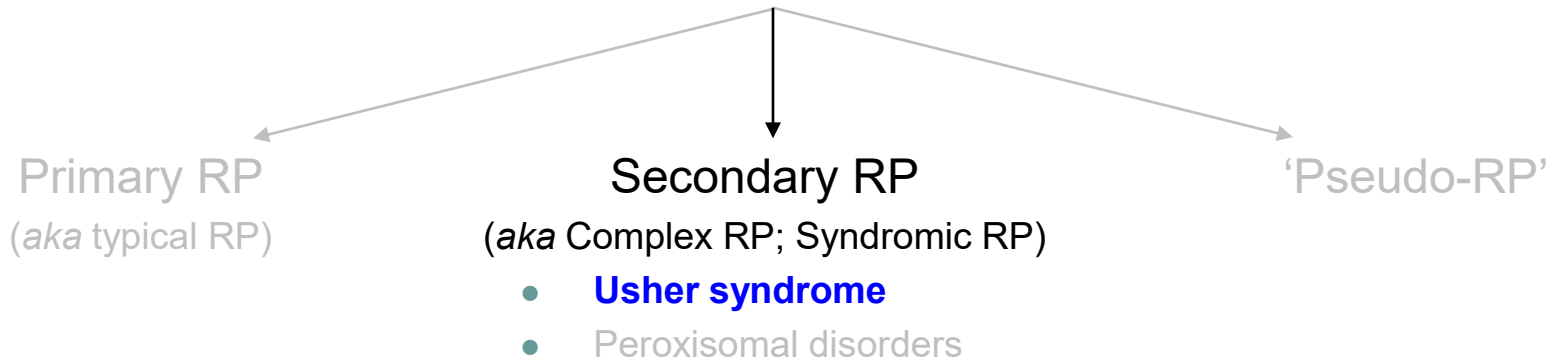
Usher syndrome = *Retinitis pigmentosa* +

two words

- Abetalipoproteinemia
--aka 'Bassen-Kornzweig dz'

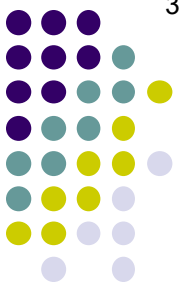


DDx for an RP-like Fundus

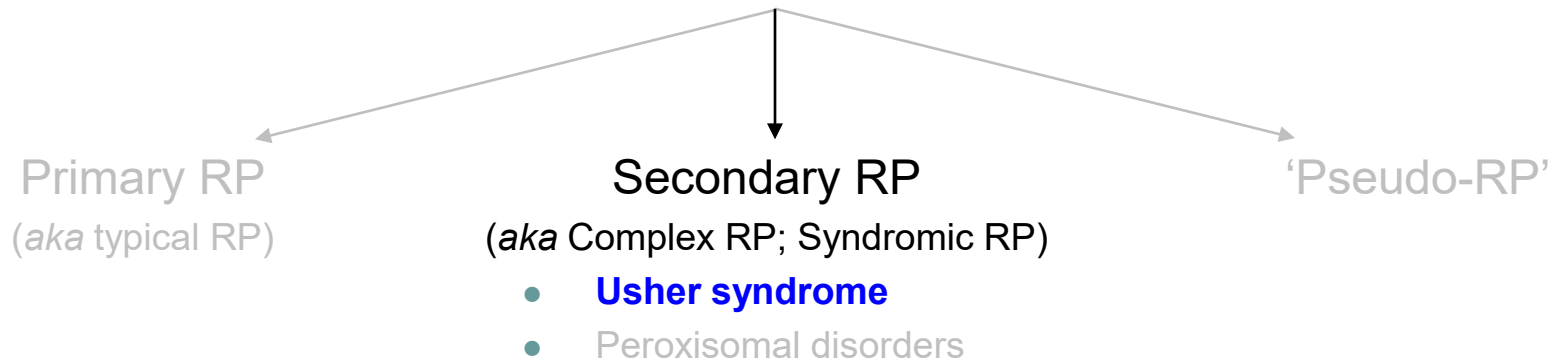


Usher syndrome = *Retinitis pigmentosa* + sensorineural deafness

- Abetalipoproteinemia
--aka 'Bassen-Kornzweig dz'



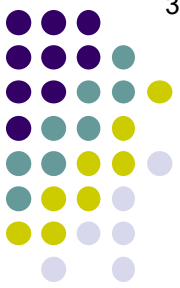
DDx for an RP-like Fundus



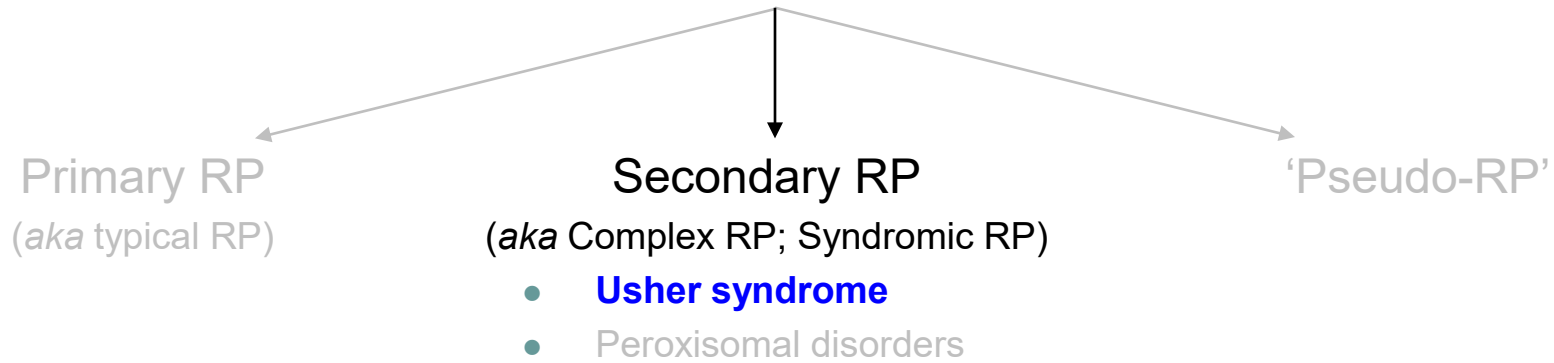
Usher syndrome = *Retinitis pigmentosa* + sensorineural deafness

Where does Usher syndrome rank as a cause of deaf-blindness in the US?

- Abetalipoproteinemia
--aka 'Bassen-Kornzweig dz'



DDx for an RP-like Fundus

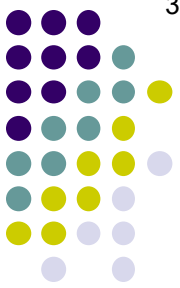


Usher syndrome = *Retinitis pigmentosa* + sensorineural deafness

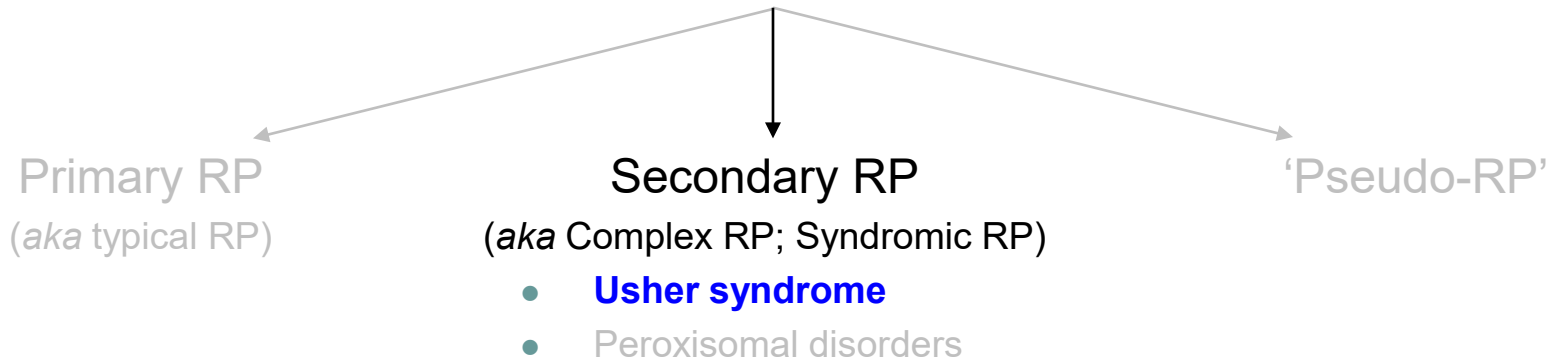
Where does Usher syndrome rank as a cause of deaf-blindness in the US?

It is the most common cause thereof

- Abetalipoproteinemia
--aka 'Bassen-Kornzweig dz'



DDx for an RP-like Fundus



Usher syndrome = *Retinitis pigmentosa* + sensorineural deafness

Where does Usher syndrome rank as a cause of deaf-blindness in the US?

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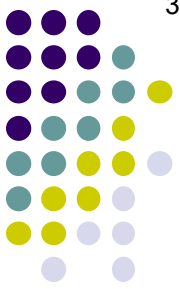
There are three types of Usher syndrome--what are they called?

--?

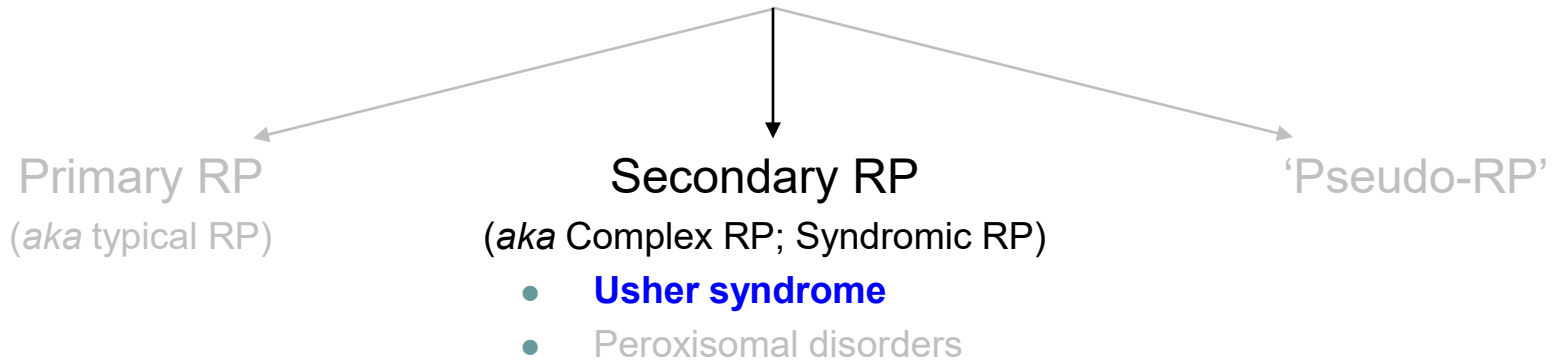
--?

--?

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DDx for an RP-like Fundus



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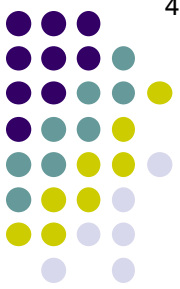
There are three types of Usher syndrome--what are they called?

--Type I

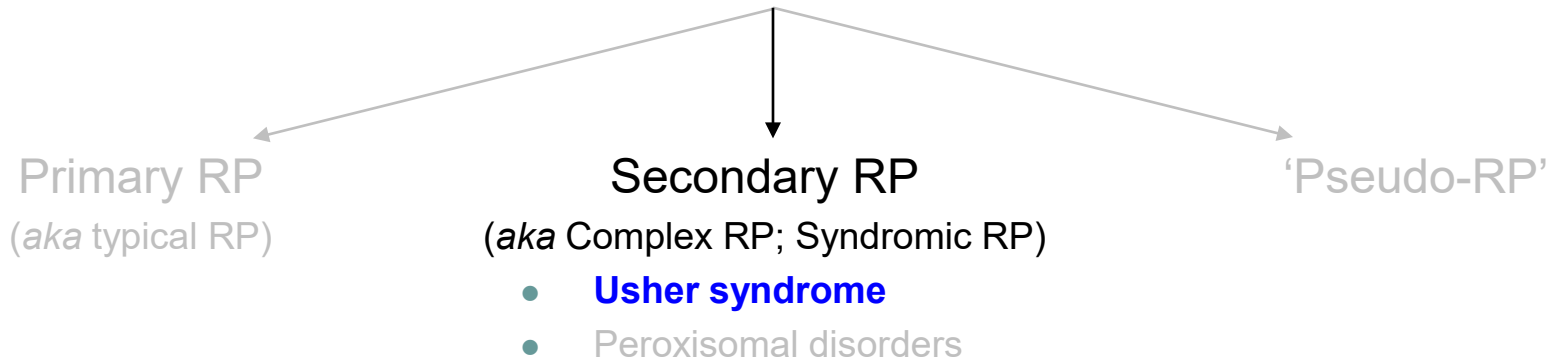
--Type II

--Type III

- Abetalipoproteinemia
--aka 'Bassen-Kornzweig dz'



DDx for an RP-like Fundus



Usher syndrome = *Retinitis pigmentosa* + sensorineural deafness

Where does Usher syndrome rank as a cause of deaf-blindness in the US?

It is the most common cause thereof

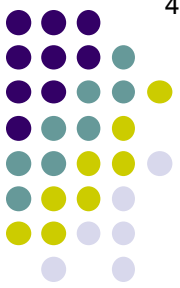
There are three types of Usher syndrome--what are they called? How do they manifest?

--**Type I** manifests...

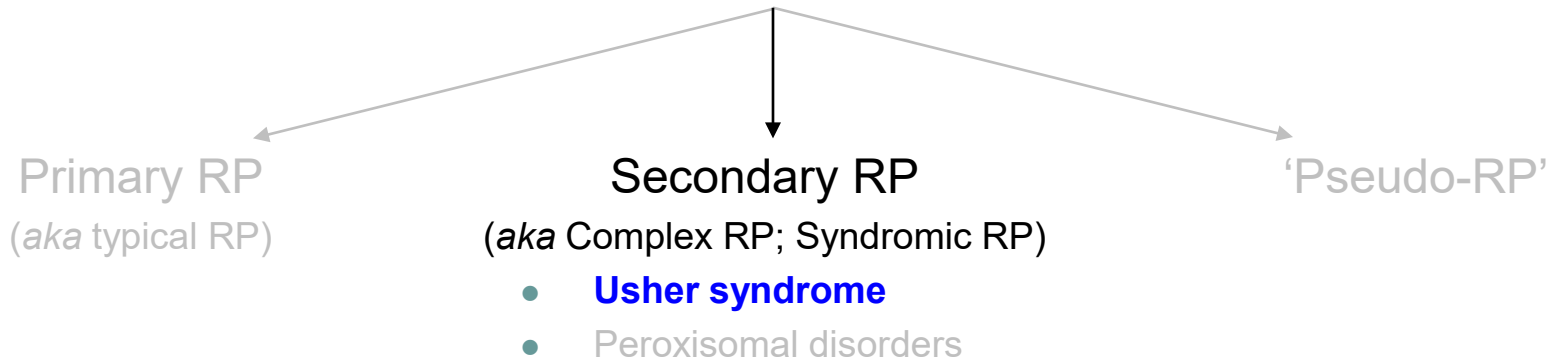
--Type II

--Type III

- Abetalipoproteinemia
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DDx for an RP-like Fundus



Usher syndrome = *Retinitis pigmentosa* + sensorineural deafness

Where does Usher syndrome rank as a cause of deaf-blindness in the US?

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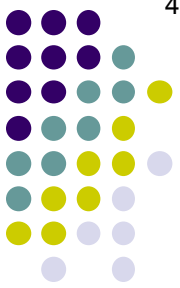
There are three types of Usher syndrome--what are they called? How do they manifest?

--**Type I** manifests...in the [] decade with [severity] hearing loss, RP and vestibular dysfunction

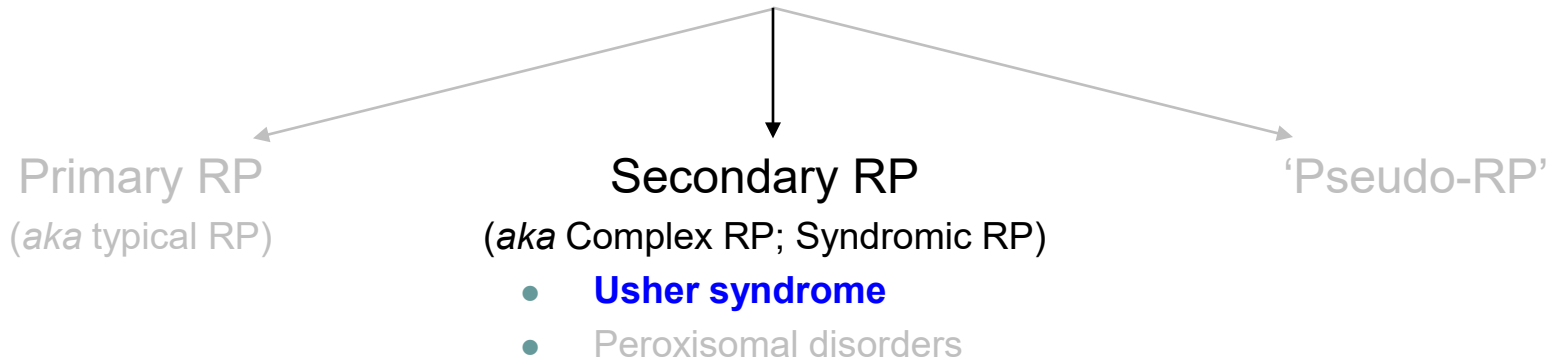
--Type II

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DDx for an RP-like Fundus



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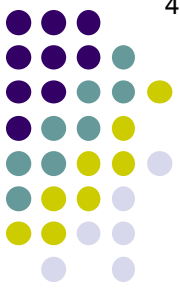
There are three types of Usher syndrome--what are they called? How do they manifest?

--**Type I** manifests...in the first decade with profound hearing loss, RP and vestibular dysfunction

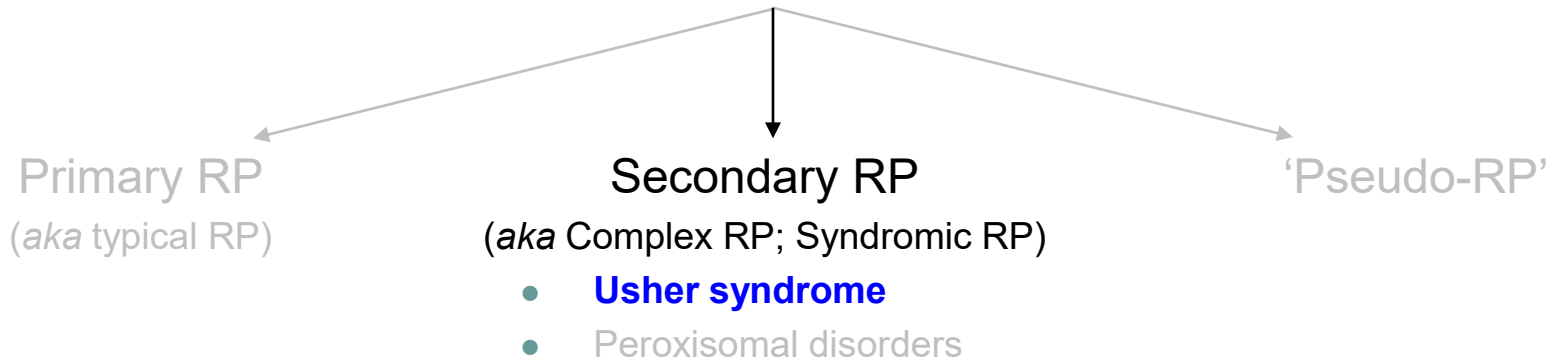
--Type II

--Type III

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DDx for an RP-like Fundus



Usher syndrome = *Retinitis pigmentosa* + sensorineural deafness

Where does Usher syndrome rank as a cause of deaf-blindness in the US?

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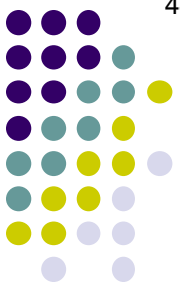
There are three types of Usher syndrome--what are they called? How do they manifest?

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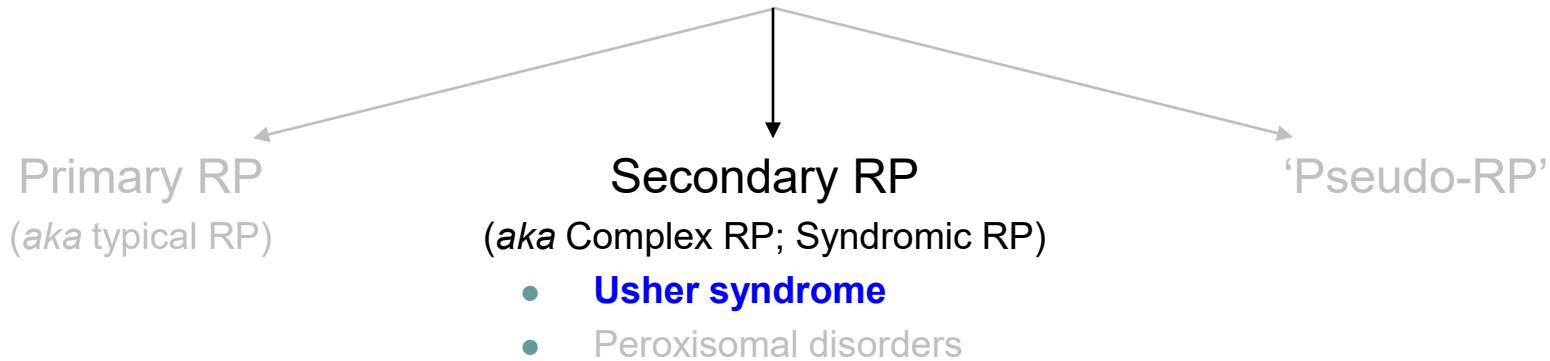
--**Type II** manifests...

--Type III

- Abetalipoproteinemia
--aka 'Bassen-Kornzweig dz'



DDx for an RP-like Fundus



Usher syndrome = *Retinitis pigmentosa* + sensorineural deafness

Where does Usher syndrome rank as a cause of deaf-blindness in the US?

It is the most common cause thereof

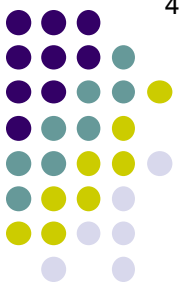
There are three types of Usher syndrome--what are they called? How do they manifest?

--**Type I** manifests...in the first decade with profound hearing loss, RP and vestibular dysfunction

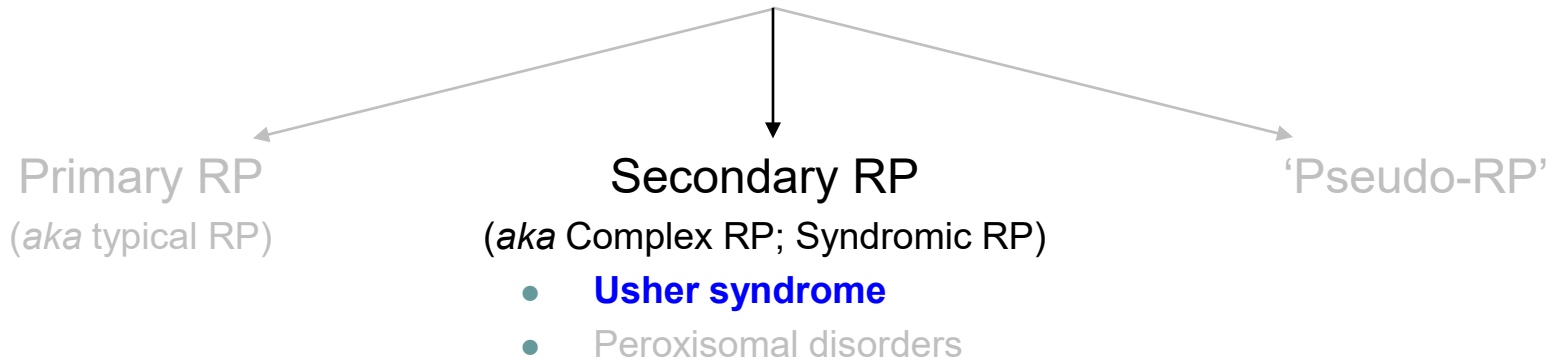
--**Type II** manifests...in the decade with severity hearing loss, RP; vestibular function is status

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Usher syndrome = *Retinitis pigmentosa* + sensorineural deafness

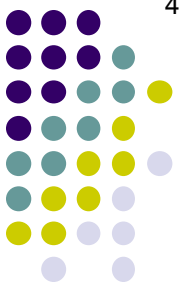
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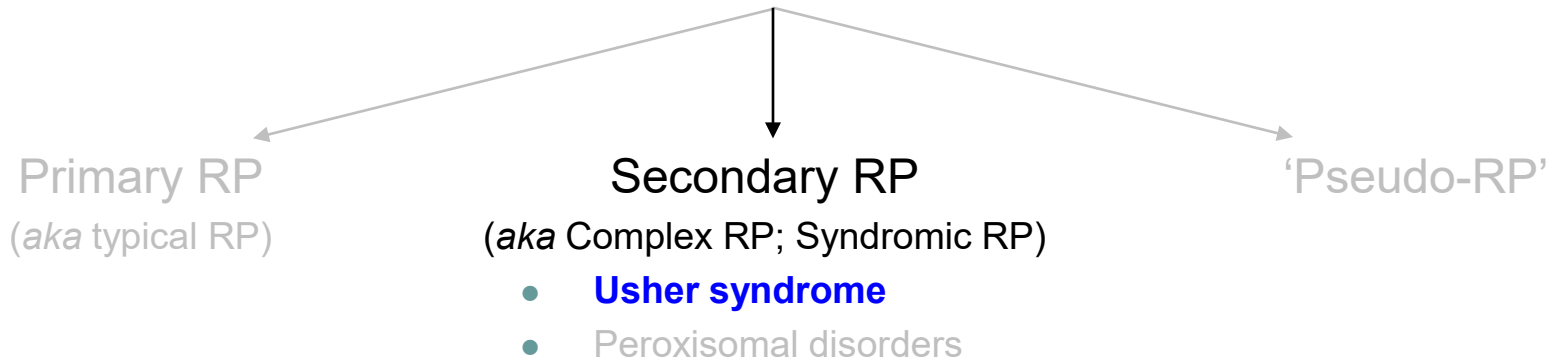
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- Type I** manifests...in the first decade with profound hearing loss, RP and vestibular dysfunction
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- Type III**

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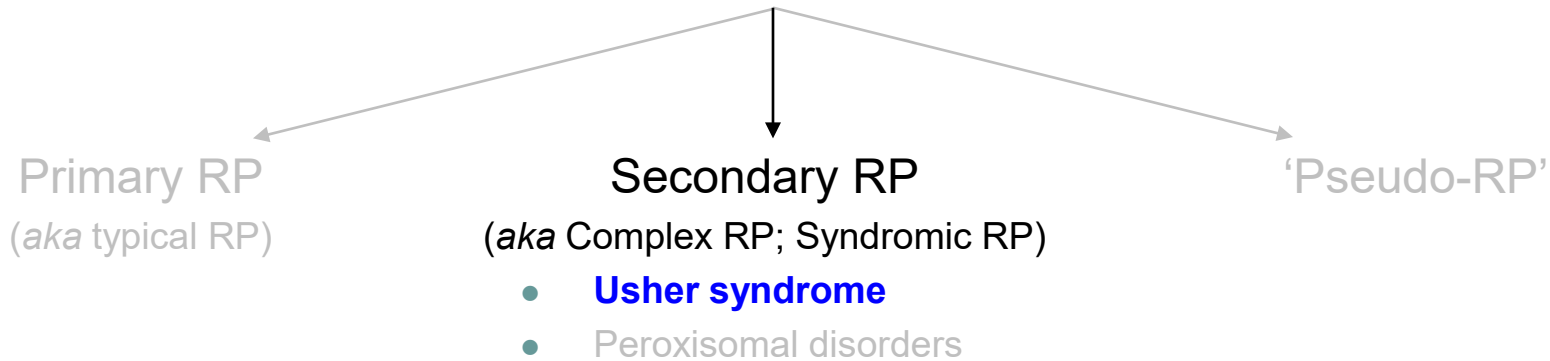
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DDx for an RP-like Fundus



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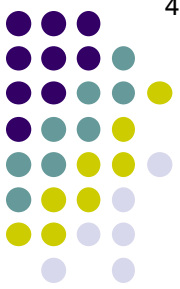
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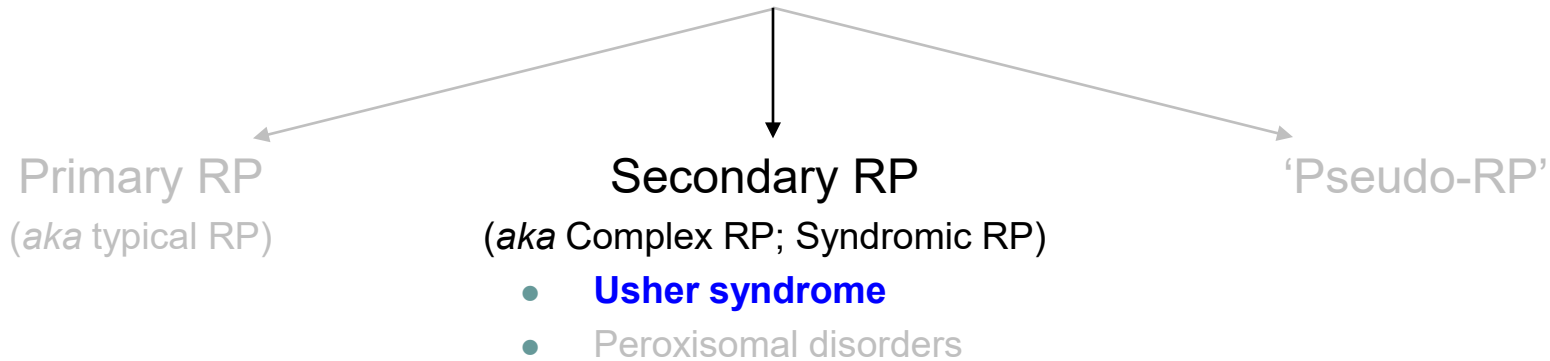
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DDx for an RP-like Fundus



Usher syndrome = *Retinitis pigmentosa* + sensorineural deafness

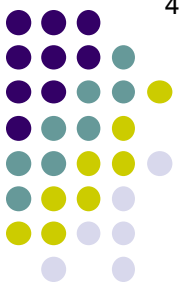
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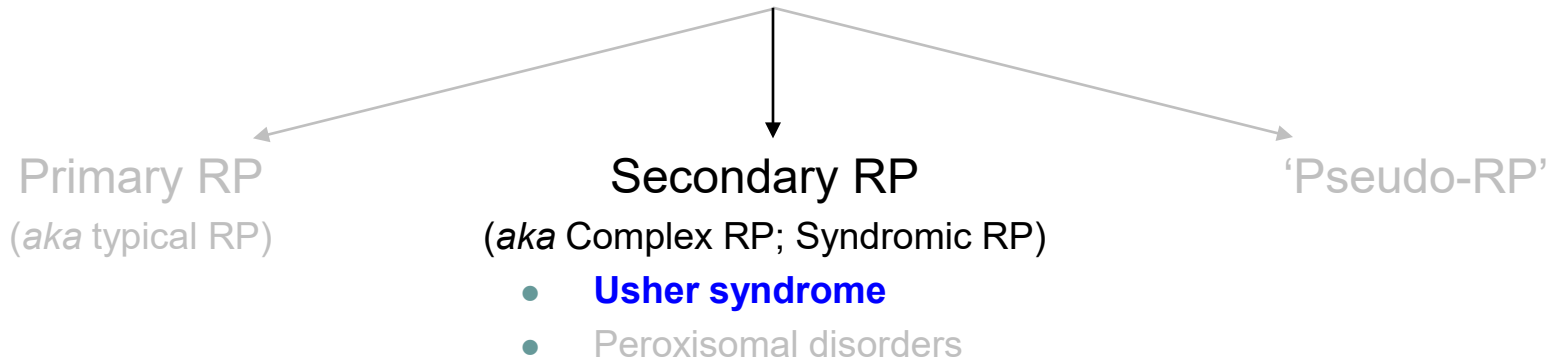
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- Type I** manifests...in the first decade with profound hearing loss, RP and vestibular dysfunction
- Type II** manifests...in the second decade with moderate hearing loss, RP; vestibular function is intact
- Type III** has...progressive hearing loss; the RP varies in severity; vestibular function is sporadic

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DDx for an RP-like Fundus



Usher syndrome = Retinitis pigmentosa + sensorineural deafness

Where does Usher syndrome manifest?
It is the most common form of RP.

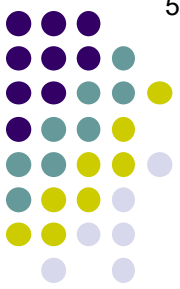
There are three types of Usher syndrome.

- Type I manifests... early, severe
- Type II manifests... intermediate
- Type III has... progressive hearing loss, the RP varies in severity, vestibular function is sporadic

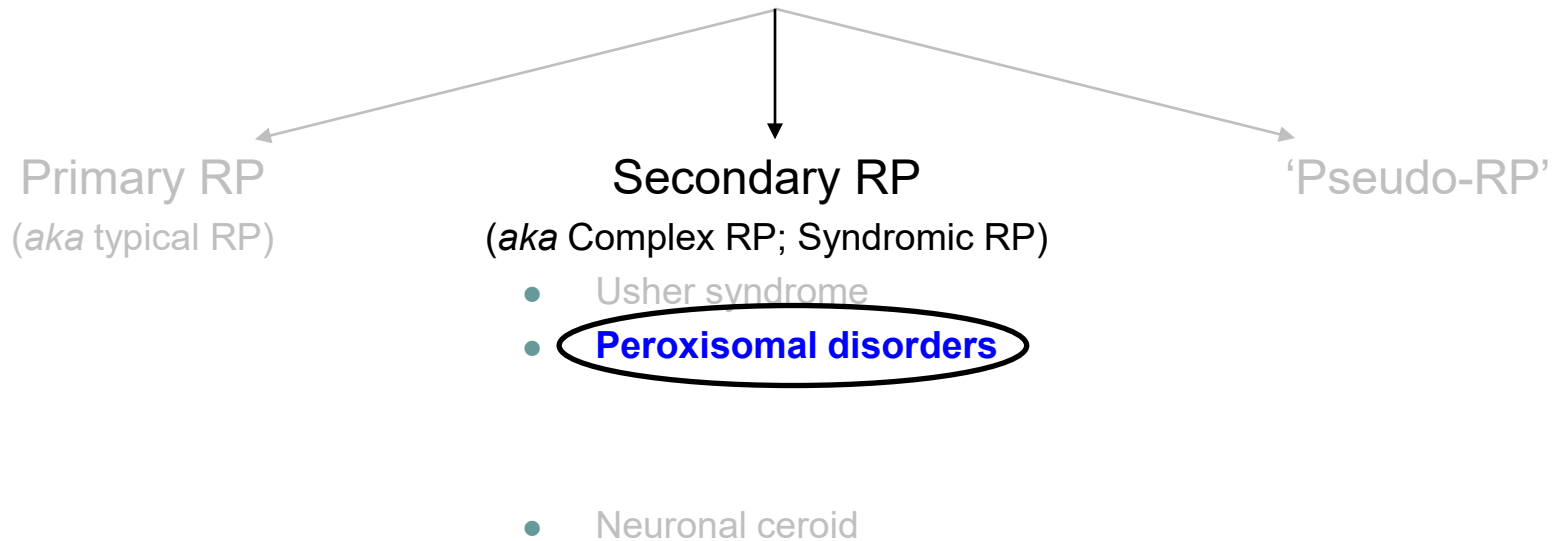
Usher syndrome t1;dr
= RP + hearing loss +/- vestibular dysfunction
 --Type I early, severe
 --Type II later, less severe
 --Type III variable

manifest?
vestibular dysfunction
vestibular function is intact
sporadic

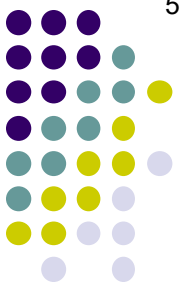
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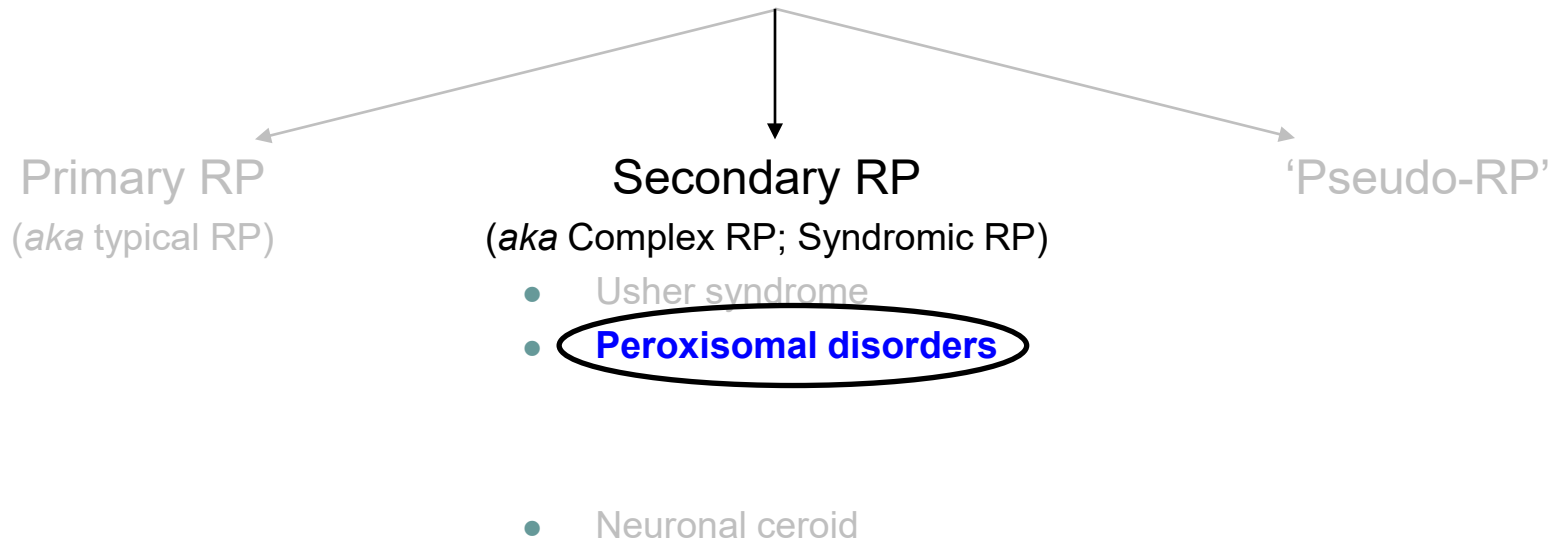
DDx for an RP-like Fundus



What are peroxisomal disorders?

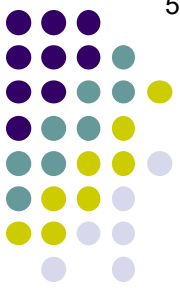


DDx for an RP-like Fundus

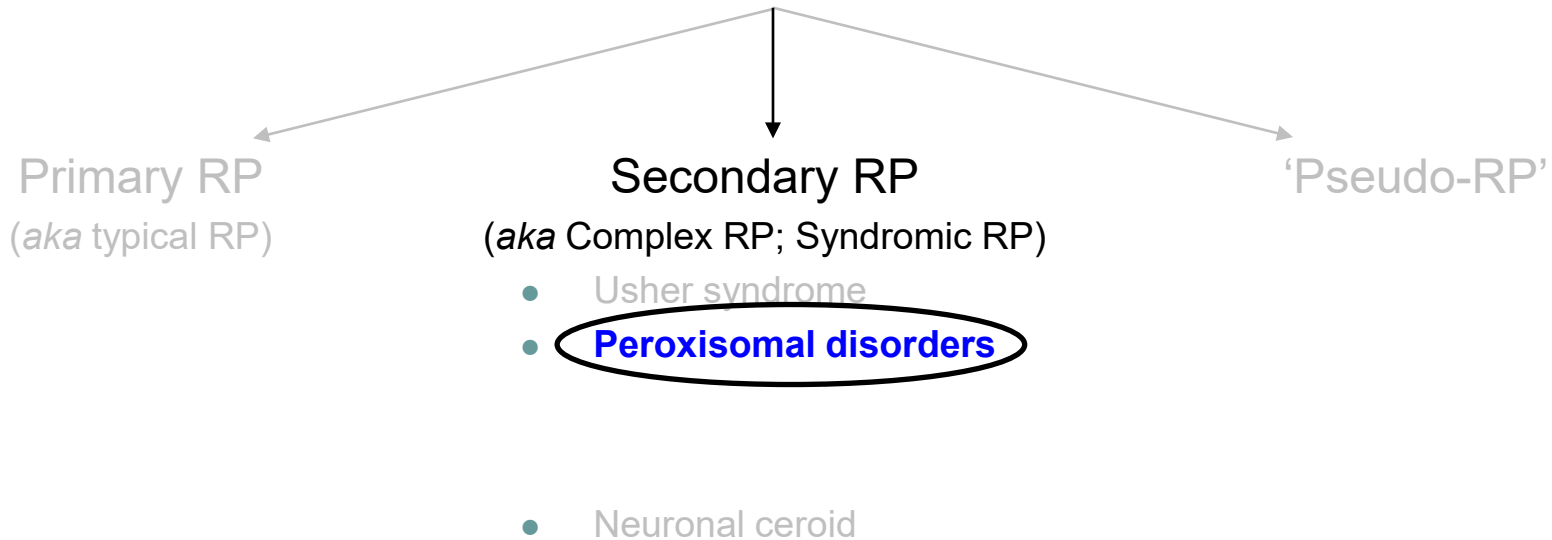


What are peroxisomal disorders?

A heterogeneous group of disorders of peroxisome function



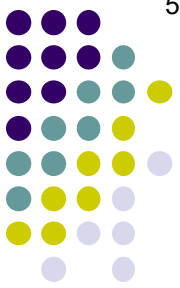
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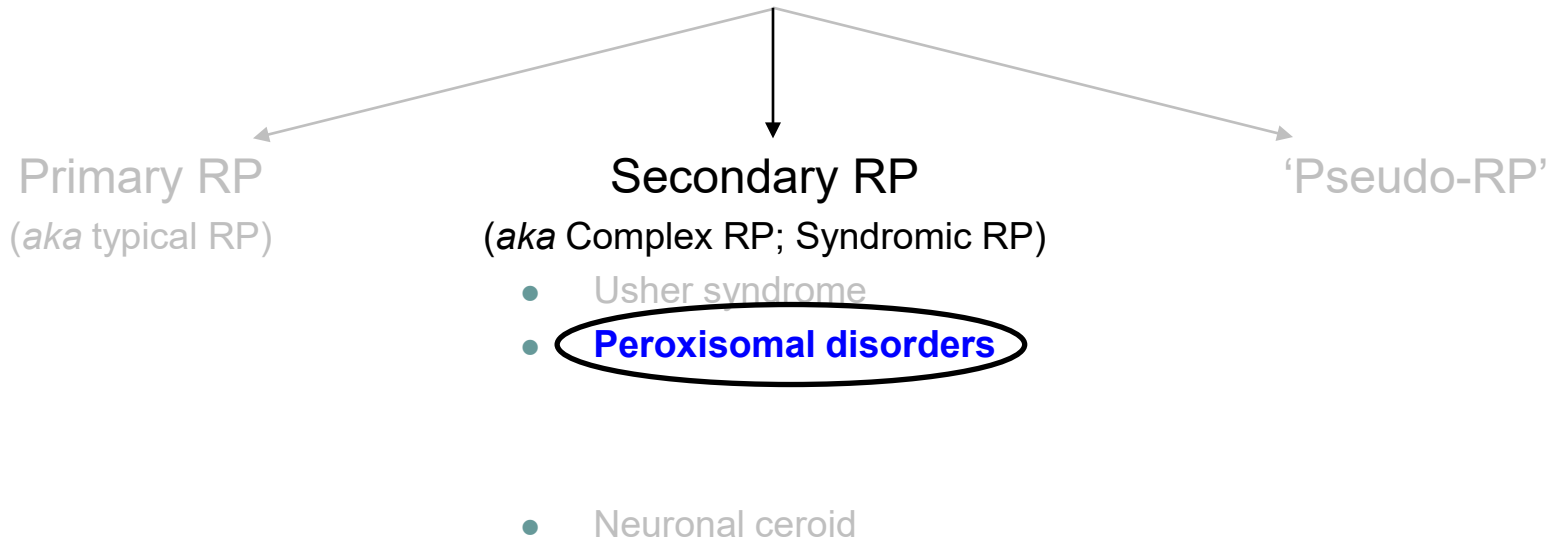
What are peroxisomal disorders?

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What is/are peroxisomes?



DDx for an RP-like Fundus

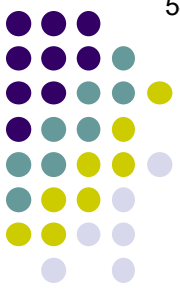


What are peroxisomal disorders?

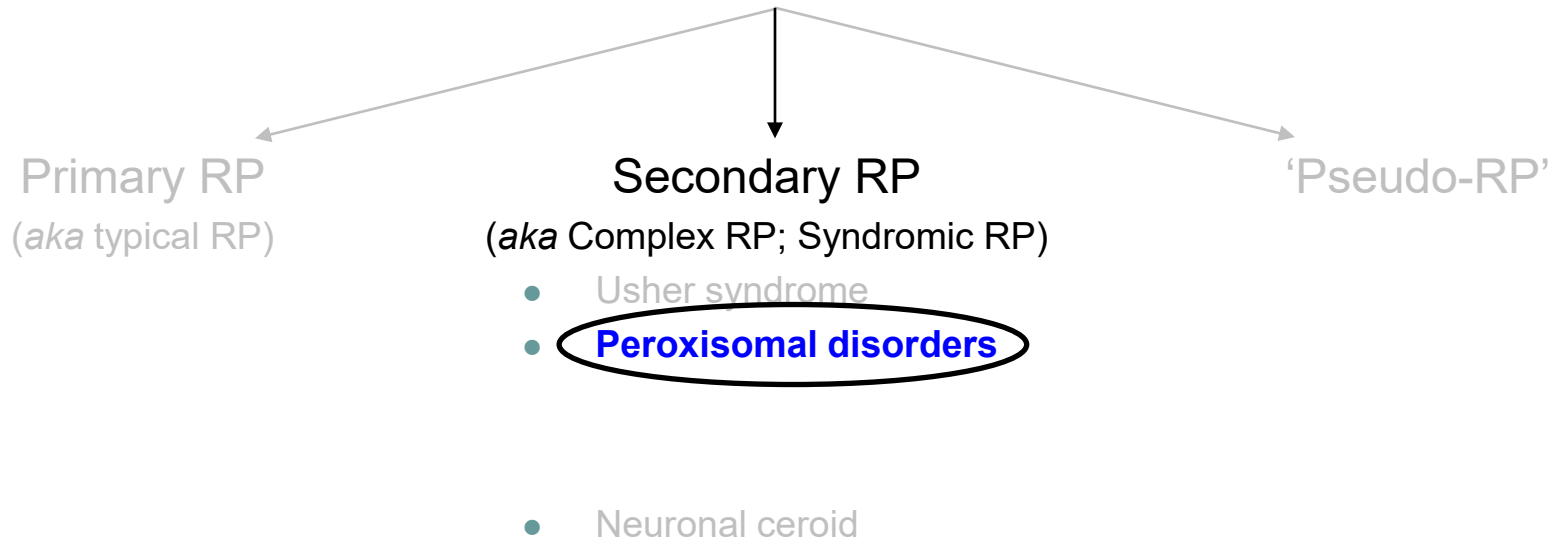
A heterogeneous group of disorders of peroxisome function

What is/are peroxisomes?

Intracellular organelles that play key roles in many aspects of cell metabolism



DDx for an RP-like Fundus



What are peroxisomal disorders?

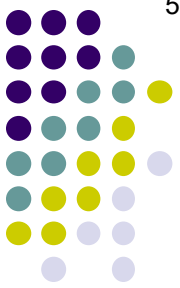
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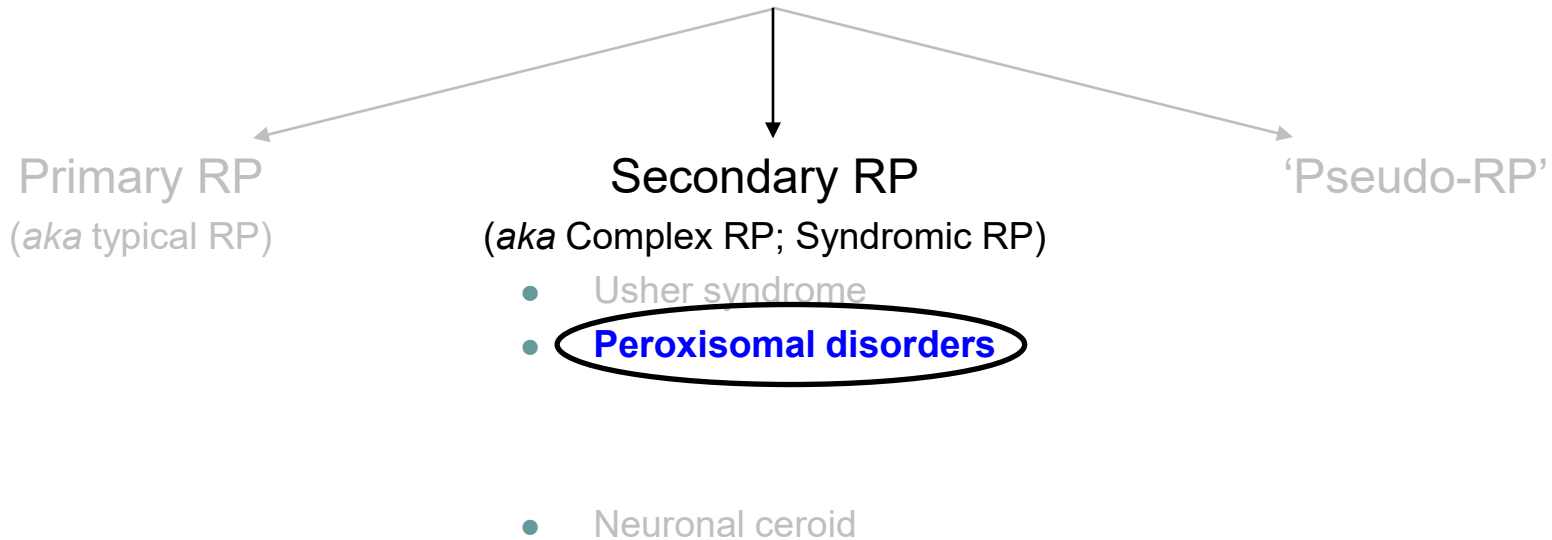
Intracellular organelles that play key roles in many aspects of cell metabolism

*What is the hallmark lab abnormality of the peroxisomal disorders that present with **LCA**?*

(LCA = Leber's congenital amaurosis, an age-related form of RP)



DDx for an RP-like Fundus



What are peroxisomal disorders?

A heterogeneous group of disorders of peroxisome function

What is/are peroxisomes?

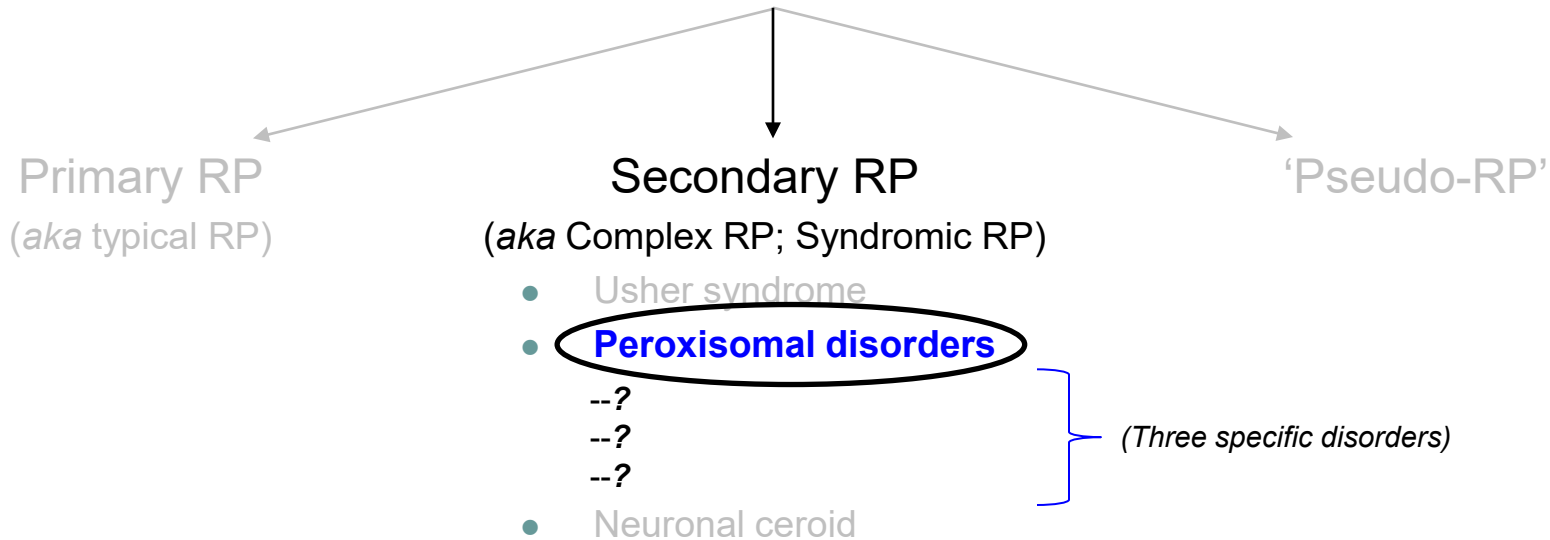
Intracellular organelles that play key roles in many aspects of cell metabolism

What is the hallmark lab abnormality of the peroxisomal disorders that present with LCA?

Abnormally high serum levels of **very long chain fatty acids** (VLCFA)



DDx for an RP-like Fundus



What are peroxisomal disorders?

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What is/are peroxisomes?

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Abnormally high serum levels of **very long chain fatty acids** (VLCFA)

What specific peroxisomal disorders can manifest an LCA-type presentation?

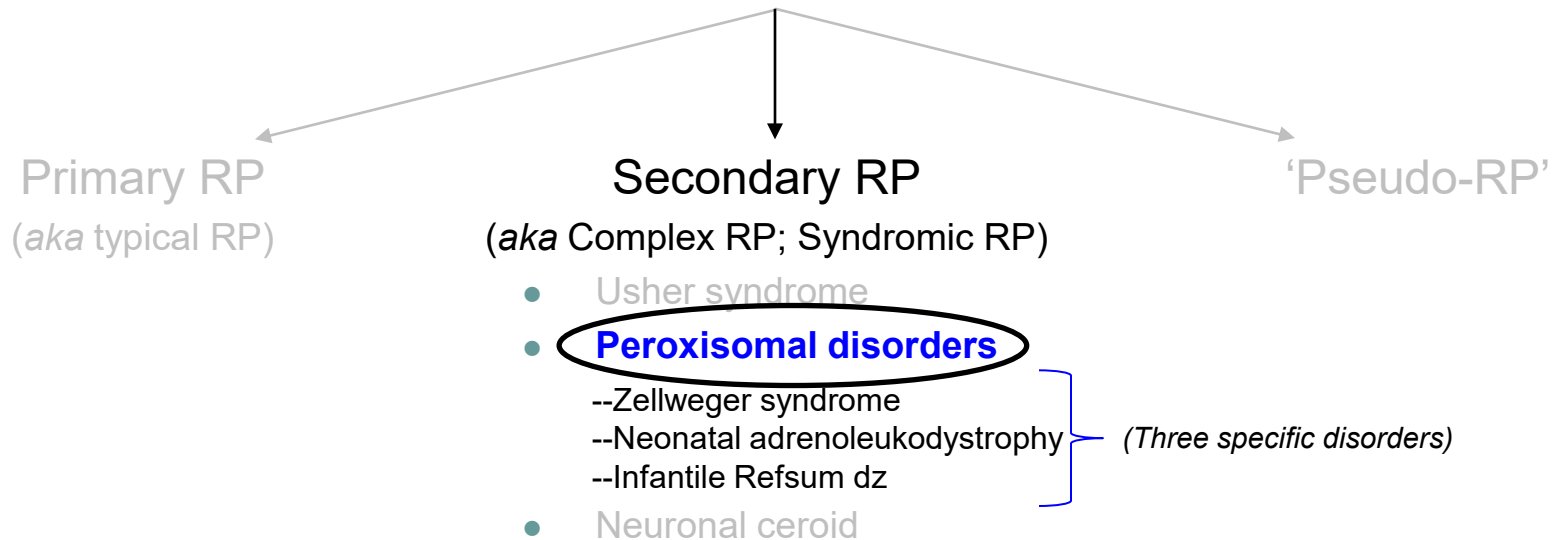
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DDx for an RP-like Fundus



What are peroxisomal disorders?

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What is/are peroxisomes?

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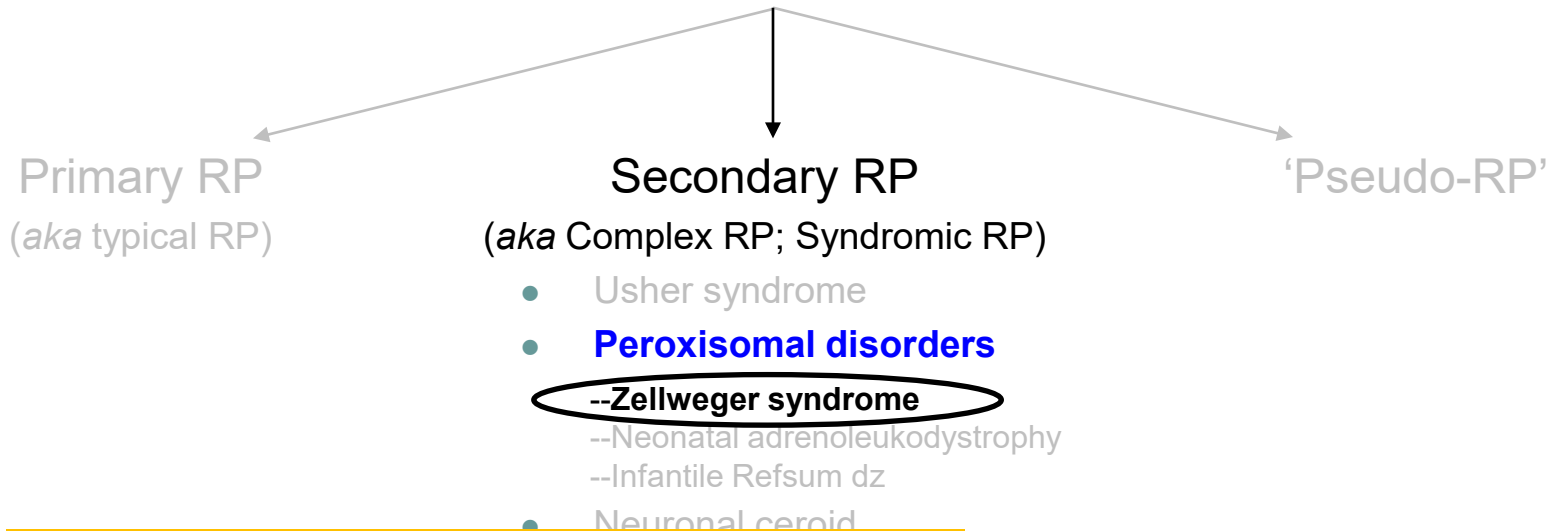
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What specific peroxisomal disorders can manifest an LCA-type presentation?

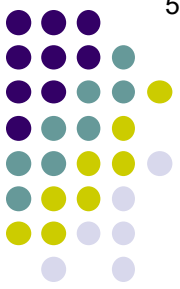
- Zellweger syndrome
- Neonatal adrenoleukodystrophy (NALD)
- Infantile Refsum dz



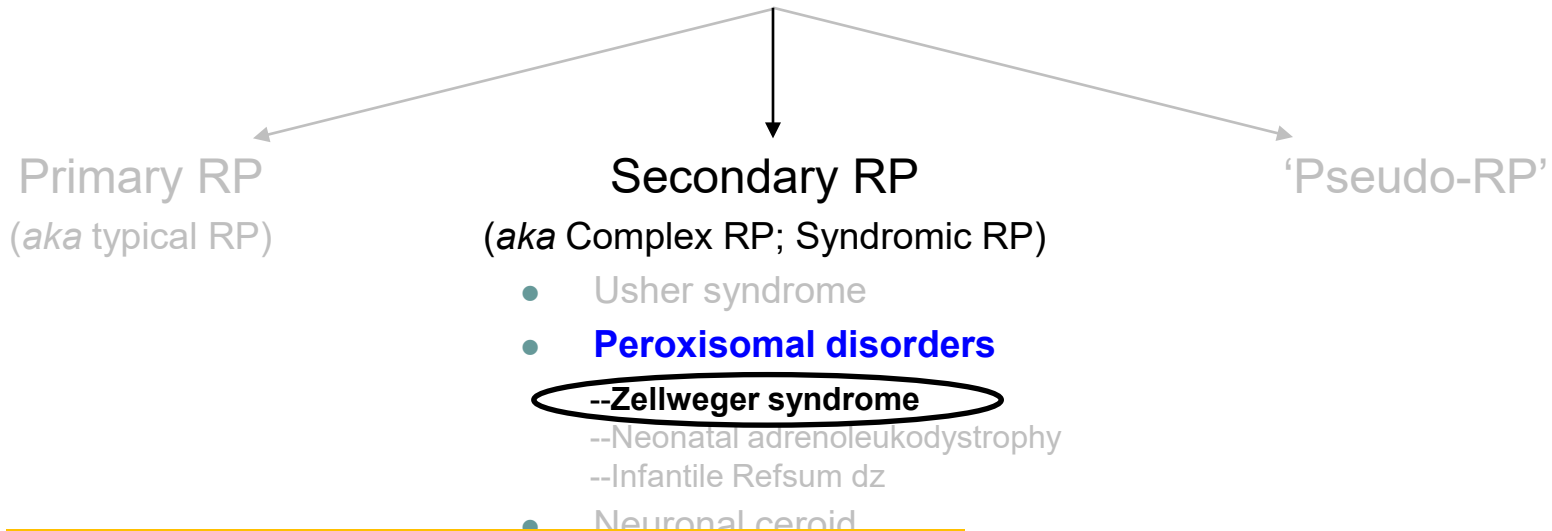
DDx for an RP-like Fundus



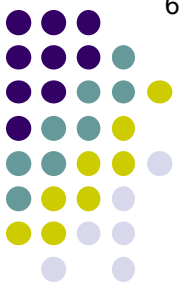
What is the noneponymous name for Zellweger syndrome?



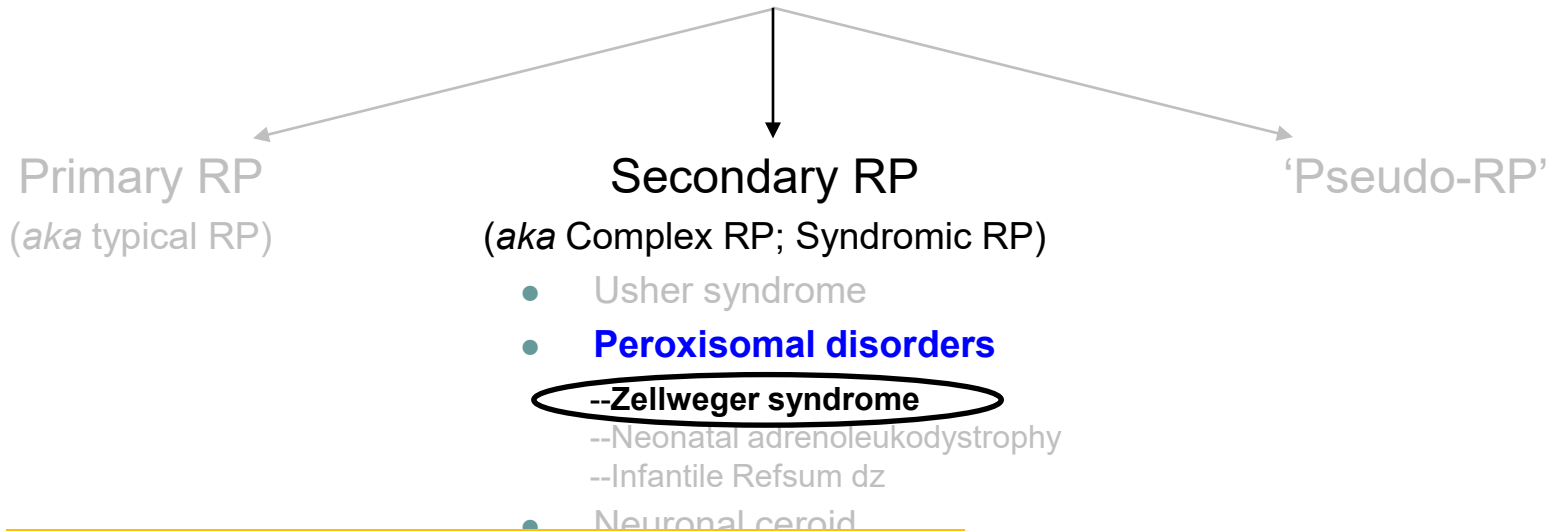
DDx for an RP-like Fundus



What is the noneponymous name for Zellweger syndrome?
Cerebrohepatorenal syndrome

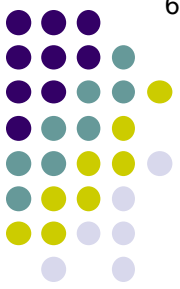


DDx for an RP-like Fundus

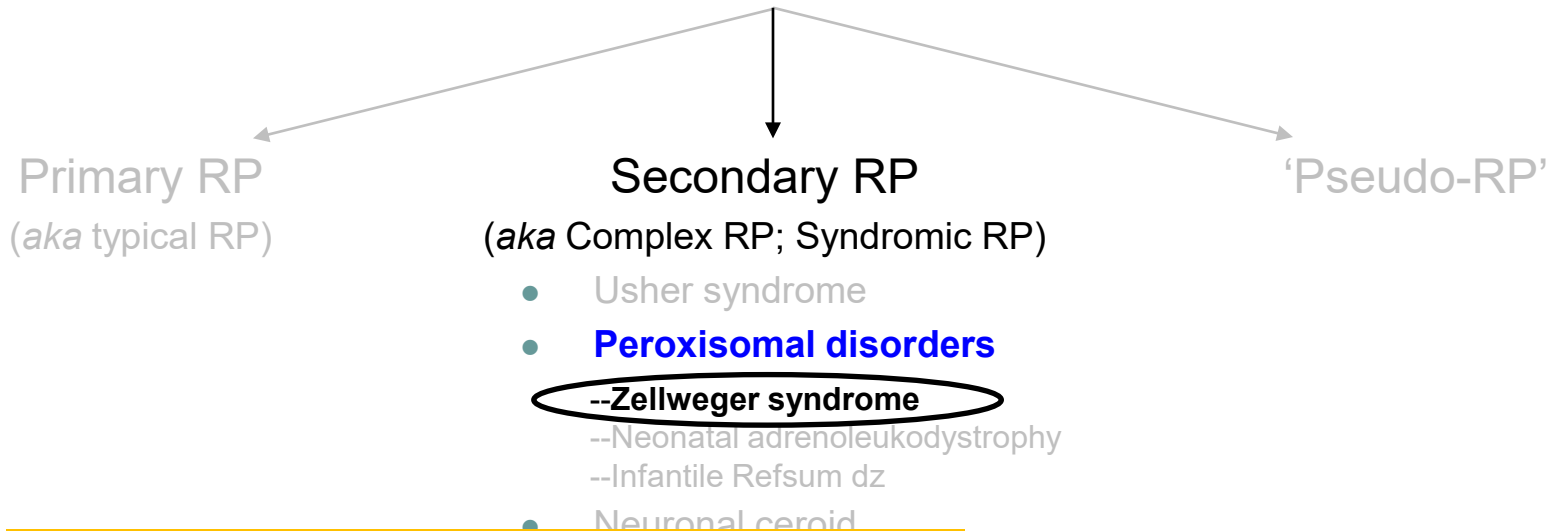


What is the noneponymous name for Zellweger syndrome?
Cerebrohepatorenal syndrome

What is its inheritance pattern?

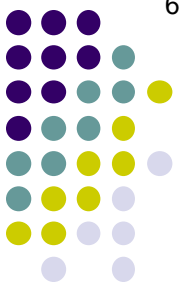


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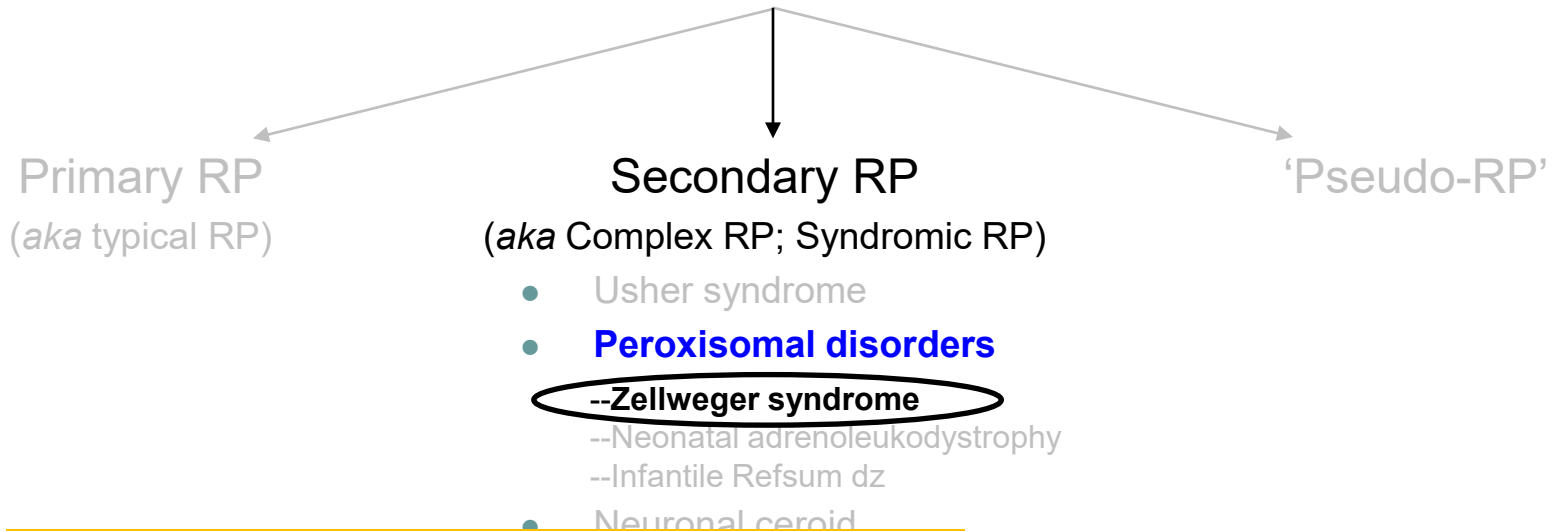


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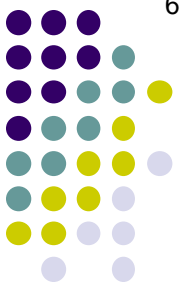
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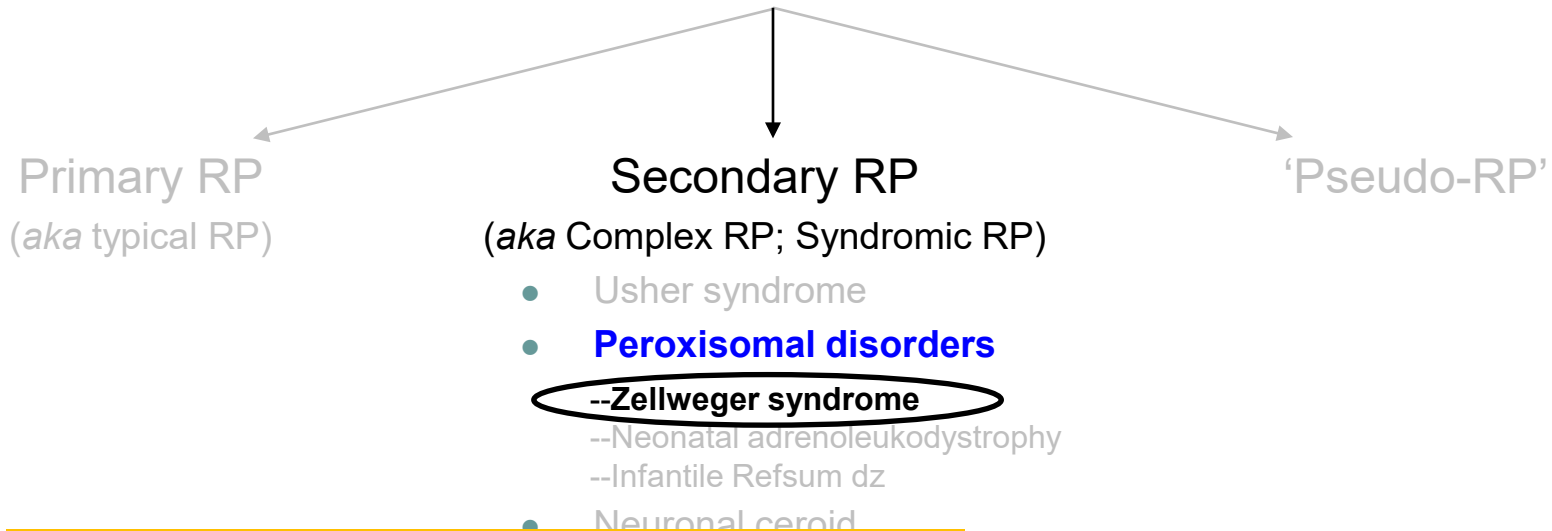
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How do Zellweger syndrome pts present?



DDx for an RP-like Fundus

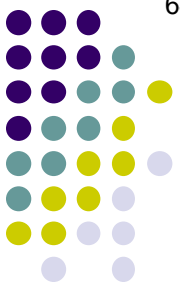


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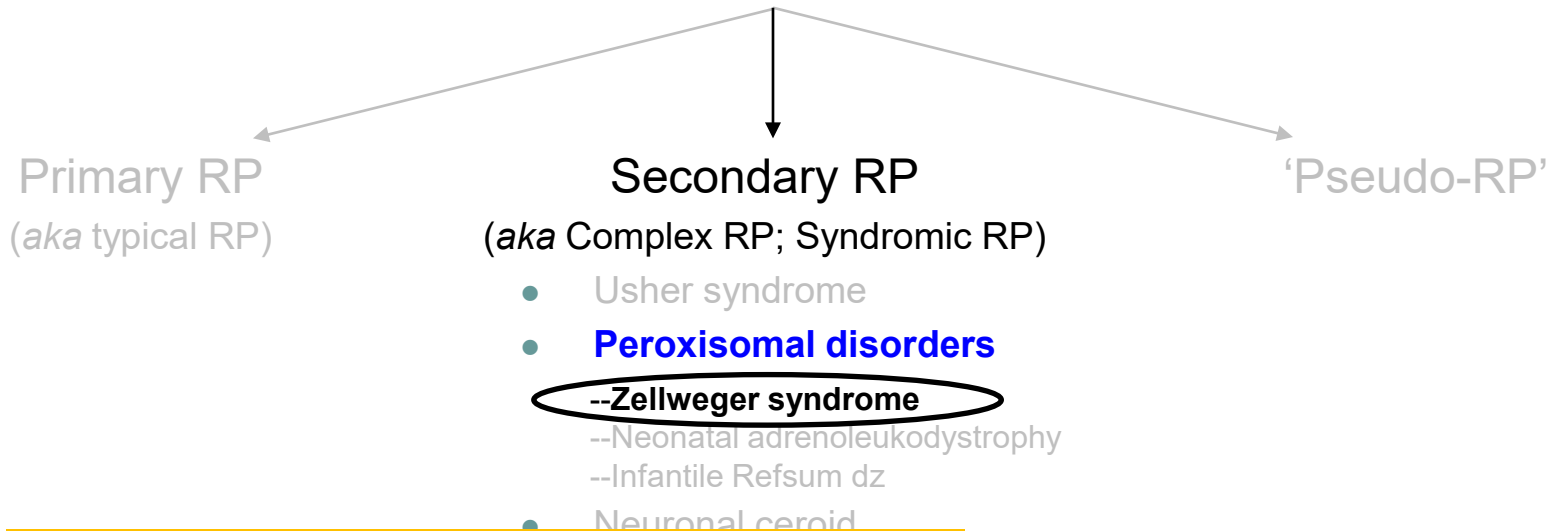
What is its inheritance pattern?
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How do Zellweger syndrome pts present?
In the 'age' period

dz'



DDx for an RP-like Fundus



What is the noneponymous name for Zellweger syndrome?
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What is its inheritance pattern?
AR

How do Zellweger syndrome pts present?

In the **neonatal** period with:

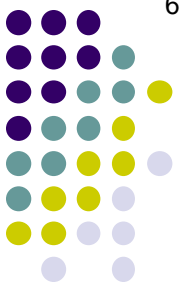
--RP-like fundus

--?

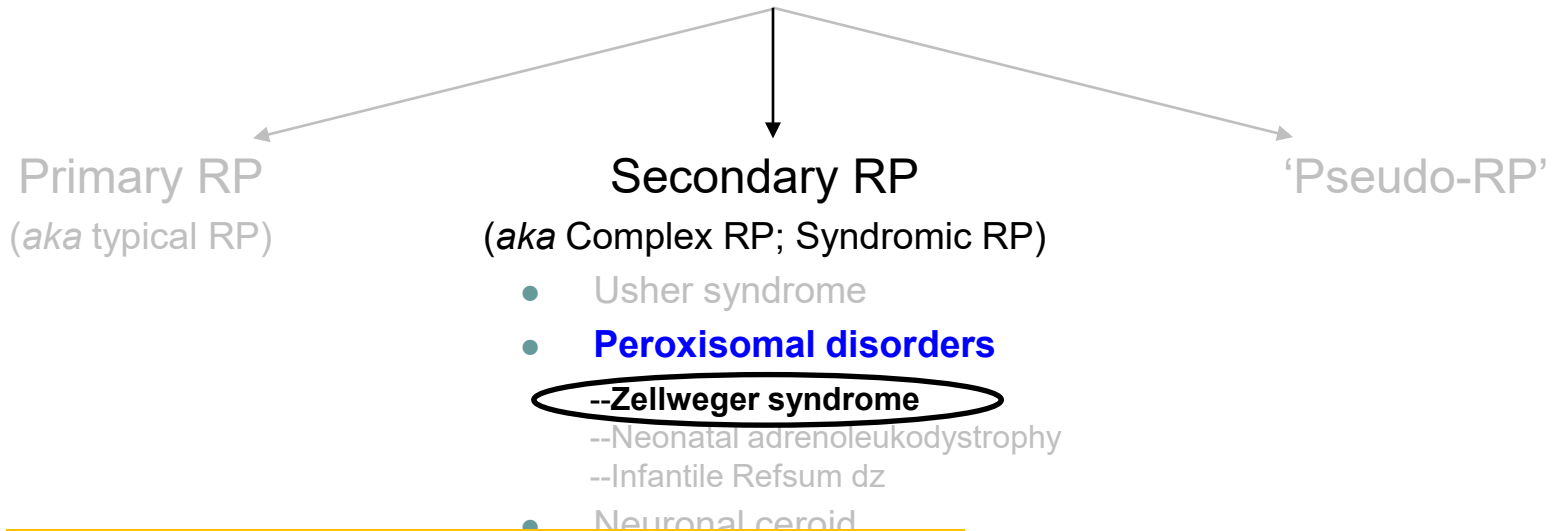
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DDx for an RP-like Fundus



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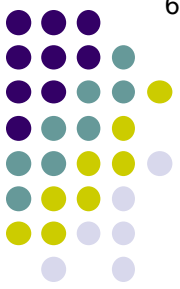
What is its inheritance pattern?
AR

How do Zellweger syndrome pts present?
In the **neonatal** period with:
 --RP-like fundus
 --Deafness
 --Hypotonia
 --Seizures
 --Abnormal facies (high forehead; hypertelorism)

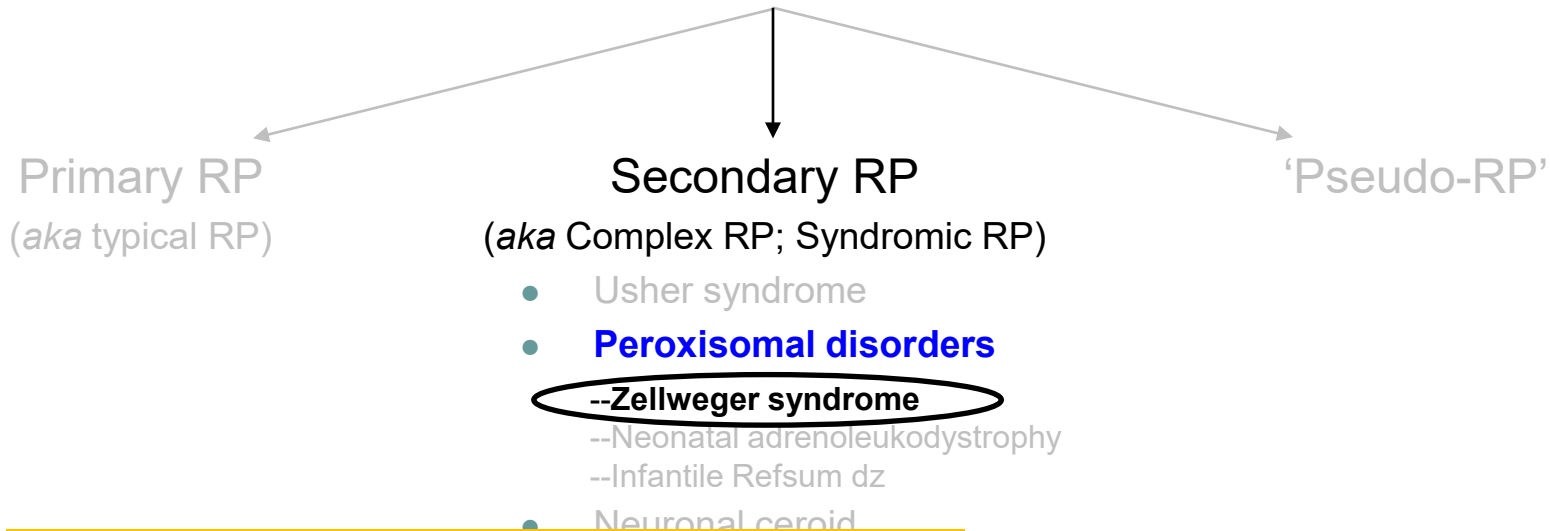
DDx for an RP-like Fundus



Zellweger syndrome facies: High forehead; hypertelorism



DDx for an RP-like Fundus



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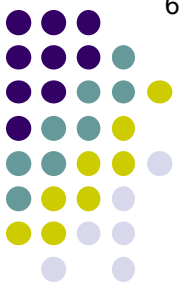
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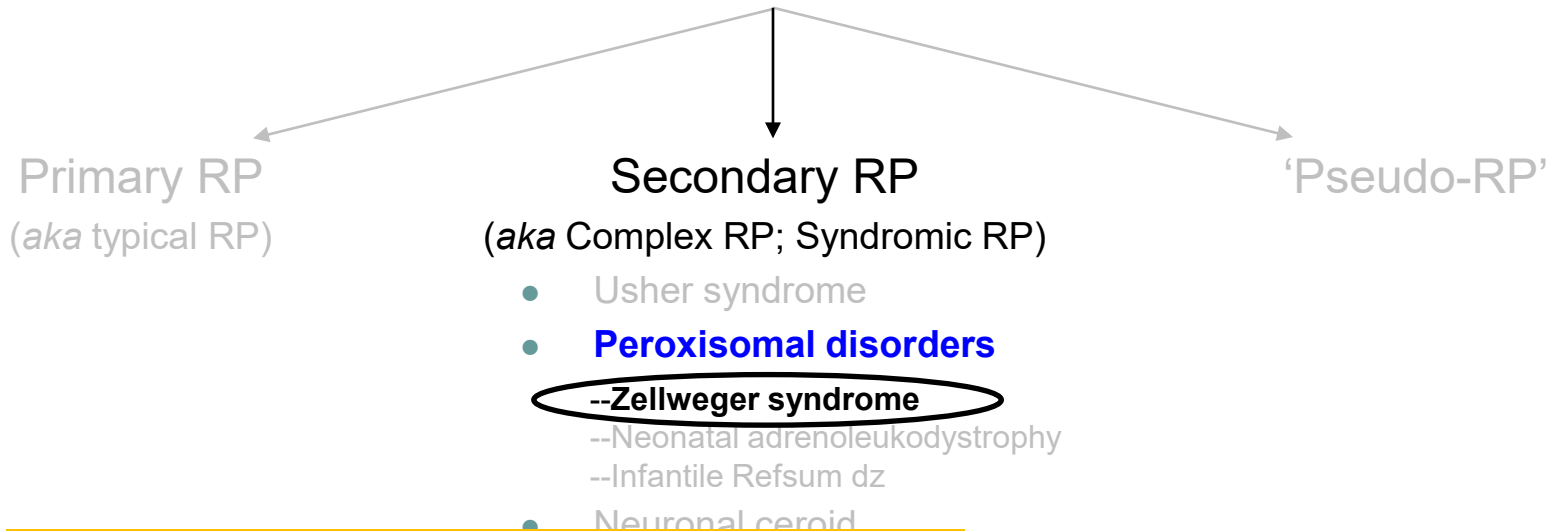
In the **neonatal** period with:

- RP-like fundus
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What is the prognosis?



DDx for an RP-like Fundus



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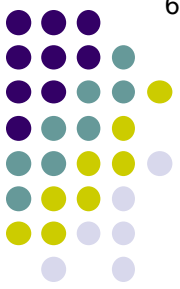
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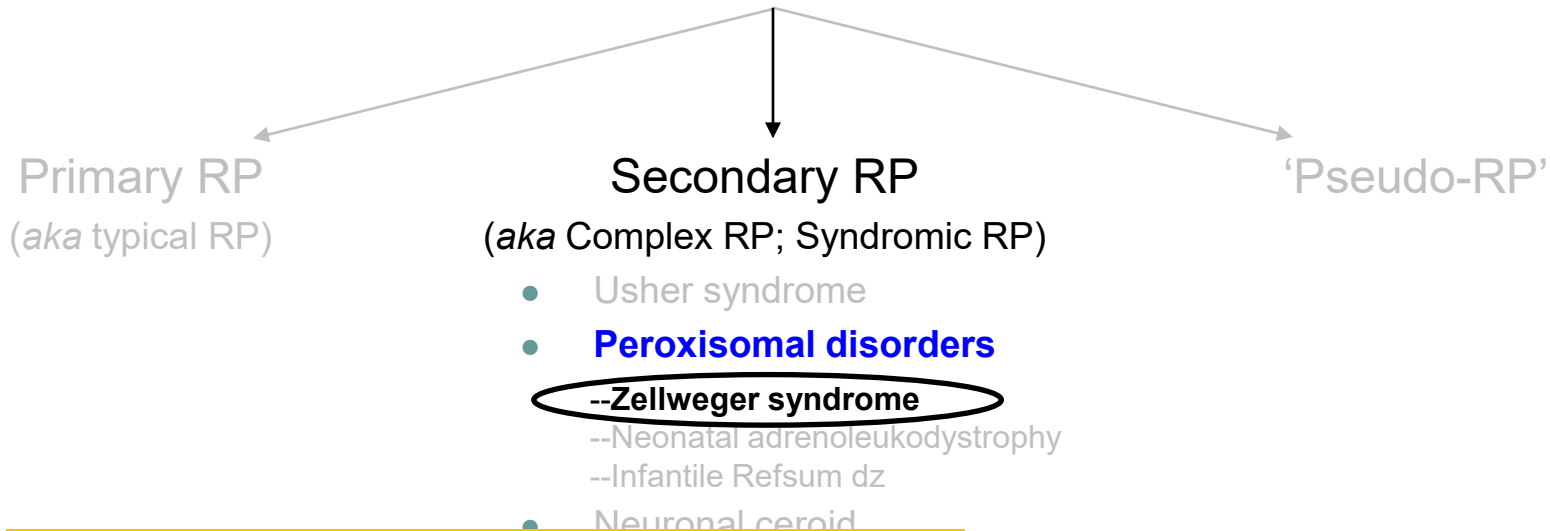
- RP-like fundus
- Deafness
- Hypotonia
- Seizures
- Abnormal facies (high forehead; hypertelorism)

What is the prognosis?

It is uniformly fatal by age 12



DDx for an RP-like Fundus

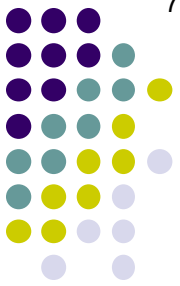


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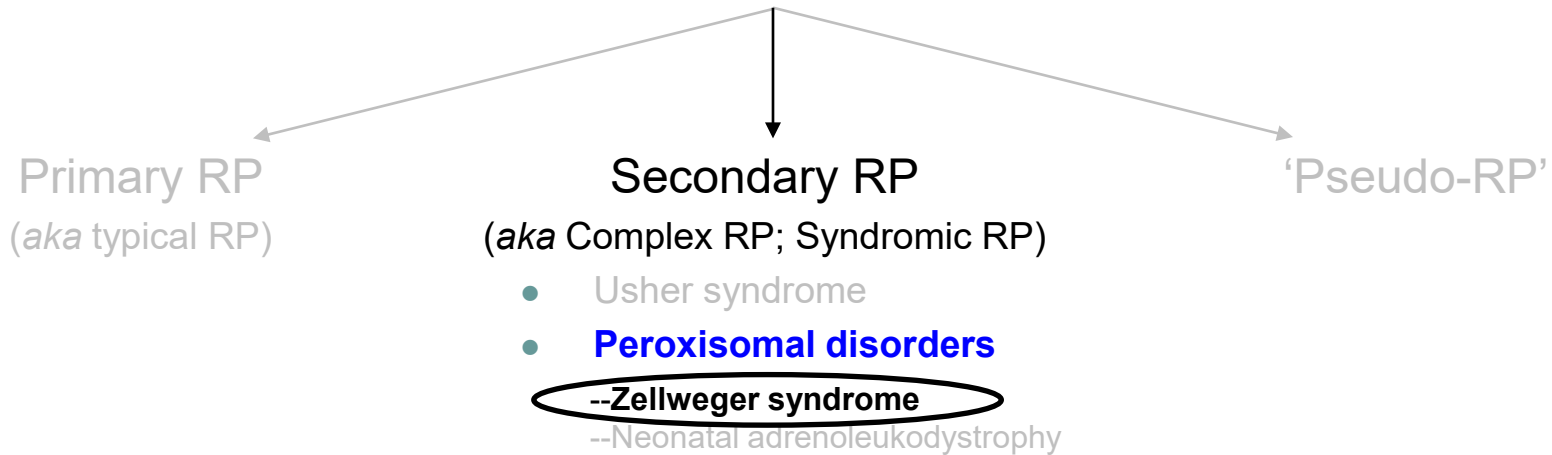
What is its inheritance pattern?
AR

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--Deafness
--Hypotonia
--Seizures
--Abnormal facies (high forehead; hypertelorism)

What is the prognosis?
It is uniformly fatal by age **1 year**



DDx for an RP-like Fundus



How is Zellweger syndrome diagnosed?

*What is the
Cerebrohepato-*

What is its inheritance pattern?
AR

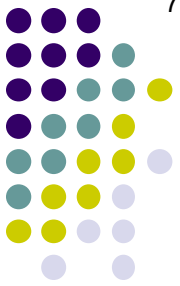
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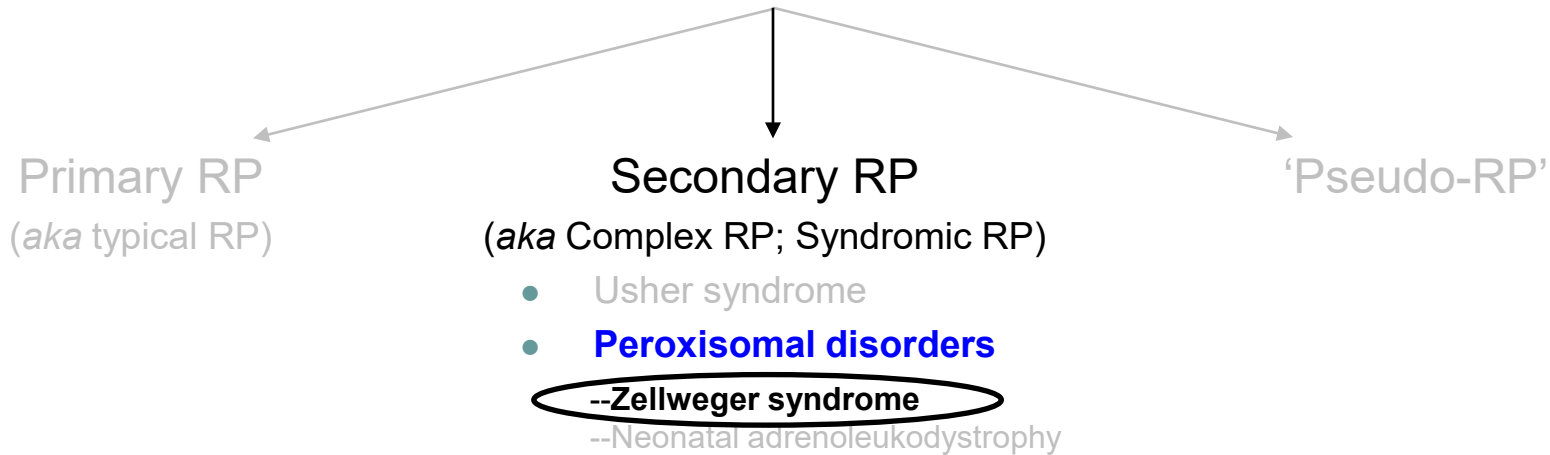
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- Deafness
- Hypotonia
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- Abnormal facies (high forehead; hypertelorism)

What is the prognosis?

It is uniformly fatal by age **1 year**



DDx for an RP-like Fundus



How is Zellweger syndrome diagnosed?

By the constellation of findings (along with elevated levels of VLCFA in the blood)

*What is the
Cerebrohepato-*

What is its inheritance pattern?
AR

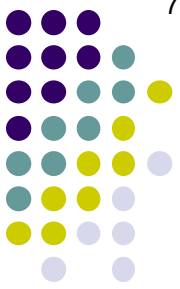
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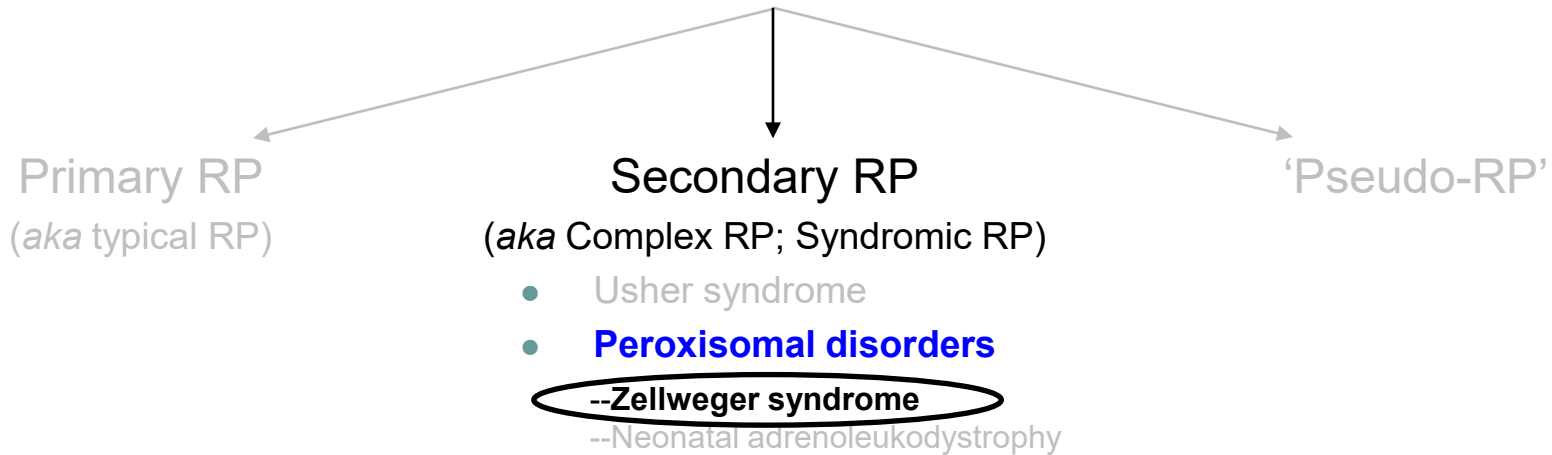
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DDx for an RP-like Fundus



How is Zellweger syndrome diagnosed?

By the constellation of findings (along with elevated levels of VLCFA in the blood)

How is Zellweger managed?

*What is the
Cerebrohepato-*

What is its inheritance pattern?
AR

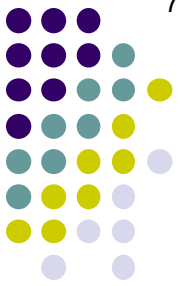
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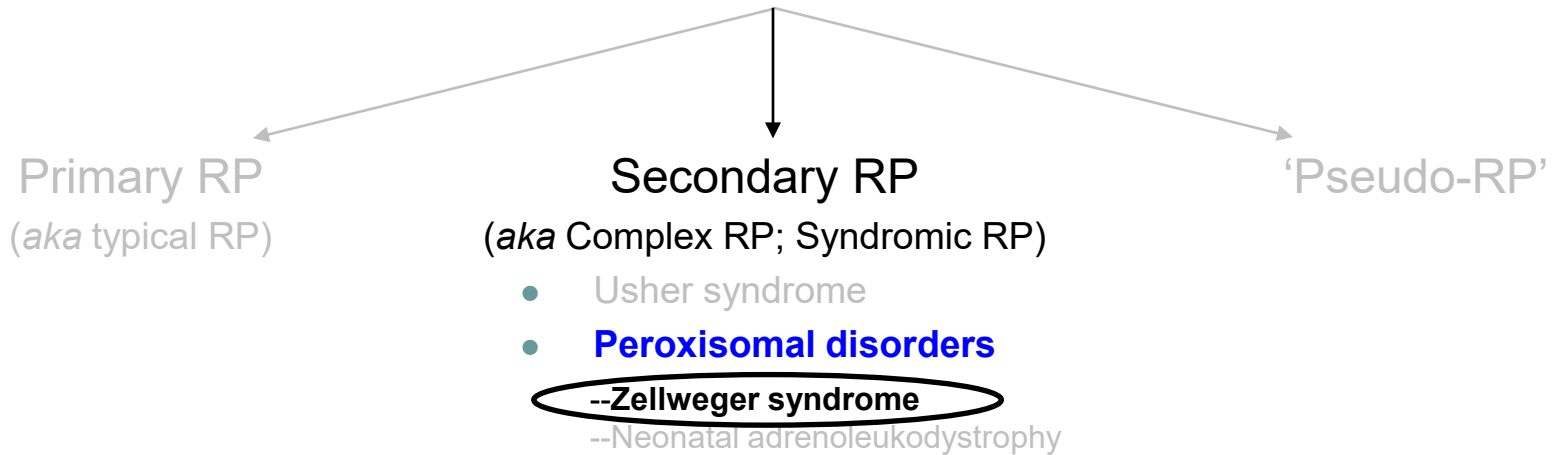
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What is the prognosis?

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DDx for an RP-like Fundus



How is Zellweger syndrome diagnosed?

By the constellation of findings (along with elevated levels of VLCFA in the blood)

How is Zellweger managed?

Supportively

What is the

Cerebrohe

What is its inheritance pattern?

AR

How do Zellweger syndrome pts present?

In the **neonatal** period with:

--RP-like fundus

--Deafness

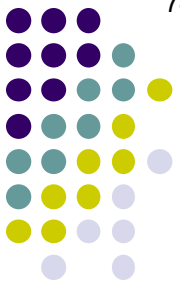
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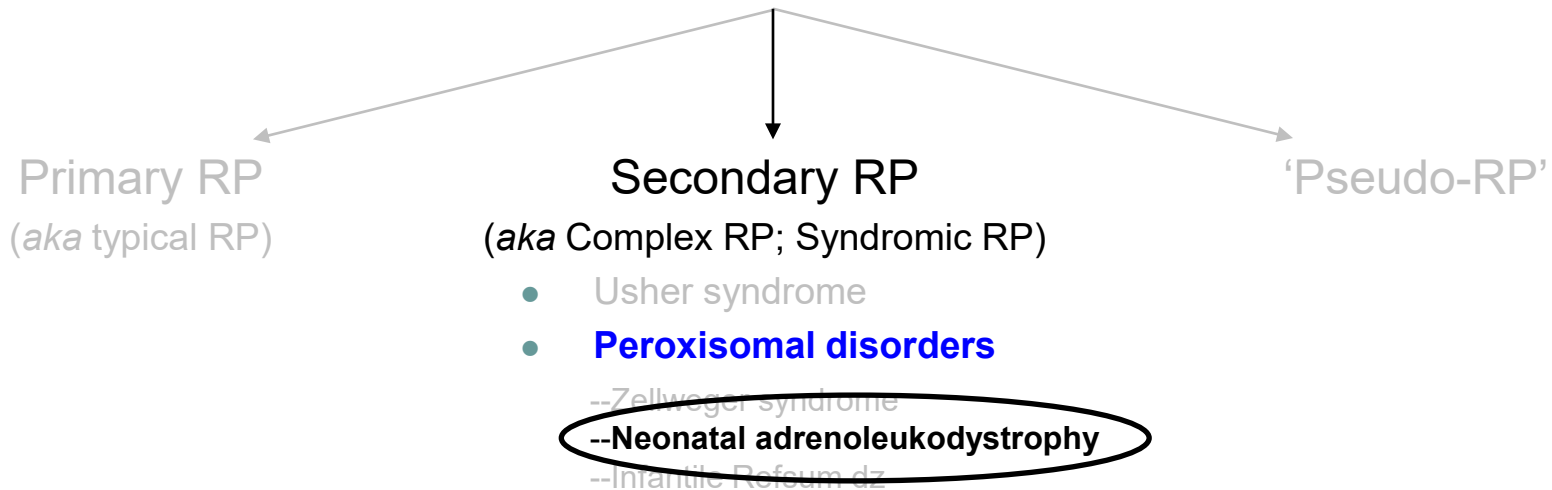
--Abnormal facies (high forehead; hypertelorism)

What is the prognosis?

It is uniformly fatal by age **1 year**



DDx for an RP-like Fundus



What is the nonet
Cerebrohepatorenal

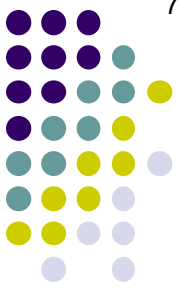
What is its inheritance
AR

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In the **neonatal** p
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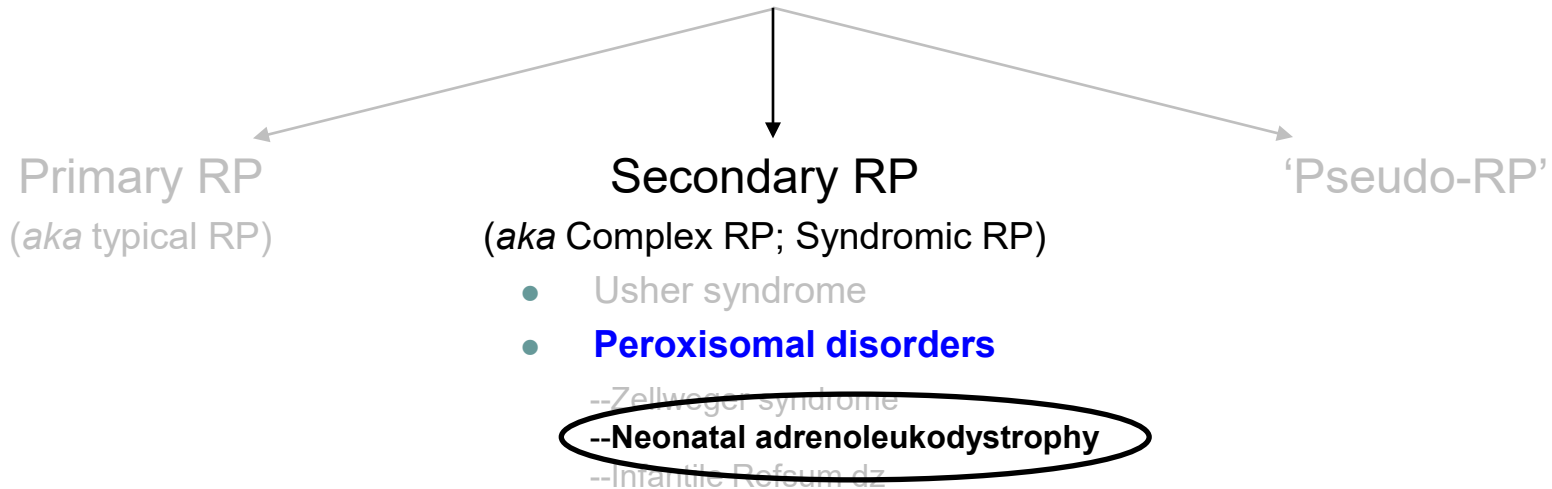
What is the prognosis

It is uniformly fatal by age **1 year**

Is NALD the same condition as adrenoleukodystrophy?



DDx for an RP-like Fundus



What is the nonexcessive
Cerebrohepatorenal

What is its inheritance?
AR

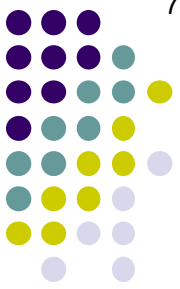
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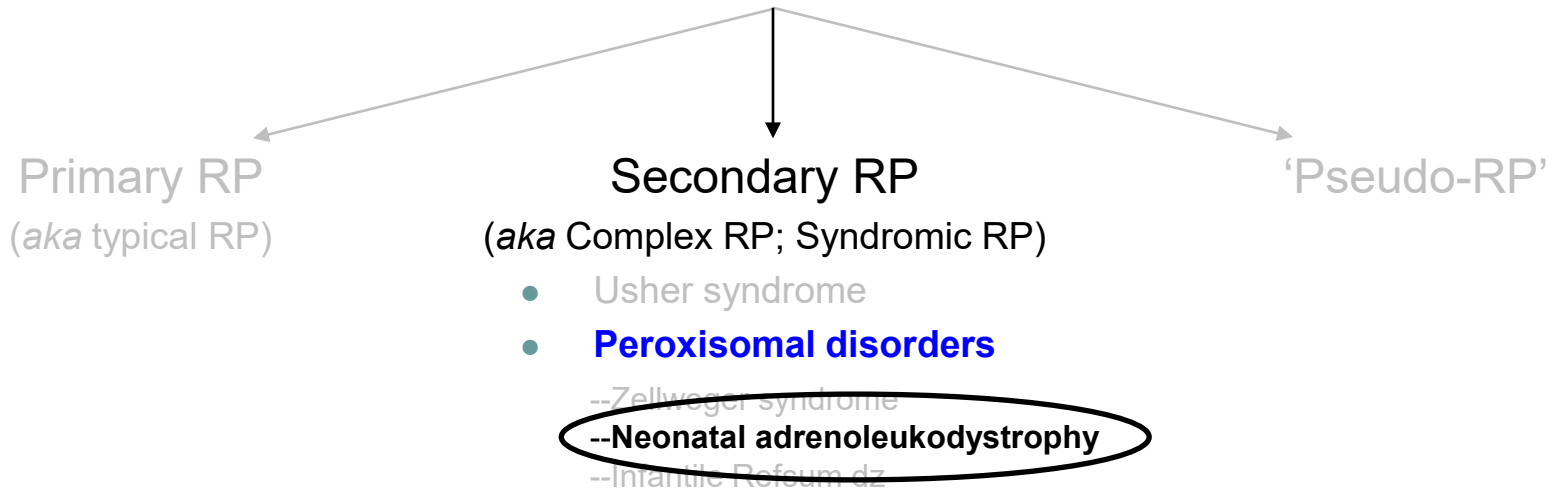
It is uniformly fatal by age **1 year**

Is NALD the same condition as adrenoleukodystrophy?

No, that is an X-linked condition that presents later in childhood



DDx for an RP-like Fundus



What is the nonep
Cerebrohepatoren

What is its inherita
AR

How do Zellweger
In the **neonatal** p
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies

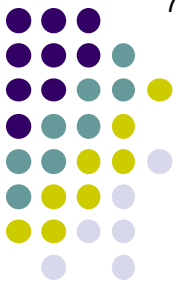
What is the progn

It is uniformly fatal by age **1 year**

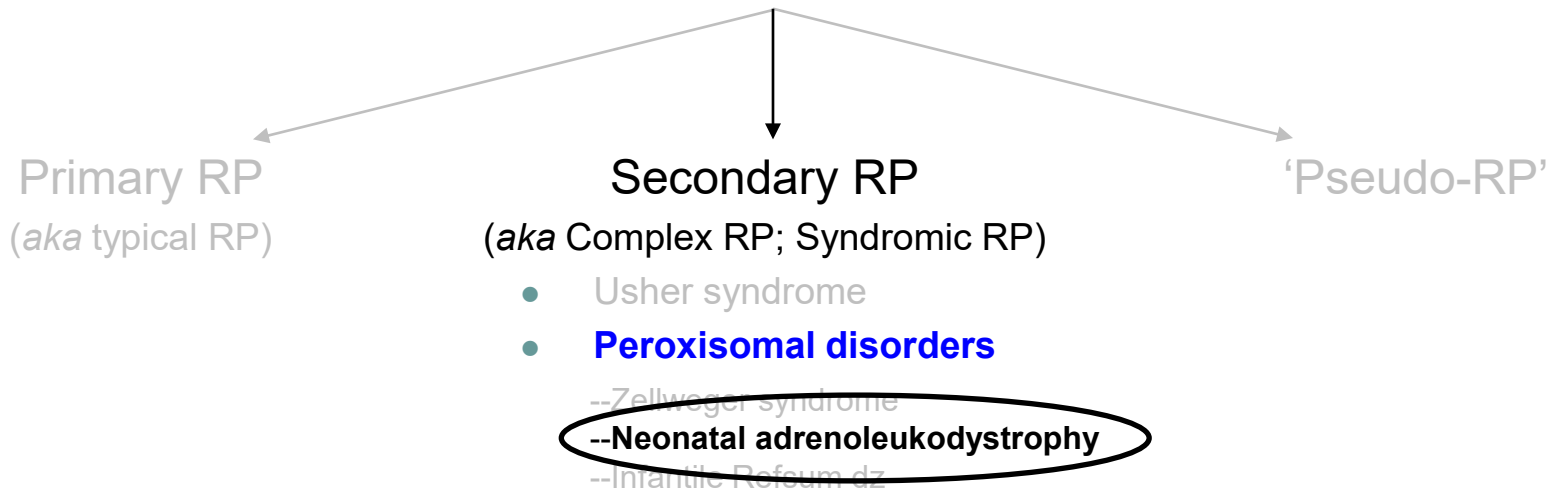
Is NALD the same condition as adrenoleukodystrophy?

No, that is an X-linked condition that presents later in childhood

What is its inheritance pattern?



DDx for an RP-like Fundus



What is the nonex...
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How do Zellweger...
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What is the progn...

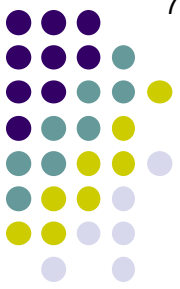
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Is NALD the same condition as adrenoleukodystrophy?

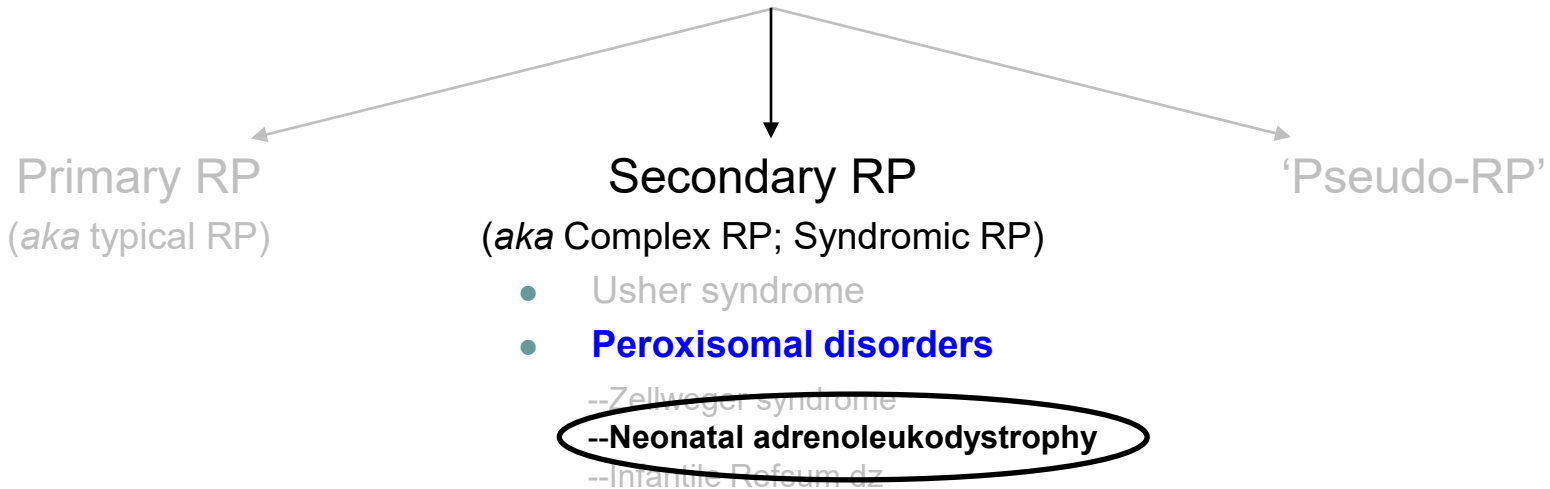
No, that is an X-linked condition that presents later in childhood

What is its inheritance pattern?

AR



DDx for an RP-like Fundus



What is the non-pigmented fundus?
Cerebrohepatorenal

Is NALD the same condition as adrenoleukodystrophy?

No, that is an X-linked condition that presents later in childhood

What is its inheritance?

AR

What is its inheritance pattern?

AR

Note: Both are inherited AR

How does Zellweger syndrome present?

In the neonatal period

--RP-like fundus

--Deafness

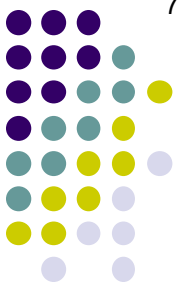
--Hypotonia

--Seizures

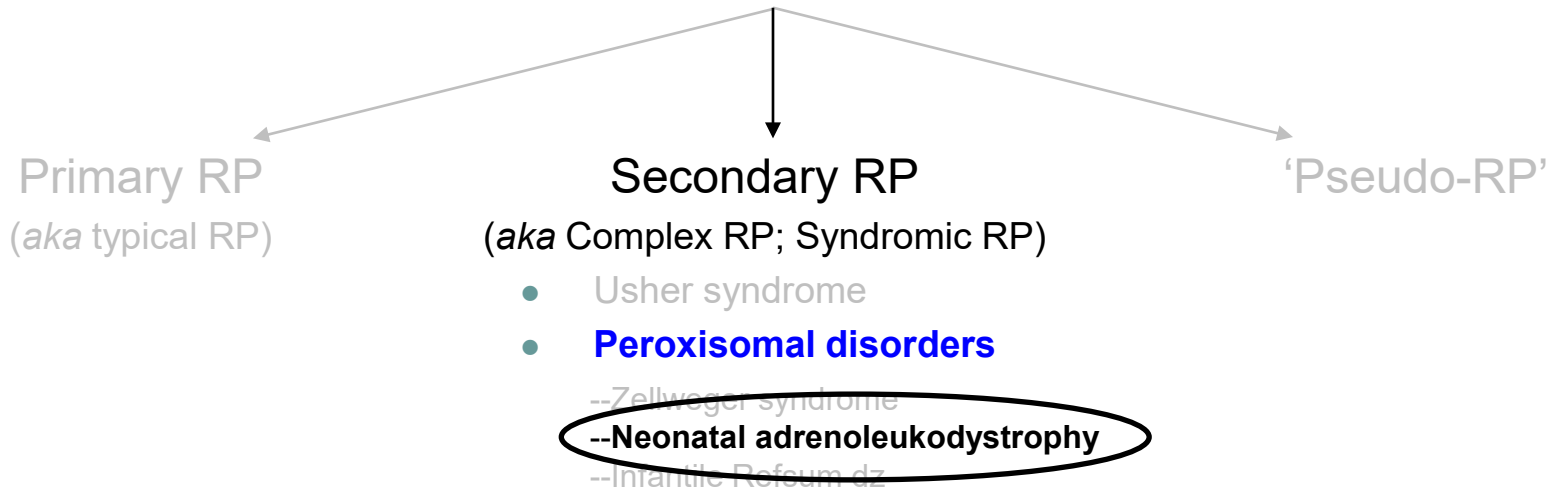
--Abnormal facies

What is the prognosis?

It is uniformly fatal by age 1 year



DDx for an RP-like Fundus



What is the nonet
Cerebrohepatorenal

What is its inheritance
AR

How do Zellweger
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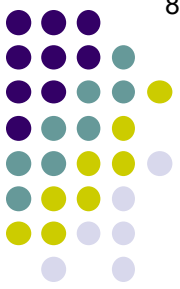
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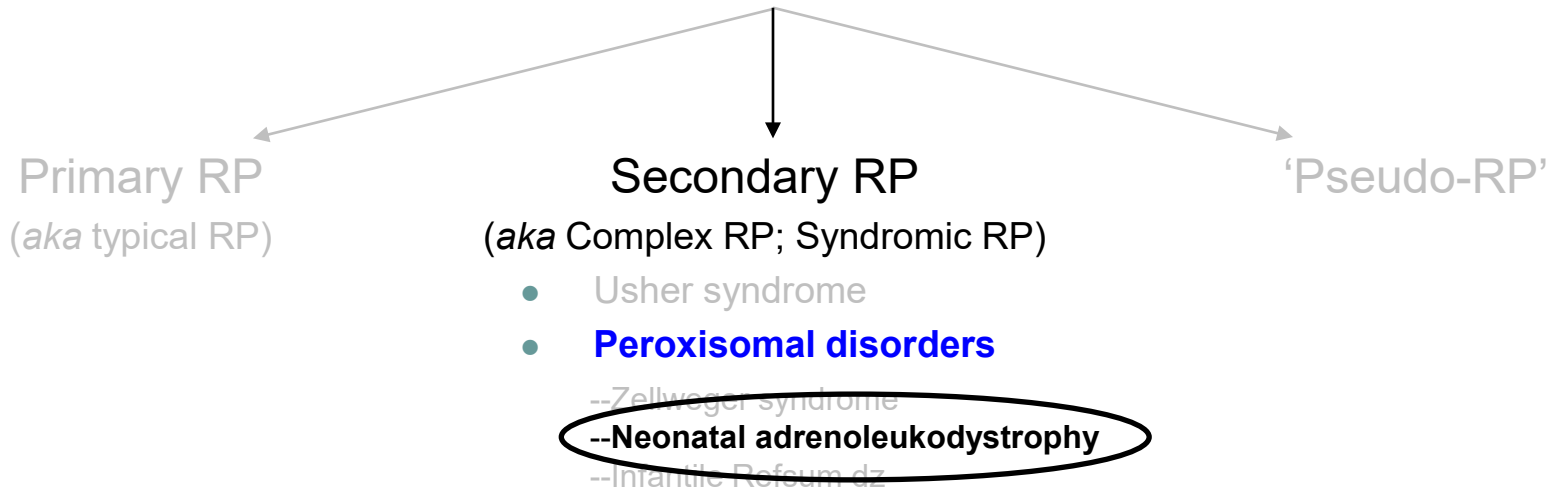
What is its inheritance pattern?

AR

How do NALD pts present?



DDx for an RP-like Fundus



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Cerebrohepatorenal

What is its inheritance
AR

How do Zellweger
In the neonatal p

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--Hypotonia
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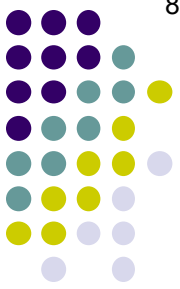
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What is its inheritance pattern?

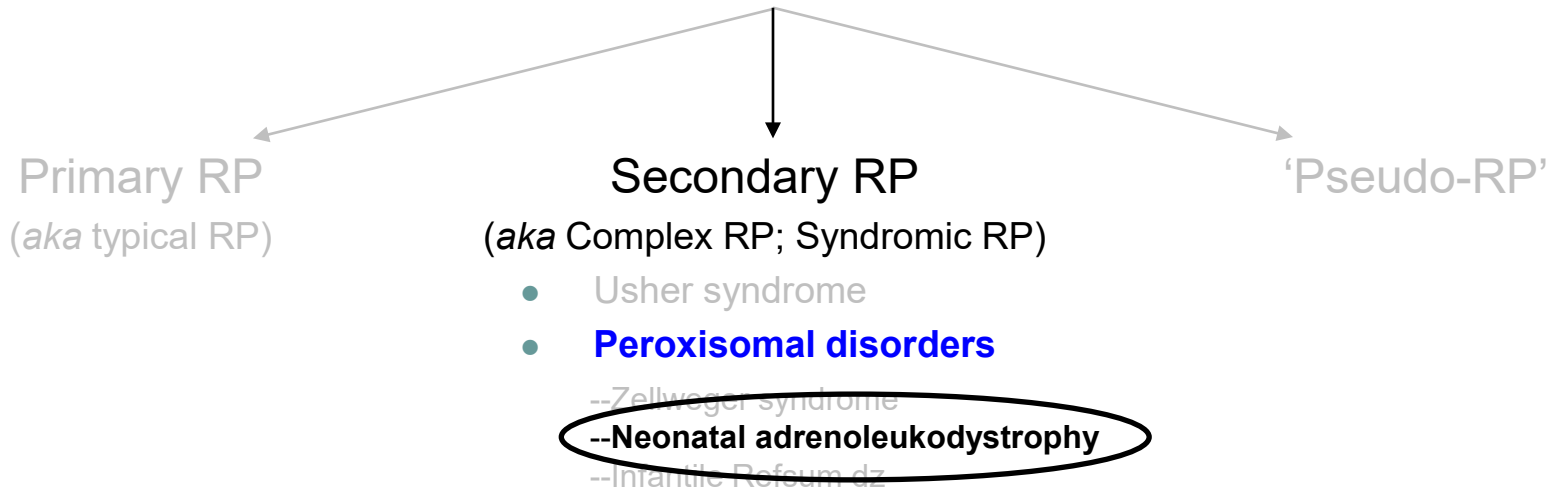
AR

How do NALD pts present?

In the 'age' period



DDx for an RP-like Fundus



What is the nonex...
Cerebrohepatoren...

What is its inherita...
AR

How do Zellweger...
In the **neonatal** p...
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies

What is the progn...

It is uniformly fatal by age **1 year**

Is NALD the same condition as adrenoleukodystrophy?

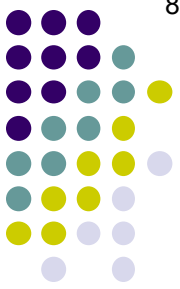
No, that is an X-linked condition that presents later in childhood

What is its inheritance pattern?

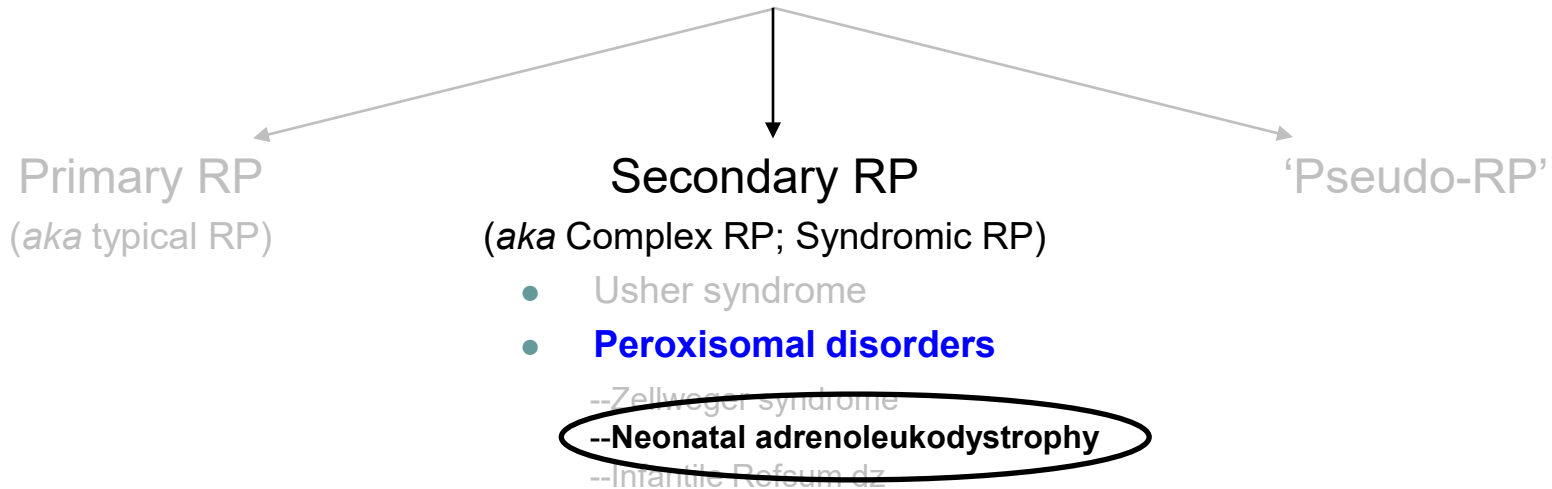
AR

How do NALD pts present?

In the **late infancy** period



DDx for an RP-like Fundus



What is the nonep...
Cerebrohepatoren...

What is its inherita...
AR

How do Zellweger...
In the **neonatal** period
--RP-like fundus

Is NALD the same condition as adrenoleukodystrophy?

No, that is an X-linked condition that presents later in childhood

What is its inheritance pattern?
AR

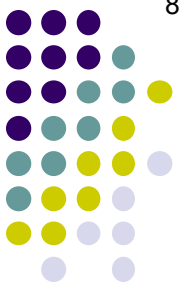
How do NALD pts present?
In the **late infancy** period

Note: NALD's onset occurs a little later than does Zellweger's

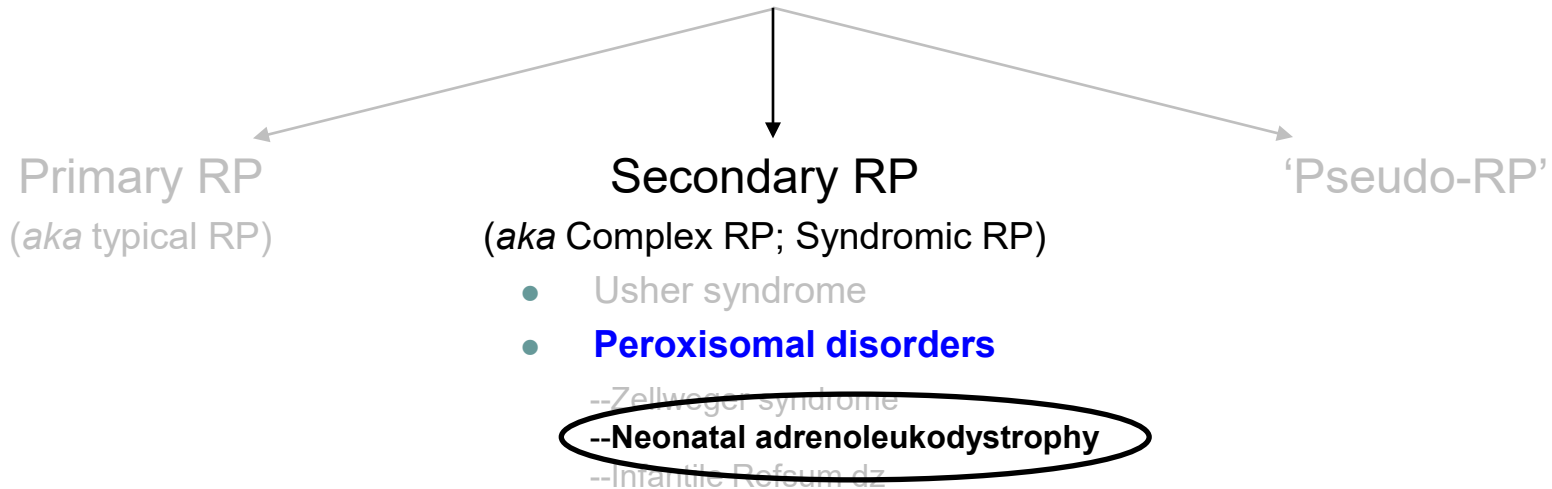
--Hypotonia
--Seizures
--Abnormal facies

What is the progn...

It is uniformly fatal by age **1 year**



DDx for an RP-like Fundus



What is the nonexcessive
Cerebrohepatorenal

What is its inheritance
AR

How do Zellweger
In the **neonatal** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies

What is the prognosis

It is uniformly fatal by age **1 year**

Is NALD the same condition as adrenoleukodystrophy?

No, that is an X-linked condition that presents later in childhood

What is its inheritance pattern?

AR

How do NALD pts present?

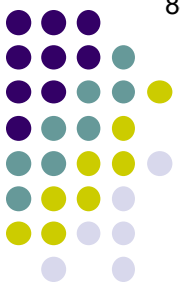
In the **late infancy** period with:

--RP-like fundus

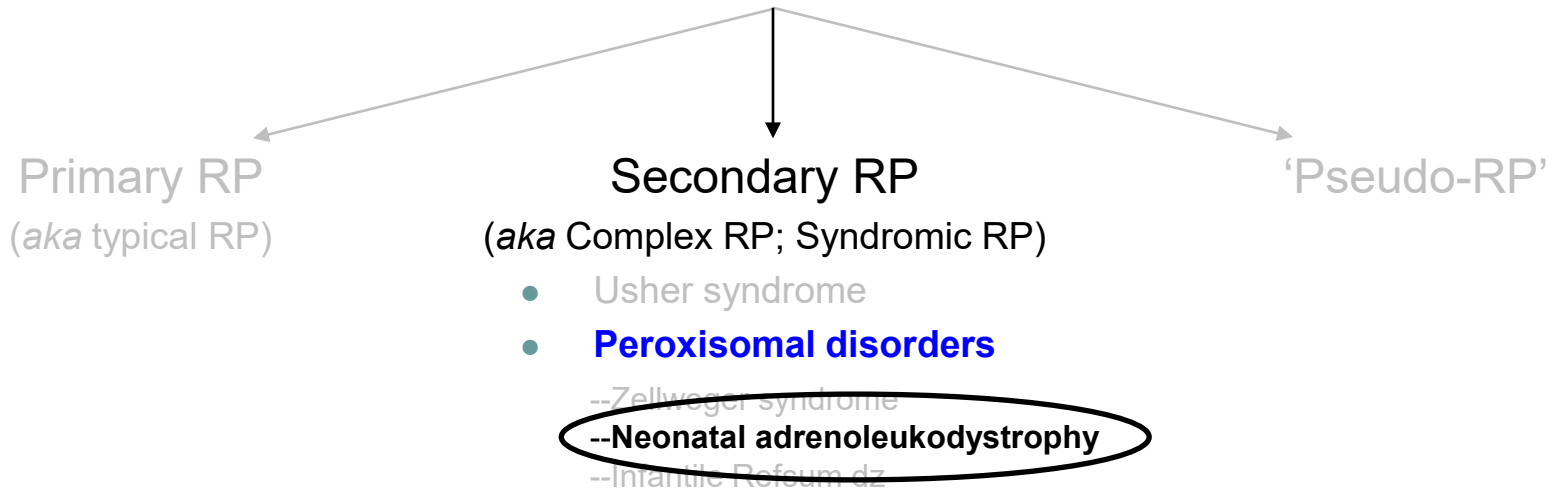
--?

--?

--?



DDx for an RP-like Fundus



What is the nonexcessive
Cerebrohepatorenal

What is its inheritance
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How do Zellweger
In the **neonatal** period
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--Seizures
--Abnormal facies

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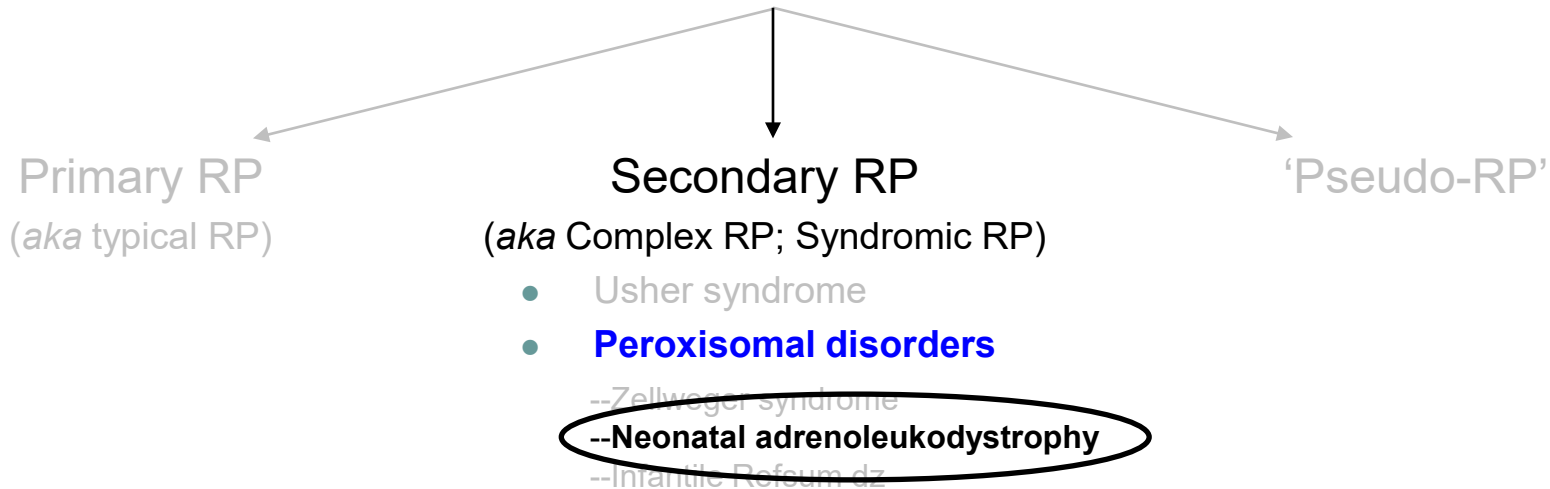
AR

How do NALD pts present?

In the **late infancy** period with:

- RP-like fundus
- Deafness
- Hypotonia
- Seizures

DDx for an RP-like Fundus



What is the nonep
Cerebrohepatoren

Is NALD the same condition as adrenoleukodystrophy?

No, that is an X-linked condition that presents later in childhood

What is its inherita
AR

What is its inheritance pattern?

AR

Note that NALD has the same S/S as Zellweger, except it's missing the last one on the list

In the neonatal p

--RP-like fundus

--RP-like fundus

--Deafness

--Deafness

--Hypotonia

--Hypotonia

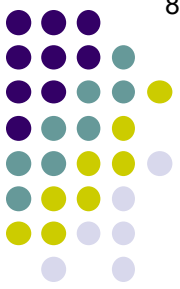
--Seizures

--Seizures

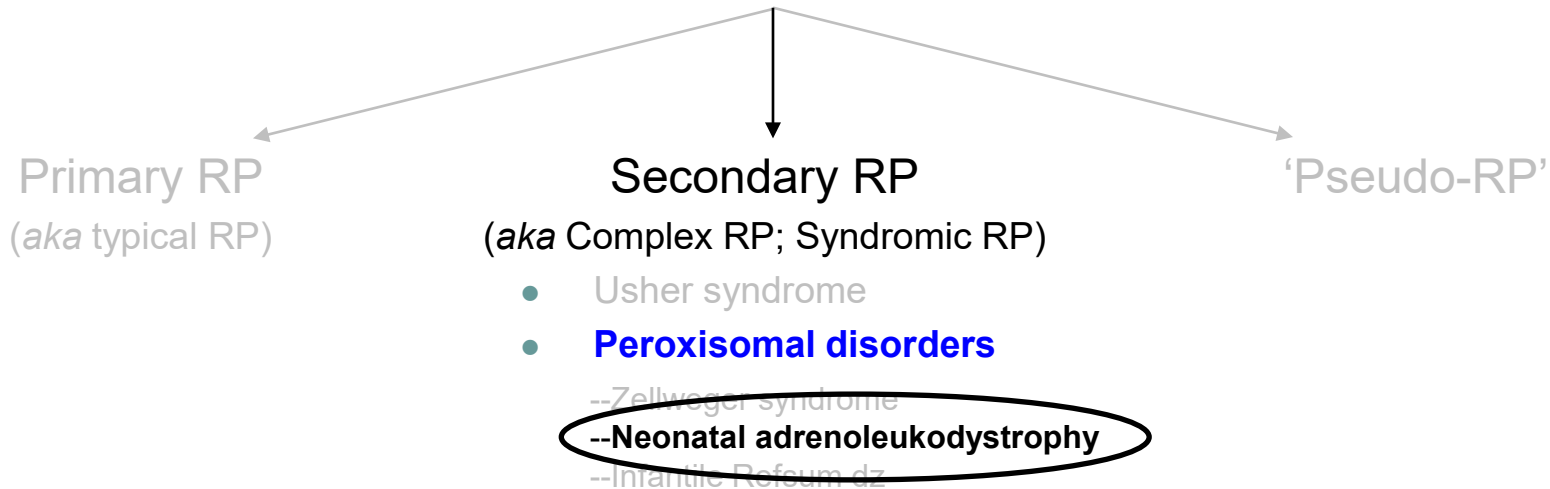
--Abnormal facies

What is the progn

It is uniformly fatal by age 1 year



DDx for an RP-like Fundus



What is the nonet
Cerebrohepatorenal

What is its inheritance
AR

How do Zellweger
In the **neonatal** p
--RP-like fundus
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--Abnormal facies

What is the progn
It is uniformly fatal by age **1 year**

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No, that is an X-linked condition that presents later in childhood

What is its inheritance pattern?

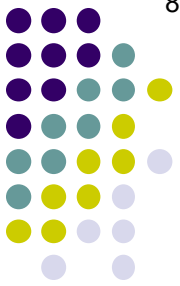
AR

How do NALD pts present?

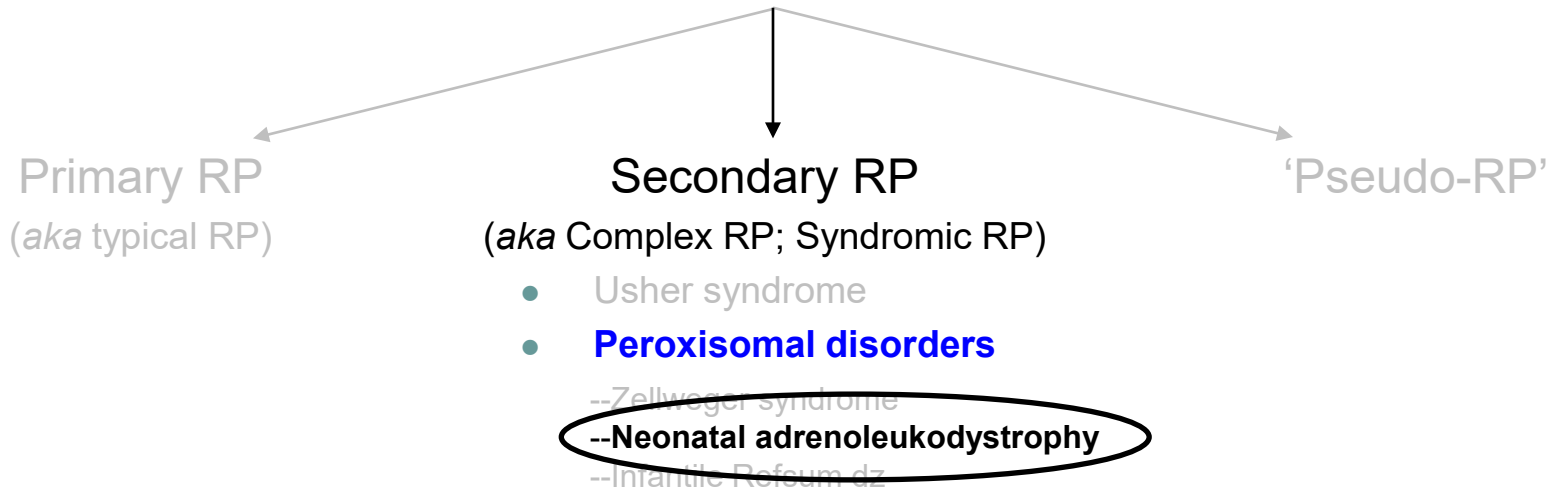
In the **late infancy** period with:

--RP-like fundus
--Deafness
--Hypotonia
--Seizures

What is the prognosis?



DDx for an RP-like Fundus



What is the nonep...
Cerebrohepatoren...

What is its inherita...
AR

How do Zellweger...
In the **neonatal** p...
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies

What is the progn...
It is uniformly fatal by age **1 year**

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What is its inheritance pattern?

AR

How do NALD pts present?

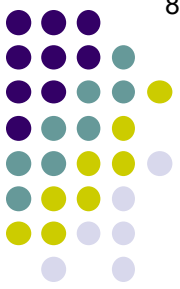
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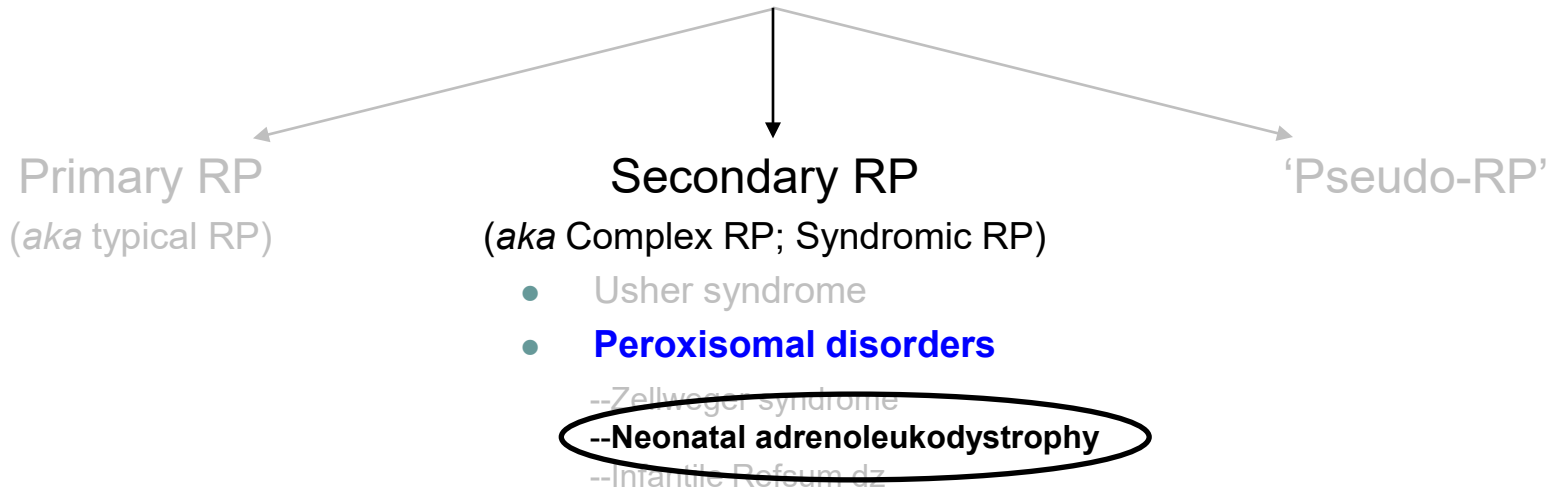
What is the prognosis?

It is uniformly fatal by





DDx for an RP-like Fundus



What is the nonep...
Cerebrohepatoren...

What is its inherita...
AR

How do Zellweger...
In the **neonatal** p...
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies

What is the progn...
It is uniformly fatal by age **1 year**

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AR

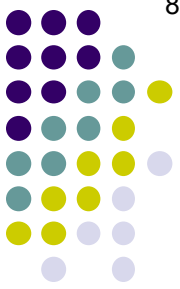
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In the **late infancy** period with:

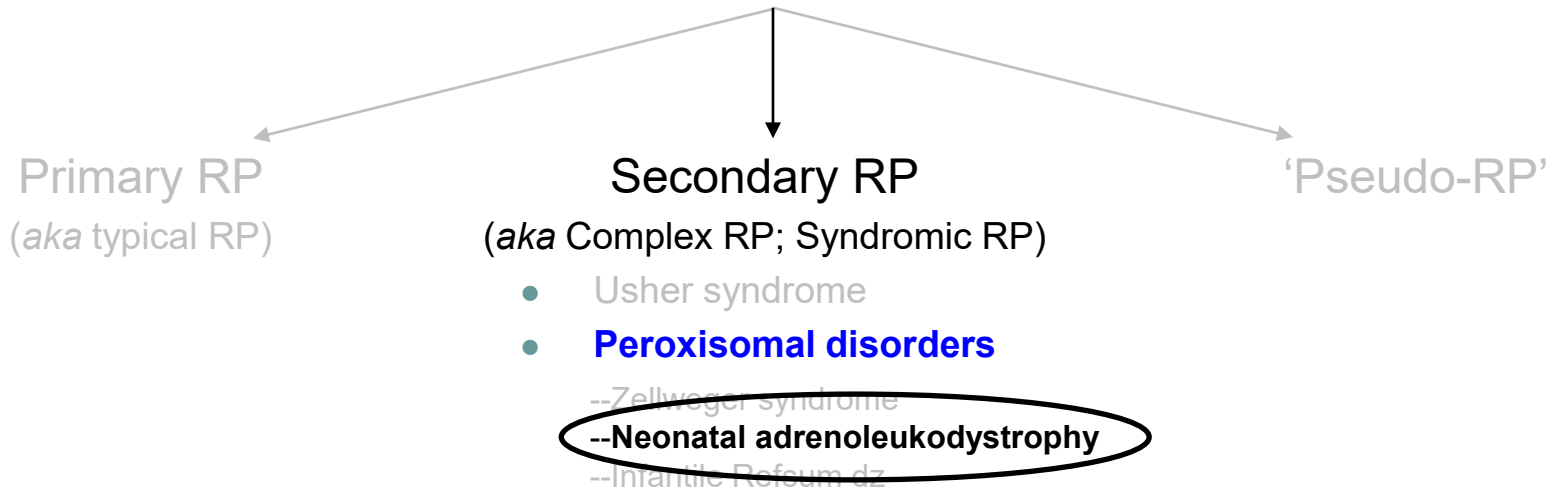
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

What is the prognosis?

It is uniformly fatal by **late childhood**



DDx for an RP-like Fundus



What is the nonet
Cerebrohepatorenal

What is its inheritance
AR

How do Zellweger
In the **neonatal** p
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal

What is the prognosis
It is uniformly

Is NALD the same condition as adrenoleukodystrophy?

No, that is an X-linked condition that presents later in childhood

What is its inheritance pattern?

AR

How do NALD pts present?

In the **late infancy** period with:

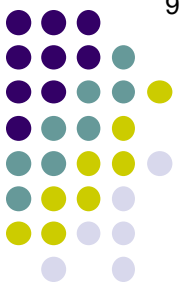
--RP-like fundus
--Deafness
--Hypotonia

And albeit dreadful, the prognosis for NALD is better than that for Zellweger

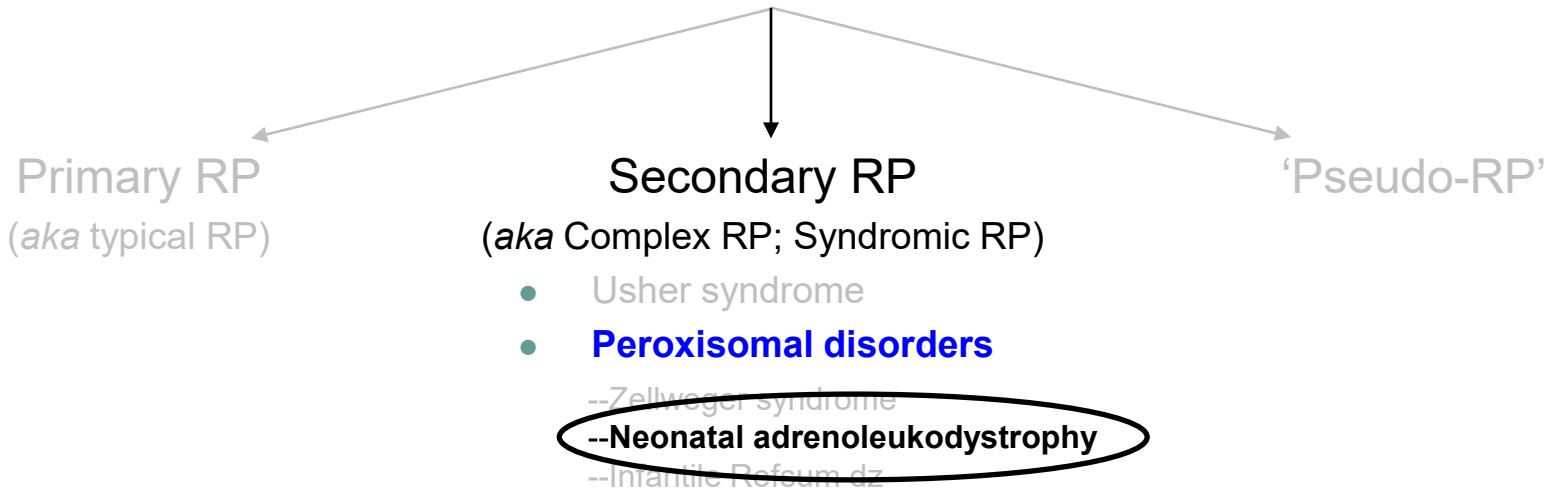
What is the prognosis?

It is uniformly **fatal by late childhood**

fatal by age 1 year



DDx for an RP-like Fundus



What is the nonep
Cerebrohepatoren

Is NALD the same condition as adrenoleukodystrophy?

No, that is an X-linked condition that presents later in childhood

What is its inherita
AR

What is its inheritance pattern?

So NALD and Zellweger are quite similar, except that NALD is a somewhat milder condition:

How do Z

--Later onset

In the ne

--One fewer S/S (= no abnormal facies)

--RP-like

--Pts live a little longer

--Deafness

--Hypotonia

--Hypotonia

--Seizures

--Seizures

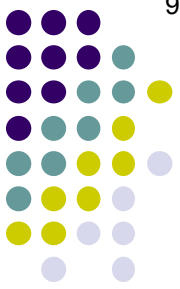
--Abnormal facies

What is the prognosis?

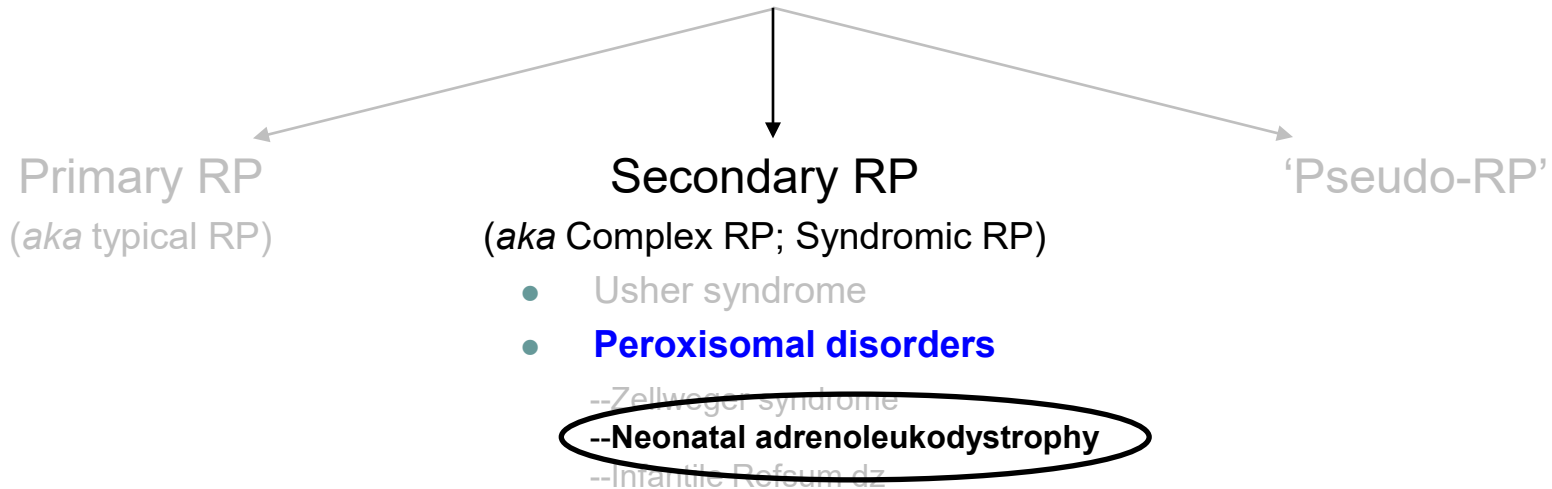
It is uniformly fatal by **late childhood**

What is the progn

It is uniformly fatal by age **1 year**



DDx for an RP-like Fundus



Why does neonatal ADRENOleukodystrophy have adreno- in the name?

What is the
Cerebrohe

What is its
AR

How do Ze
In the neo

--RP-like fu
--Deafness

--Hypotonia
--Seizures

--Abnormal facies

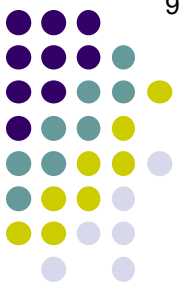
What is the progn

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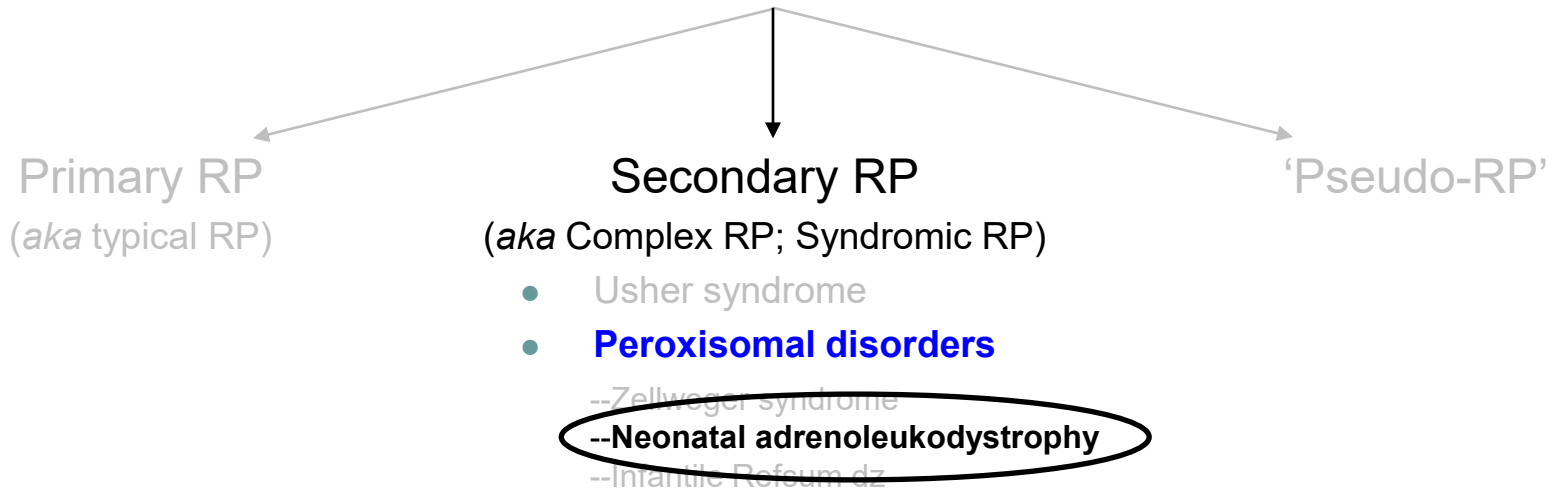
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DDx for an RP-like Fundus



Why does neonatal ADRENOleukodystrophy have adreno- in the name?

In NALD, the VLCFAs impair the function of adrenal glands by compromising the integrity of adrenal-cell membranes

What is the
Cerebrohe

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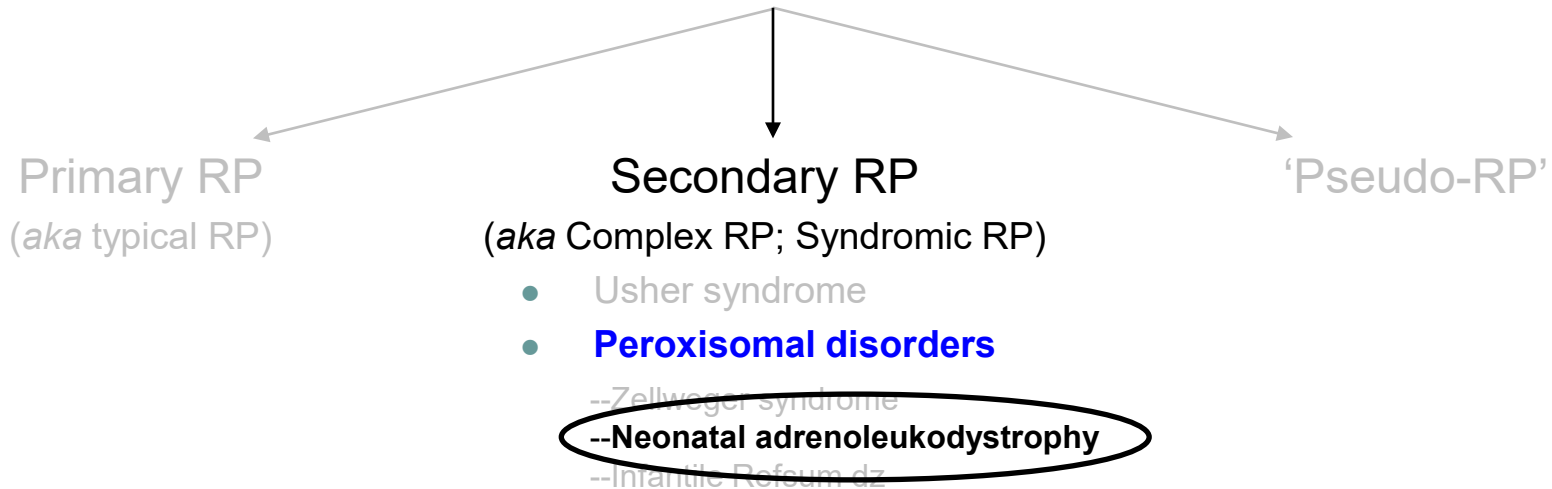
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DDx for an RP-like Fundus



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- Hypotonia
- Seizures

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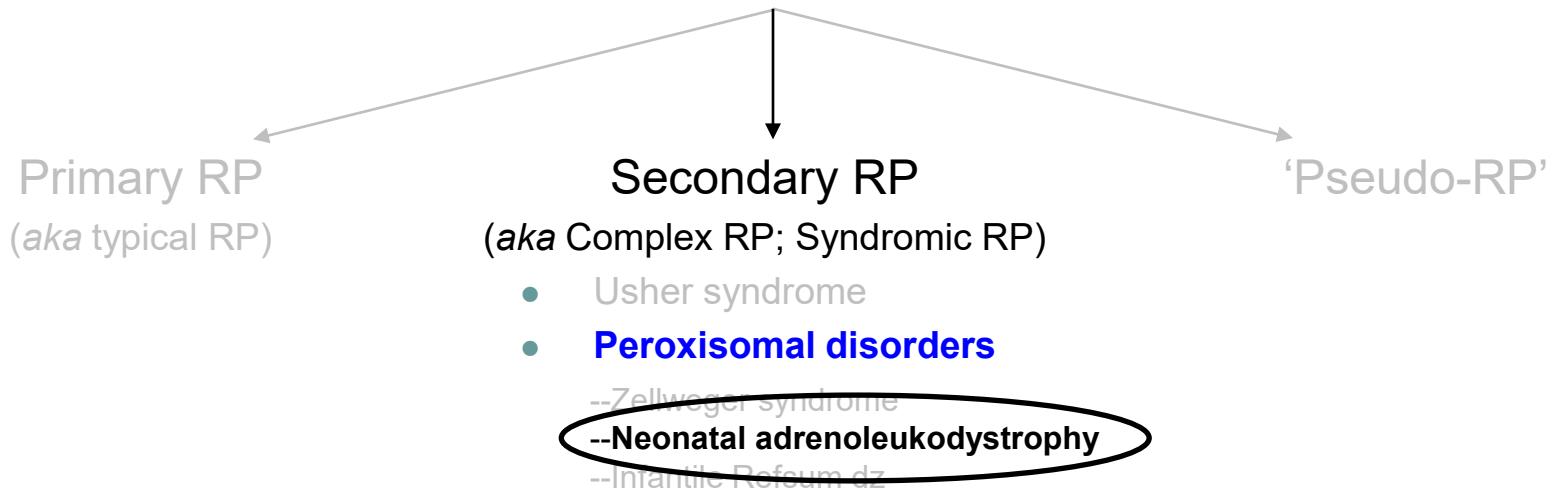
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How is NALD diagnosed?

Via its clinical presentation, coupled with MRI of the brain revealing gross white-matter abnormalities, and the elevated serum VLCFAs

- Hypotonia
- Seizures

What is the prognosis?

It is uniformly fatal by **late childhood**

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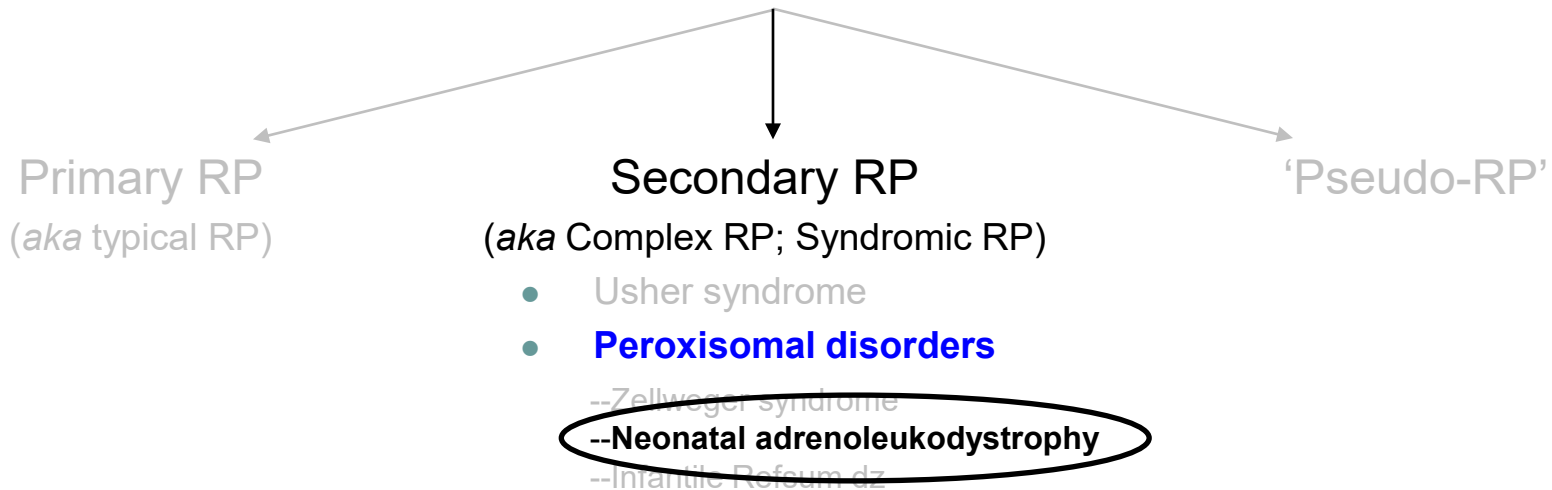
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- Hypotonia
- Seizures

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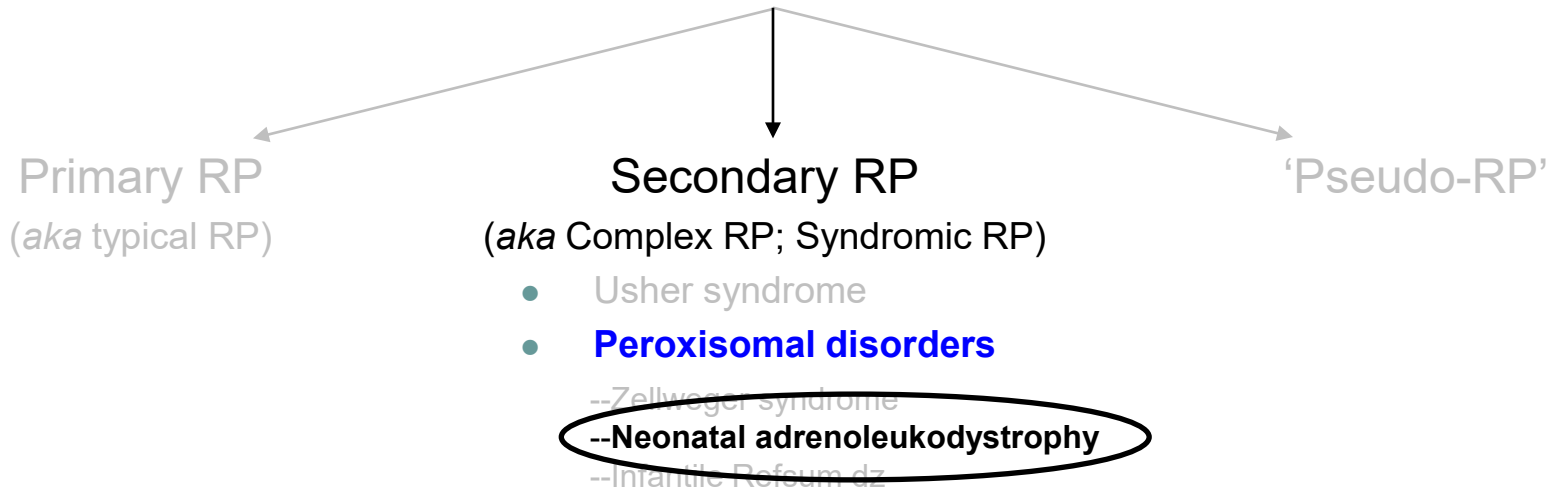
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How is NALD diagnosed?

Via its clinical presentation, coupled with MRI of the brain revealing gross white-matter abnormalities, and the elevated serum VLCFAs

How is NALD managed?

Supportively (just like Zellweger)

--Hypotonia

--Seizures

What is the prognosis?

It is uniformly fatal by **late childhood**

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Cerebrohe

What is its
AR

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In the neo

--RP-like fu

--Deafness

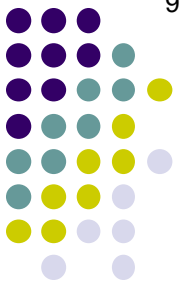
--Hypotonia

--Seizures

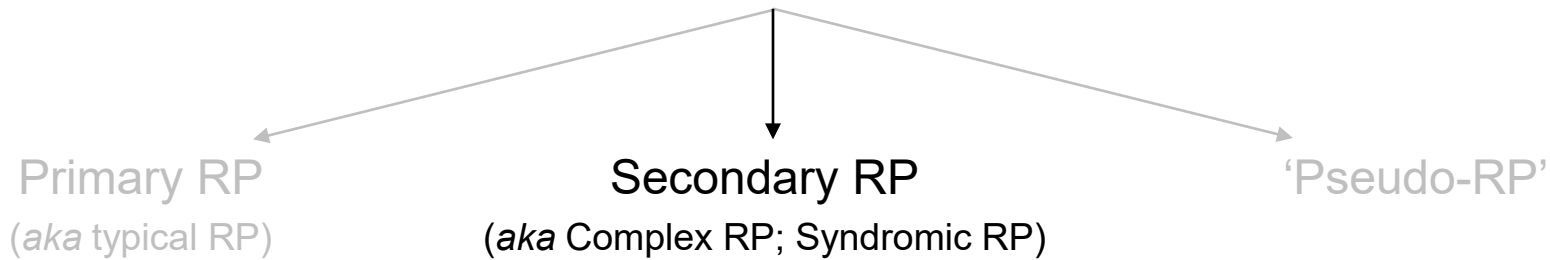
--Abnormal facies

What is the progn

It is uniformly fatal by age **1 year**



DDx for an RP-like Fundus



- Usher syndrome
- **Peroxisomal disorders**
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz** = adult-onset Refsum?

Is NALD the same condition as adrenoleukodystrophy?

Before we get into it: Is infantile Refsum dz the same as adult-onset Refsum dz?

What is its inheritance pattern?
AR

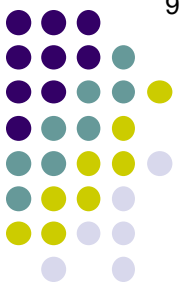
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--Seizures
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What is the prognosis?
It is uniformly fatal by age **1 year**

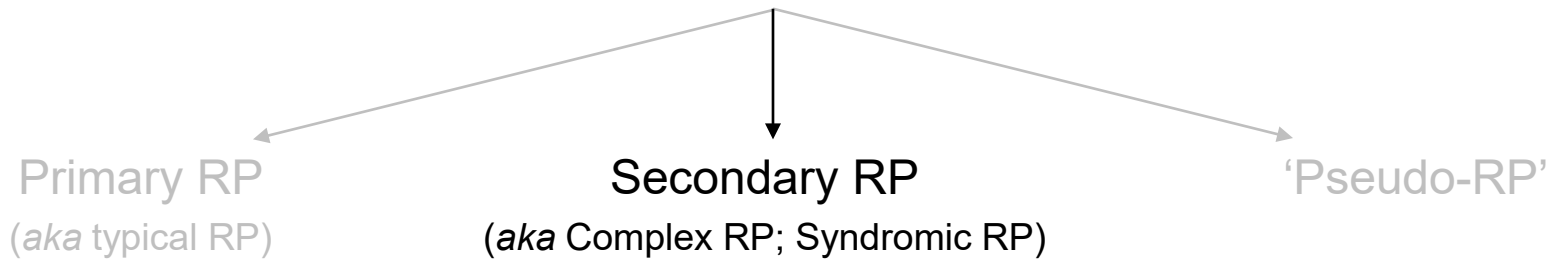
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How do NALD pts present?
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--RP-like fundus
--Deafness
--Hypotonia
--Seizures

What is the prognosis?
It is uniformly fatal by **late childhood**



DDx for an RP-like Fundus



- Usher syndrome
- **Peroxisomal disorders**
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz** = adult-onset Refsum? No!

Is NALD the same condition as adrenoleukodystrophy?

Before we get into it: Is infantile Refsum dz the same as adult-onset Refsum dz?
No

What is its inheritance pattern?
AR

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--Abnormal facies

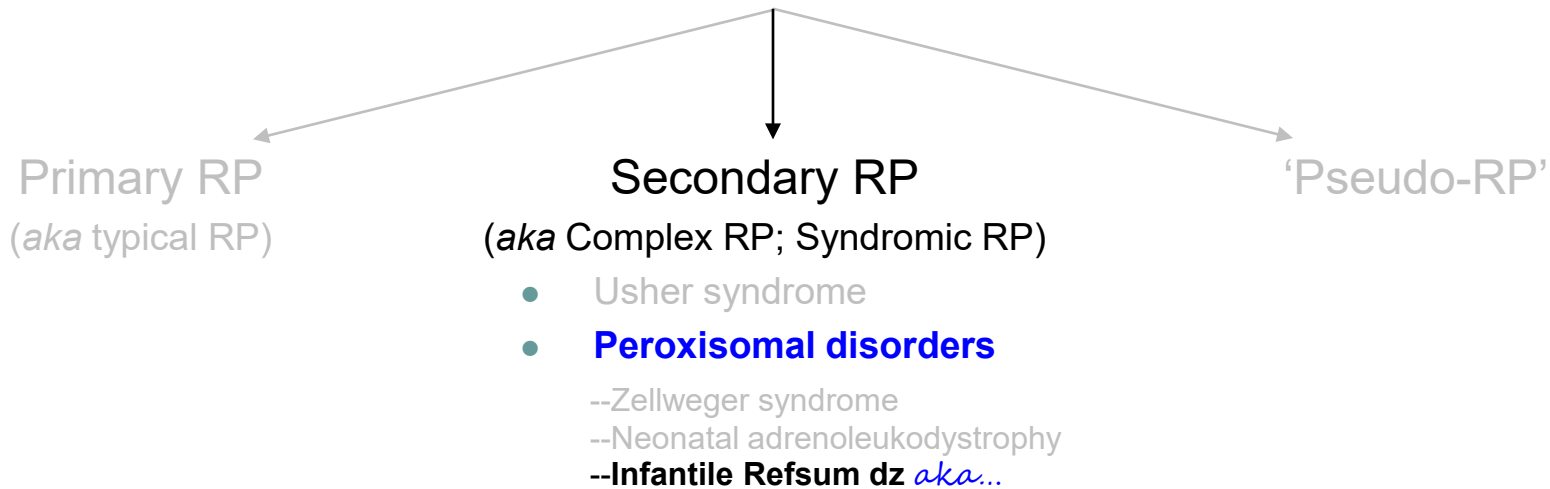
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--Seizures

What is the prognosis?
It is uniformly fatal by **late childhood**

DDx for an RP-like Fundus



What is the noneponymous name for NALD?
Cerebrohepato-renal disease

What is its inheritance?
AR

How do Zellweger pts present?
In the **neonatal** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies

What is the prognosis?
It is uniformly fatal by age **1 year**

Is NALD the same condition as NALD?
No, that is an X-linked condition

What is its inheritance?
AR

How do NALD pts present?
In the **late infancy** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

What is the prognosis?
It is uniformly fatal by **late childhood**

By what noneponymous name is infantile Refsum disease known?

DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP
(aka Complex RP; Syndromic RP)

- Usher syndrome
- **Peroxisomal disorders**
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

'Pseudo-RP'



What is the noneponymous name of NALD?
Cerebrohepato-renal (X-linked adrenoleukodystrophy)

What is its inheritance?
AR

How do Zellweger syndrome and NALD present?
In the **neonatal** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies (in NALD)

What is the prognosis?
It is uniformly fatal by age **1 year**

Is NALD the same condition as infantile Refsum disease?
No, that is an X-linked condition

What is its inheritance?
AR

How do NALD pts present?
In the **late infancy** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

What is the prognosis?
It is uniformly fatal by **late childhood**

By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP
(aka Complex RP; Syndromic RP)

- Usher syndrome
- **Peroxisomal disorders**
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

'Pseudo-RP'



What is the noneponymous name of NALD?
Cerebrohepato-renal (X-linked adrenoleukodystrophy)

What is its inheritance pattern?
AR

How do Zellweger syndrome and NALD present?
In the **neonatal** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies (in NALD)

What is the prognosis for NALD?
It is uniformly fatal by age **1 year**

Is NALD the same condition as infantile Refsum disease?
No, that is an X-linked condition

What is its inheritance pattern?
AR

How do NALD pts present?
In the **late infancy** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

What is the prognosis for NALD?
It is uniformly fatal by age **late childhood**

By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

What is its inheritance pattern?

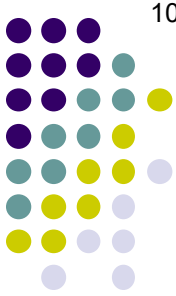
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 - Zellweger syndrome
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 - Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

'Pseudo-RP'



What is the noneponymous name of Cerebrohepato-renal (CH) disease?

Is NALD the same condition?
No, that is an X-linked adrenoleukodystrophy

By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

What is its inheritance pattern?
AR

What is its inheritance pattern?
AR

What is its inheritance pattern?
AR

How do Zellweger syndrome and NALD present?
In the **neonatal** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies (large head)

How do NALD pts present?
In the **late infancy** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

What is the prognosis?

It is uniformly fatal by **late childhood**

What is the prognosis?
It is uniformly fatal by age **1 year**

DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP
(aka Complex RP; Syndromic RP)

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 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

'Pseudo-RP'

What is the noneponymous name for Cerebrohepato-renal (Zellweger) syndrome?

Is NALD the same condition?
No, that is an X-linked adrenoleukodystrophy

By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

What is its inheritance pattern?

AR

What is its inheritance pattern?

AR

What is its inheritance pattern?

AR

Like Zellweger's and NALD, infantile Refsum's is inherited AR

How do Zellweger's and NALD differ?

In the **neonatal** period

--RP-like fundus

--Deafness

--Hypotonia

--Seizures

--Abnormal facies

In the **late infancy** period

--RP-like fundus

--Deafness

--Hypotonia

--Seizures

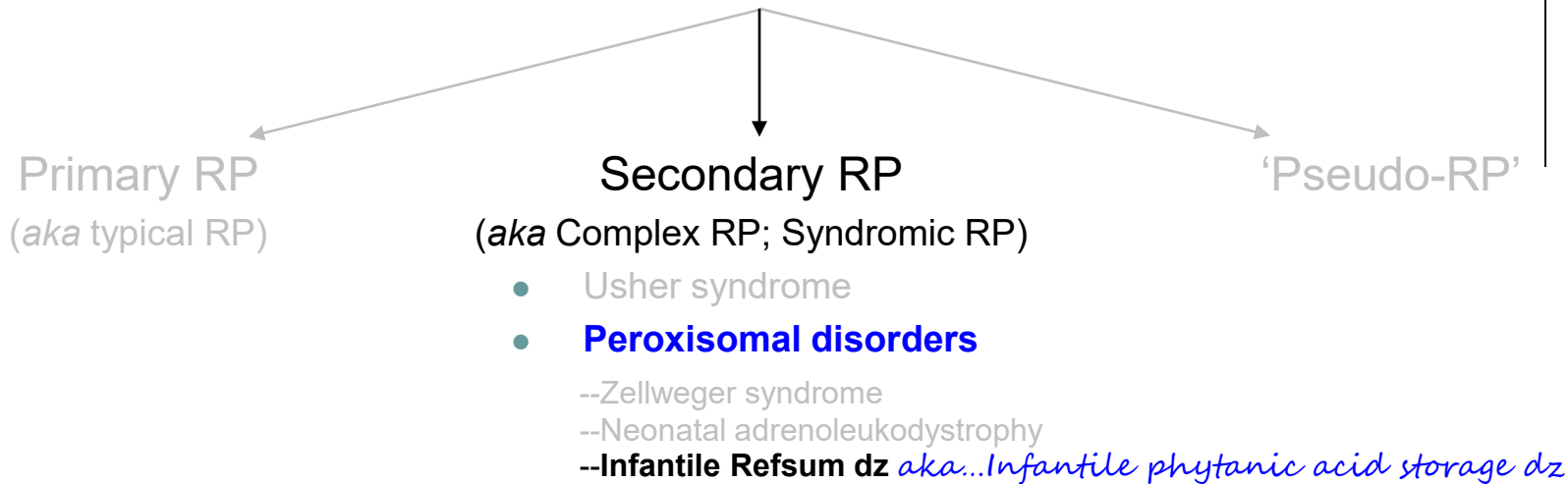
What is the prognosis?

It is uniformly fatal by **late childhood**

What is the prognosis?

It is uniformly fatal by age **1 year**

DDx for an RP-like Fundus



What is the noneponymous name of NALD?
Cerebrohepato-renal (X-linked adrenoleukodystrophy)

What is its inheritance pattern?
AR

How do Zellweger syndrome pts present?
In the **neonatal** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies (leopard facies)

What is the prognosis for Zellweger syndrome?
It is uniformly fatal by age **1 year**

Is NALD the same condition as infantile Refsum disease?
No, that is an X-linked condition

What is its inheritance pattern?
AR

How do NALD pts present?
In the **late infancy** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

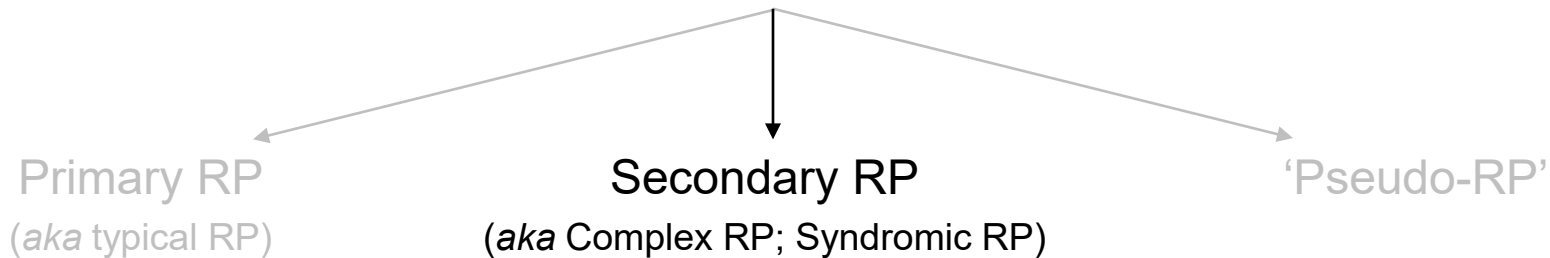
What is the prognosis for NALD?
It is uniformly fatal by age **late childhood**

By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

What is its inheritance pattern?
AR

How do infantile Refsum dz pts present?

DDx for an RP-like Fundus



- Usher syndrome
- **Peroxisomal disorders**

--Zellweger syndrome

--Neonatal adrenoleukodystrophy

--**Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

What is the noneponymous name of NALD?
Cerebrohepato-renal (Zellweger) syndrome

What is its inheritance pattern?
AR

How do Zellweger syndrome pts present?
In the **neonatal** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies

What is the prognosis?
It is uniformly fatal by age **1 year**

Is NALD the same condition as infantile Refsum disease?
No, that is an X-linked condition

What is its inheritance pattern?
AR

How do NALD pts present?
In the **late infancy** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

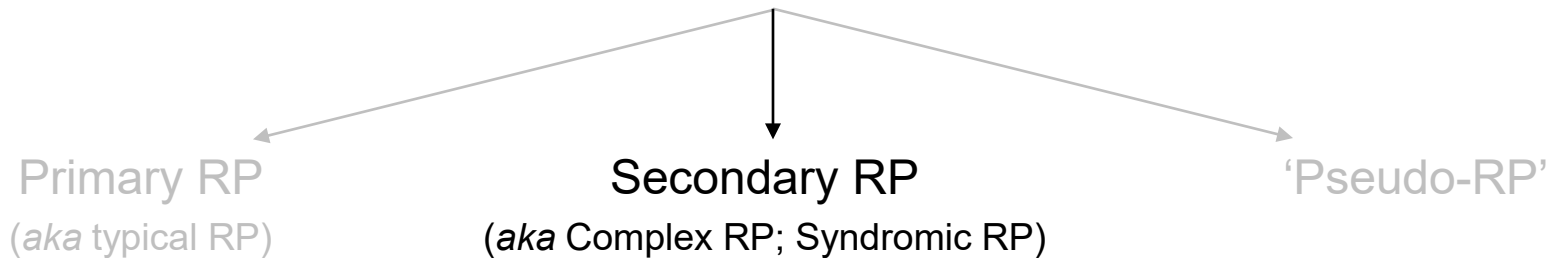
What is the prognosis?
It is uniformly fatal by **late childhood**

By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

What is its inheritance pattern?
AR

How do infantile Refsum dz pts present?
In the **'age'** period

DDx for an RP-like Fundus



- Usher syndrome
- **Peroxisomal disorders**

--Zellweger syndrome

--Neonatal adrenoleukodystrophy

--**Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

What is the noneponymous name of NALD?
Cerebrohepato-renal (X-linked adrenoleukodystrophy)

Is NALD the same condition as infantile Refsum disease?
No, that is an X-linked condition

By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

What is its inheritance pattern?
AR

What is its inheritance pattern?
AR

What is its inheritance pattern?
AR

How do Zellweger syndrome pts present?
In the **neonatal** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies (lemon-shaped)

How do NALD pts present?
In the **late infancy** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

How do infantile Refsum dz pts present?
In the **early childhood** period

What is the prognosis for NALD?
It is uniformly fatal by age **1 year**

What is the prognosis for NALD?
It is uniformly fatal by age **1 year**

What is the prognosis for infantile Refsum dz?
It is uniformly fatal by **late childhood**

DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP
(aka Complex RP; Syndromic RP)

- Usher syndrome
- **Peroxisomal disorders**
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

'Pseudo-RP'

What is the noneponymous name of Cerebrohepato-renal (Zellweger) syndrome?

What is its inheritance pattern?

How do Zellweger syndrome pts present? In the **neonatal** period

--Deafness
--Hypoplasia of the corpus callosum
--Seizures
--Abnormal facies

What is the prognosis? It is uniformly fatal by age **1 year**

Is NALD the same condition as Zellweger syndrome? No, that is an X-linked condition

What is its inheritance pattern? AR

How do NALD pts present? In the **late infancy** period

What is the prognosis? It is uniformly fatal by **late childhood**

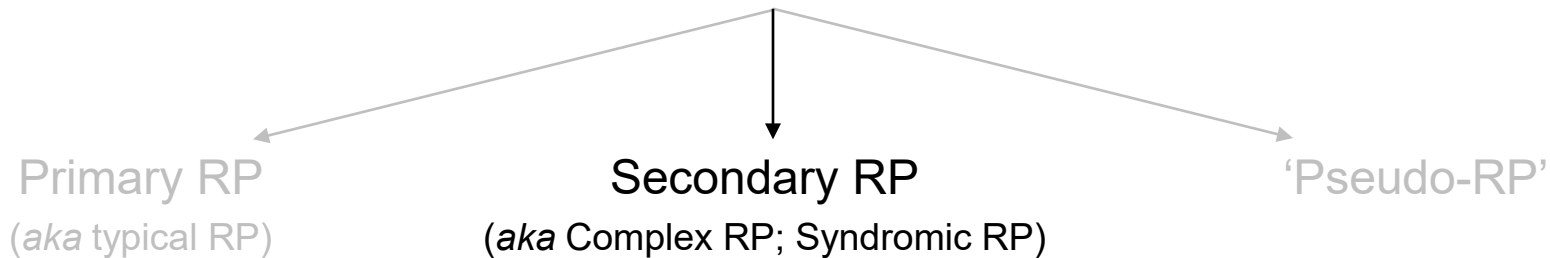
By what noneponymous name is infantile Refsum disease known? Infantile phytanic acid storage disease

What is its inheritance pattern? AR

How do infantile Refsum dz pts present? In the **early childhood** period

Just as NALD's onset is a little later than Zellweger's, infantile Refsum's is a little later than that of NALD

DDx for an RP-like Fundus



- Usher syndrome
- **Peroxisomal disorders**

--Zellweger syndrome

--Neonatal adrenoleukodystrophy

--**Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

What is the noneponymous name of NALD?
Cerebrohepato-renal

Is NALD the same condition as infantile Refsum disease?
No, that is an X-linked

By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

What is its inheritance pattern?
AR

What is its inheritance pattern?
AR

What is its inheritance pattern?
AR

How do Zellweger syndrome pts present?
In the **neonatal** period with:
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies

How do NALD pts present?
In the **late infancy** period with:
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

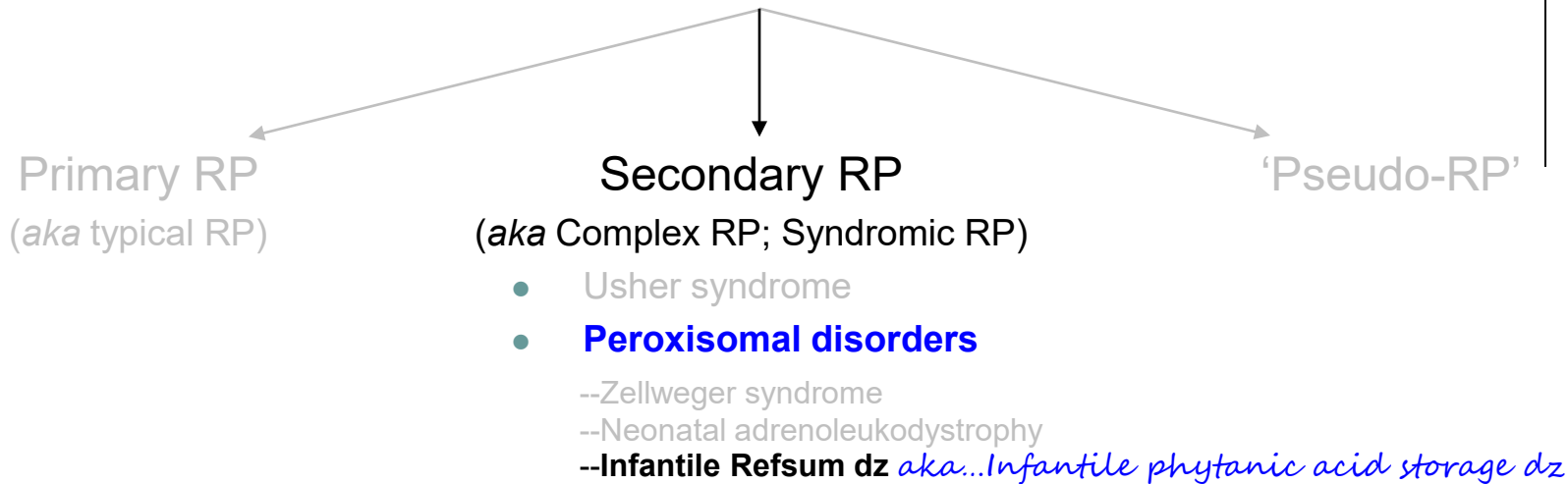
How do infantile Refsum dz pts present?
In the **early childhood** period with:
--RP-like fundus
--?
--?

What is the prognosis for NALD?
It is uniformly fatal by age **1 year**

What is the prognosis for infantile Refsum disease?
It is uniformly fatal by **late childhood**

What is the prognosis for infantile Refsum disease?
It is uniformly fatal by age **1 year**

DDx for an RP-like Fundus



What is the noneponymous name of NALD?
Cerebrohepato-renal (Zellweger) syndrome

What is its inheritance pattern?
AR

How do Zellweger syndrome pts present?
In the **neonatal** period with:
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies (large forehead, epicanthic folds)

What is the prognosis?
It is uniformly fatal by age **1 year**

Is NALD the same condition as infantile Refsum disease?
No, that is an X-linked condition

What is its inheritance pattern?
AR

How do NALD pts present?
In the **late infancy** period with:
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

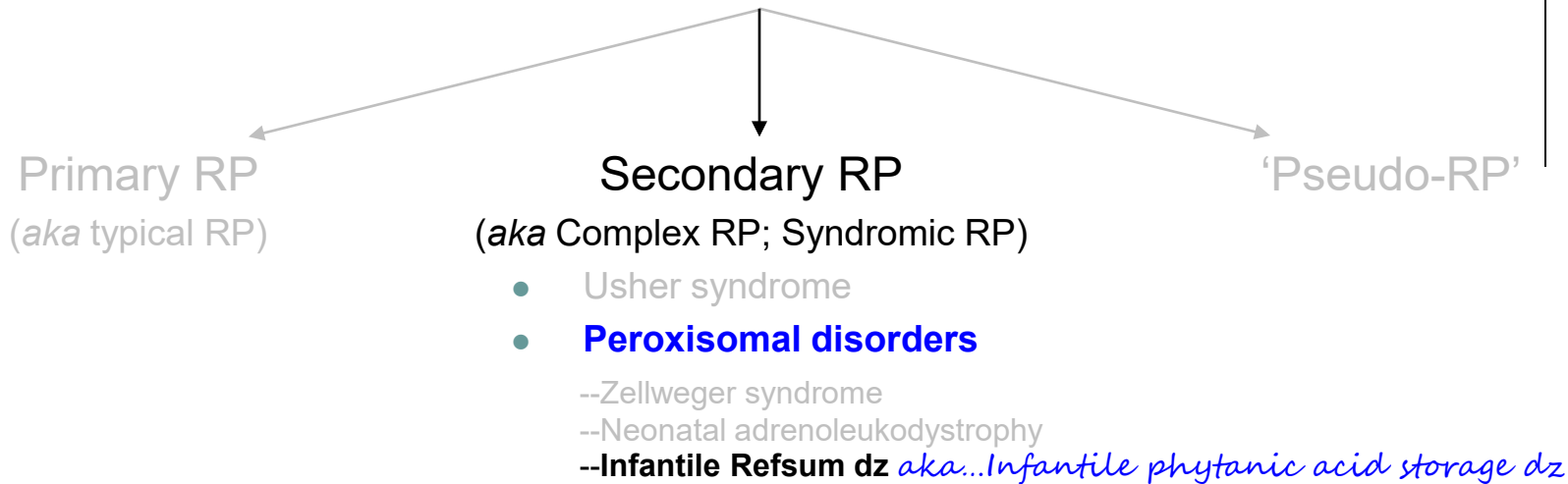
What is the prognosis?
It is uniformly fatal by **late childhood**

By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

What is its inheritance pattern?
AR

How do infantile Refsum dz pts present?
In the **early childhood** period with:
--RP-like fundus
--Deafness
--Hypotonia

DDx for an RP-like Fundus



What is the noneponymous name for Cerebrohepato-renal (NALD)?

Is NALD the same condition as Zellweger? No, that is an X-linked condition.

By what noneponymous name is infantile Refsum disease known? Infantile phytanic acid storage disease

And just as NALD has the same S/S as Zellweger save one, so too with infantile Refsum--it has the same as NALD, except, again, for the last one on the list (note that this means it has the same S/S as Zellweger, save **two**)

In the neonatal period

--RP-like fundus
--Deafness
--Hypotonia
~~--Seizures~~
~~--Abnormal facies~~

In the late infancy

--RP-like fundus
--Deafness
--Hypotonia
~~--Seizures~~

By what noneponymous name is infantile Refsum disease known? Infantile phytanic acid storage disease

--RP-like fundus
--Deafness
--Hypotonia

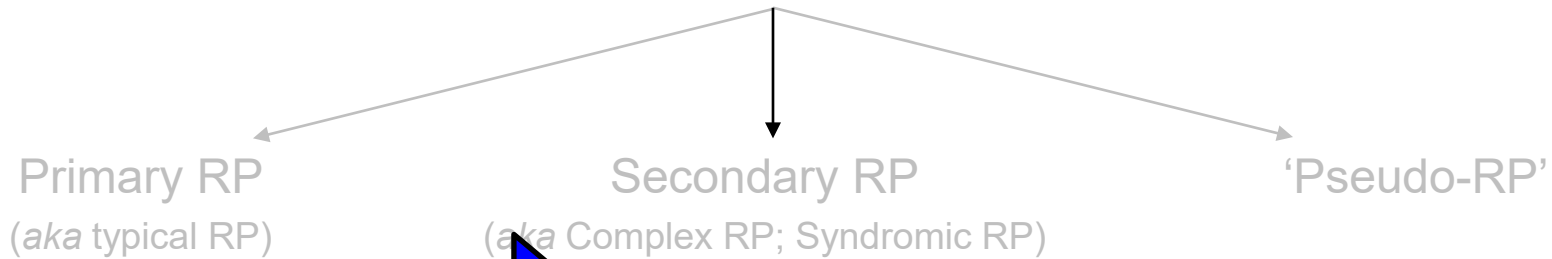
What is the prognosis for NALD?

It is uniformly fatal by late childhood

What is the prognosis for Zellweger?

It is uniformly fatal by age 1 year

DDx for an RP-like Fundus



Usher syndrome

Peroxisomal disorders

--Zellweger syndrome

--Neonatal adrenoleukodystrophy

--**Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

Note that all three peroxisomal disorders involve **deafness**. Thus, if faced with a deaf-blind pt in clinic or on the OKAP/Boards, **don't automatically assume it's Usher syndrome!**

In the **neonatal** period

--RP-like fundus

Deafness

--Hypotonia

--Seizures

--Abnormal facies

In the **late infancy** period

--RP-like fundus

Deafness

--Hypotonia

--Seizures

What is the prognosis?

It is uniformly fatal by **late childhood**

What is the prognosis?

It is uniformly fatal by age **1 year**

By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

What is its inheritance pattern?

pts present?

od with:

--RP-like fundus

Deafness

--Hypotonia

DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP
(aka Complex RP; Syndromic RP)

- Usher syndrome
- **Peroxisomal disorders**
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

'Pseudo-RP'



What is the noneponymous name for NALD?
Cerebrohepato-renal (Zellweger) syndrome

What is its inheritance pattern?
AR

How do Zellweger syndrome pts present?
In the **neonatal** period with:
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies (large, prominent ears)

What is the prognosis?
It is uniformly fatal by age **1 year**

Is NALD the same condition as infantile Refsum disease?
No, that is an X-linked condition

What is its inheritance pattern?
AR

How do NALD pts present?
In the **late infancy** period with:
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

What is the prognosis?
It is uniformly fatal by age **late childhood**

By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

What is its inheritance pattern?
AR

How do infantile Refsum dz pts present?
In the **early childhood** period with:
--RP-like fundus
--Deafness
--Hypotonia

What is the prognosis?

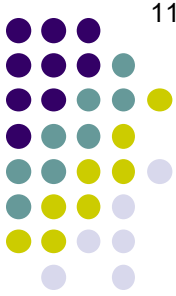
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Primary RP
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- Usher syndrome
- **Peroxisomal disorders**
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

'Pseudo-RP'



What is the noneponymous name of the disease?
Cerebrohepato-renal (Zellweger) syndrome

What is its inheritance pattern?
AR

How do Zellweger syndrome pts present?
In the **neonatal** period with:
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies (large head)

What is the prognosis?
It is uniformly fatal by age **1 year**

Is NALD the same condition?
No, that is an X-linked condition

What is its inheritance pattern?
AR

How do NALD pts present?
In the **late infancy** period with:
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

What is the prognosis?
It is uniformly fatal by **late childhood**

By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

What is its inheritance pattern?
AR

How do infantile Refsum dz pts present?
In the **early childhood** period with:
--RP-like fundus
--Deafness
--Hypotonia

What is the prognosis?

It is uniformly fatal by **late childhood** (if treatment is unsuccessful)

DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP
(aka Complex RP; Syndromic RP)

- Usher syndrome
- **Peroxisomal disorders**
 - Zellweger syndrome
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 - Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

'Pseudo-RP'



What is the noneponymous name of the disease?
Cerebrohepato-renal (Zellweger) syndrome

What is its inheritance pattern?
AR

How do Zellweger syndrome pts present?
In the **neonatal** period with:
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies (large head)

What is the prognosis?
It is uniformly fatal by age **1 year**

Is NALD the same condition?
No, that is an X-linked condition

What is its inheritance pattern?
AR

How do NALD pts present?
In the **late infancy** period with:
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

What is the prognosis?
It is uniformly fatal by **late childhood**

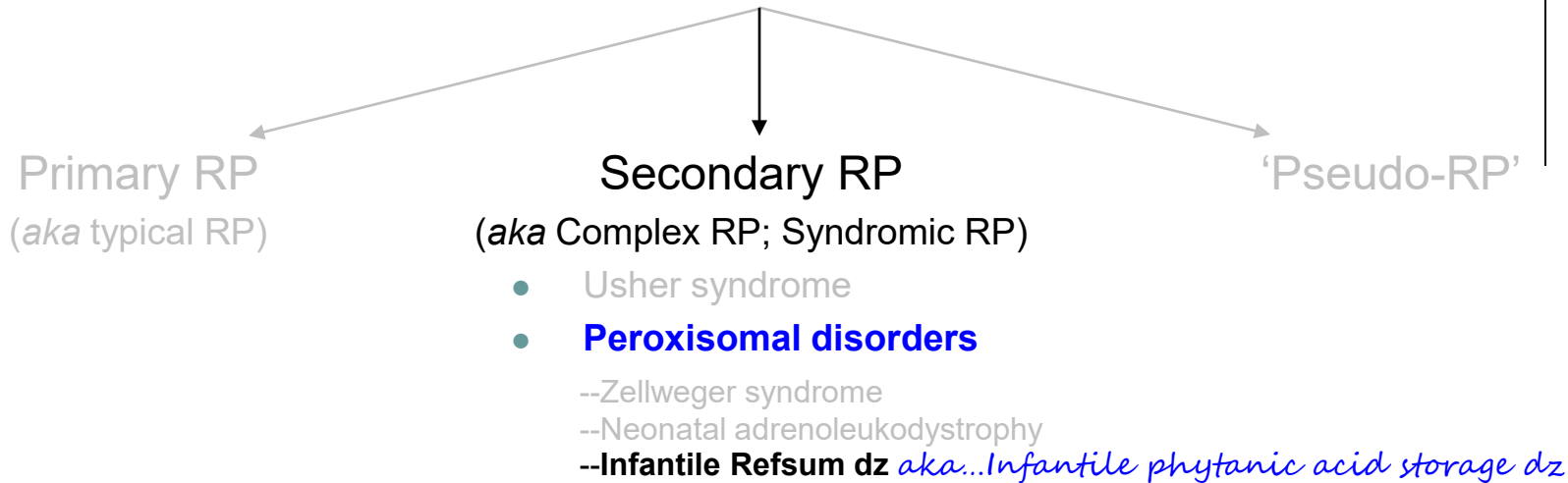
By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

What is its inheritance pattern?
AR

How do infantile Refsum dz pts present?
In the **early childhood** period with:
--RP-like fundus
--Deafness
--Hypotonia

What is the prognosis?
It is uniformly fatal by **early adulthood** (if treatment is unsuccessful)

DDx for an RP-like Fundus



What is the noneponymous name for NALD?
Cerebrohepato-renal (Zellweger) syndrome

What is its inheritance pattern?
AR

How do Zellweger syndrome pts present?
In the **neonatal** period with:

--RP-like fundus
--Deafness
--Hypoplasia of the corpus callosum
--Seizures

--Abnormal facies (large forehead, epicanthic folds)

What is the prognosis for Zellweger syndrome?
It is uniformly **fatal by age 1 year**

Is NALD the same as infantile Refsum disease?
No, that is an X-linked disorder

What is its inheritance pattern?
AR

How do NALD pts present?
In the **late infancy** period with:
--RP-like fundus

What is the prognosis for NALD?
It is uniformly **fatal by late childhood**

By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

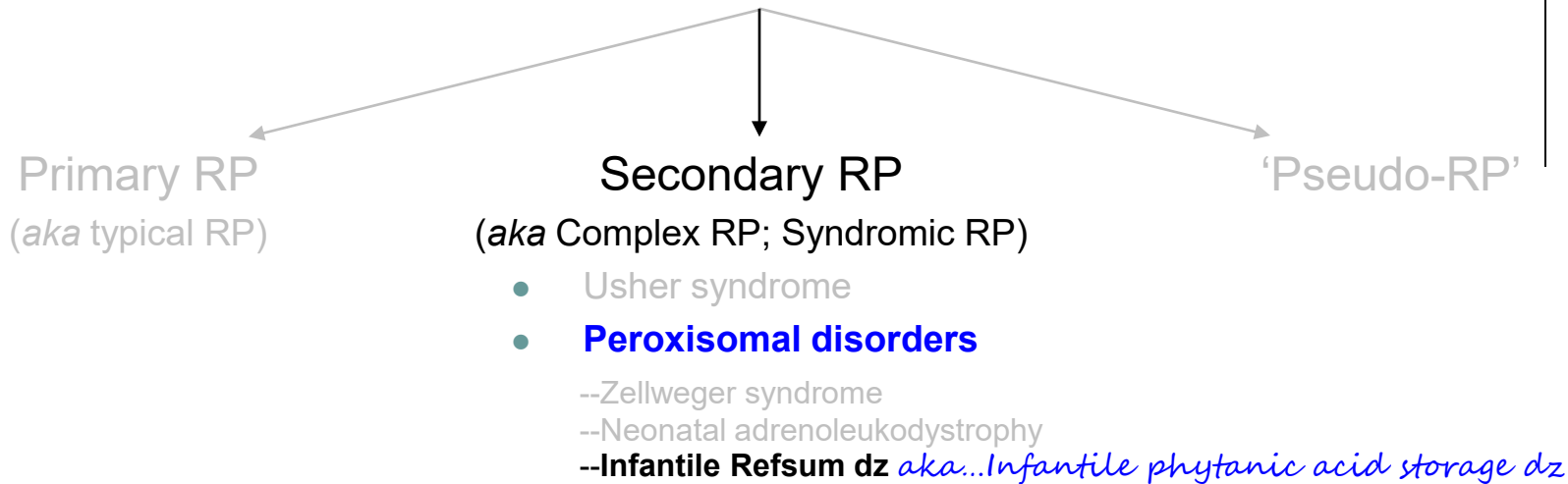
What is its inheritance pattern?
AR

How do infantile Refsum dz pts present?
In the **early childhood** period with:
--RP-like fundus

What is the prognosis for infantile Refsum disease?
It is uniformly **fatal by early adulthood** (treatment is unsuccessful)

And just as the prognosis for NALD was better than for Zellweger, so too in turn is the prognosis for infantile Refsum better than that for NALD

DDx for an RP-like Fundus



What is the noneponymous name for Cerebrohepato-renal (CH) disease?

What is its inheritance pattern?

How do Zellweger syndrome and NALD differ?
In the **neonatal** period:
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies

What is the prognosis?
It is uniformly fatal by age **1 year**

Is NALD the same condition as CHD?
No, that is an X-linked condition

What is its inheritance pattern?
AR

How do Zellweger syndrome and NALD differ?
In the **neonatal** period:
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

What is the prognosis?
It is uniformly fatal by age **late childhood**

By what noneponymous name is infantile Refsum disease known?
Infantile phytanic acid storage disease

What is its inheritance pattern?
AR

So infantile Refsum and NALD are quite similar, except that infantile Refsum is a somewhat milder condition:
--Later onset
--One fewer S/S (= no seizures)
--Pts live longer

--Hypotonia

What is the prognosis?

It is uniformly fatal by **early adulthood** (if treatment is unsuccessful)

DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP
(aka Complex RP; Syndromic RP)

- Usher syndrome
- **Peroxisomal disorders**
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

'Pseudo-RP'



How is infantile Refsum diagnosed?

What is the nonperoxisomal
Cerebrohepato-renal

What is its inheritance
AR

How do Zellweger
In the **neonatal** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies

What is the prognosis?
It is uniformly fatal by age **1 year**

What is its inheritance
AR

How do NALD pts present?
In the **late infancy** period
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

What is the prognosis?
It is uniformly fatal by **late childhood**

What is its inheritance pattern?
AR

How do infantile Refsum dz pts present?
In the **early childhood** period with:
--RP-like fundus
--Deafness
--Hypotonia

What is the prognosis?

It is uniformly fatal by **early adulthood** (if treatment is unsuccessful)

Is infantile Refsum disease known?

DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP
(aka Complex RP; Syndromic RP)

- Usher syndrome
- **Peroxisomal disorders**
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

Refsum disease known?

How is infantile Refsum diagnosed?

Via elevated serum phytanic acid levels (and VLCFAs)

What is its inheritance pattern?
AR

What is its inheritance pattern?
AR

How do NALD pts present?
In the **late infancy** period with:

- RP-like fundus
- Deafness
- Hypotonia
- Seizures

How do infantile Refsum dz pts present?

In the **early childhood** period with:

- RP-like fundus
- Deafness
- Hypotonia

What is the prognosis?

It is uniformly fatal by **early adulthood** (if treatment is unsuccessful)

What is the prognosis?

It is uniformly fatal by **late childhood**

What is the nonperoxisomal
Cerebrohepato-renal

What is its inheritance pattern?
AR

How do Zellweger

In the **neonatal** period

- RP-like fundus
- Deafness
- Hypotonia
- Seizures
- Abnormal facies

What is the prognosis?

It is uniformly fatal by age **1 year**

DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP
(aka Complex RP; Syndromic RP)

- Usher syndrome
- **Peroxisomal disorders**
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

'Pseudo-RP'



What is the nonep...
Cerebrohepatoren...

What is its inherita...
AR

How do Zellweger...
In the **neonatal** p...
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies

What is the progn...
It is uniformly fatal by age **1 year**

Is...
How is infantile Refsum diagnosed?

N...
Via elevated serum phytanic acid levels (and VLCFAs)

What is its inheritance...
AR

How do NALD pts pr...
In the **late infancy**...
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

What is the prognosi...
It is uniformly fatal by **late childhood**

What is its inheritance pattern?
AR

How do infantile Refsum dz pts present?

In the...
--RP-like
--Deafn...
--Hypot...

What is the prognosis?

It is uniformly fatal by **early adulthood**

Hold up—you can treat this one??!! How is infantile Refsum treated?

Refsum disease known?

(if treatment is unsuccessful)

DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP
(aka Complex RP; Syndromic RP)

- Usher syndrome
- **Peroxisomal disorders**
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz** aka...*Infantile phytanic acid storage dz*

'Pseudo-RP'



What is the nonep...
Cerebrohepatoren...

What is its inherita...
AR

How do Zellweger...
In the **neonatal** p...
--RP-like fundus
--Deafness
--Hypotonia
--Seizures
--Abnormal facies

What is the progn...
It is uniformly fatal by age **1 year**

How is infantile Refsum diagnosed?

N Via **elevated serum phytanic acid levels** (and VLCFAs)

What is its inheritance...
AR

How do NALD pts pr...
In the **late infancy**
--RP-like fundus
--Deafness
--Hypotonia
--Seizures

What is the prognosi...
It is uniformly fatal by **late childhood**

What is its inheritance pattern?
AR

How do infantile Refsum dz pts present?

In the...
--RP-like
--Deafn...
--Hypot...

What is the prognosis?

It is uniformly fatal by **early adulthood**

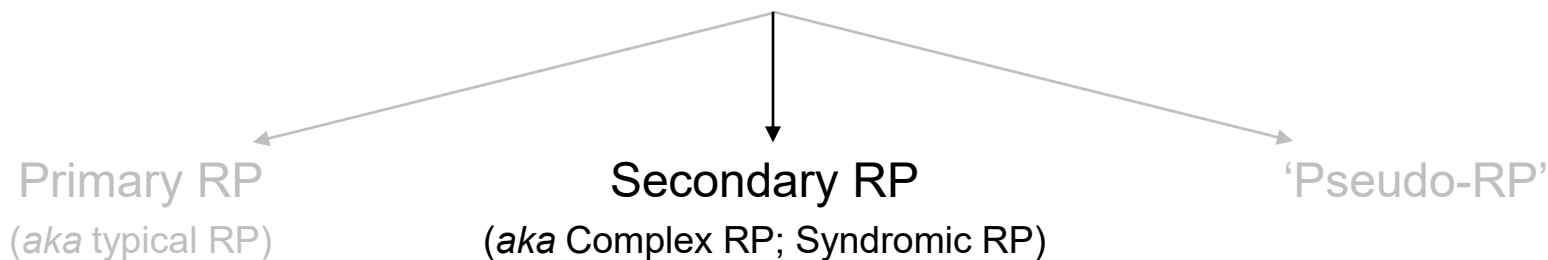
Hold up—you can treat this one??!! How is infantile Refsum treated?

Dietary restriction of phytanic acid and phytol (a phytanic acid precursor); plasmapheresis may be employed acutely

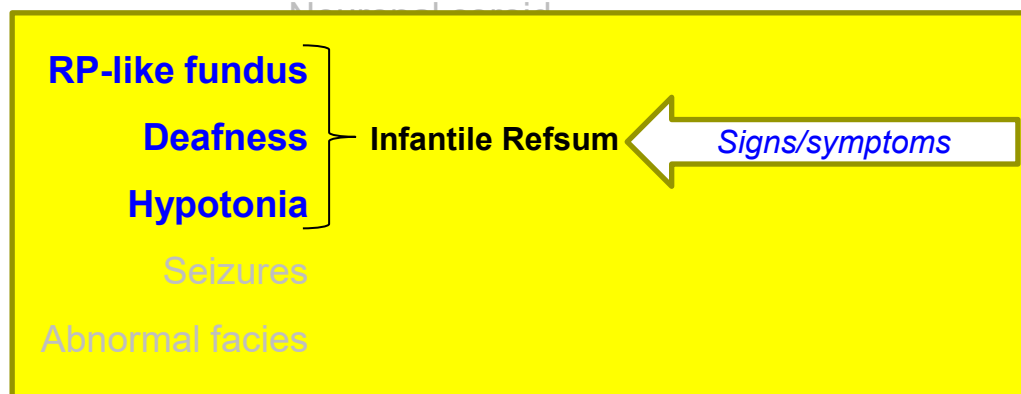
(if **treatment** is unsuccessful)



DDx for an RP-like Fundus



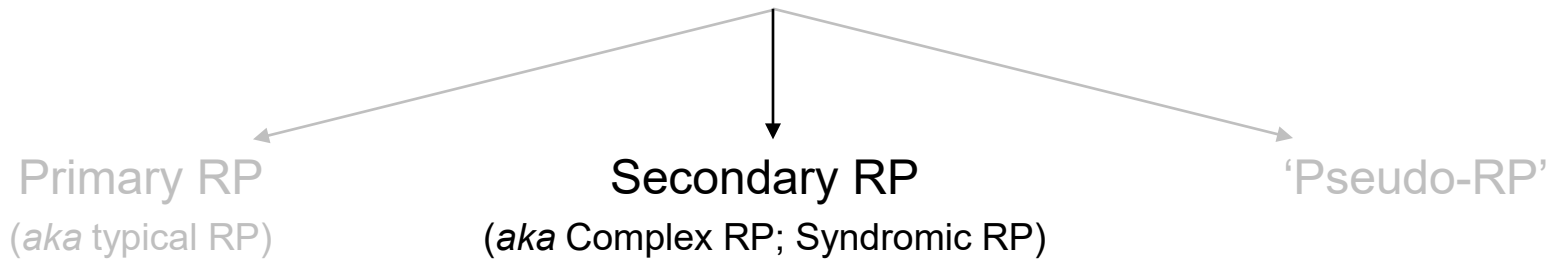
- Usher syndrome
- **Peroxisomal disorders**
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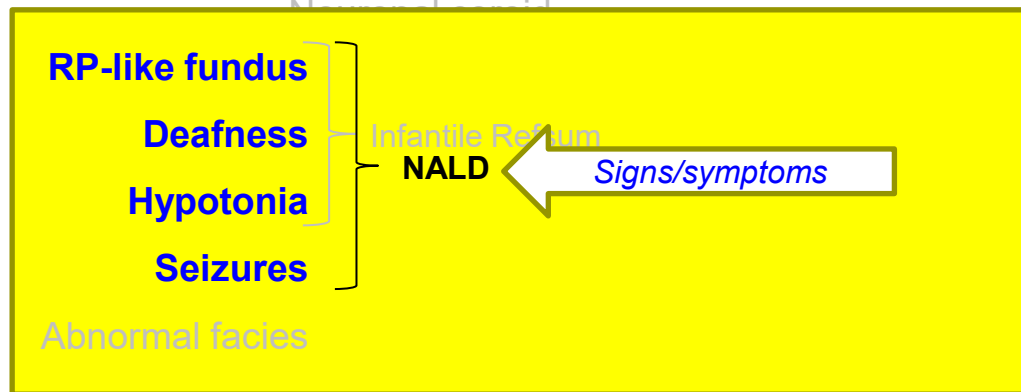
Peroxisomal disorders tl;dr

(Review slides—no questions)

DDx for an RP-like Fundus



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Peroxisomal disorders tl;dr

(Review slides—no questions)



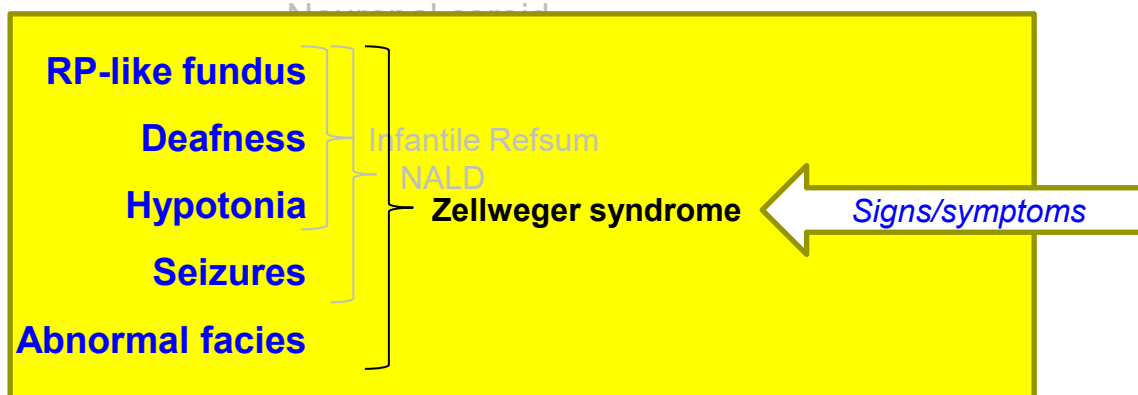
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Secondary RP
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'Pseudo-RP'

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Peroxisomal disorders tl;dr

(Review slides—no questions)



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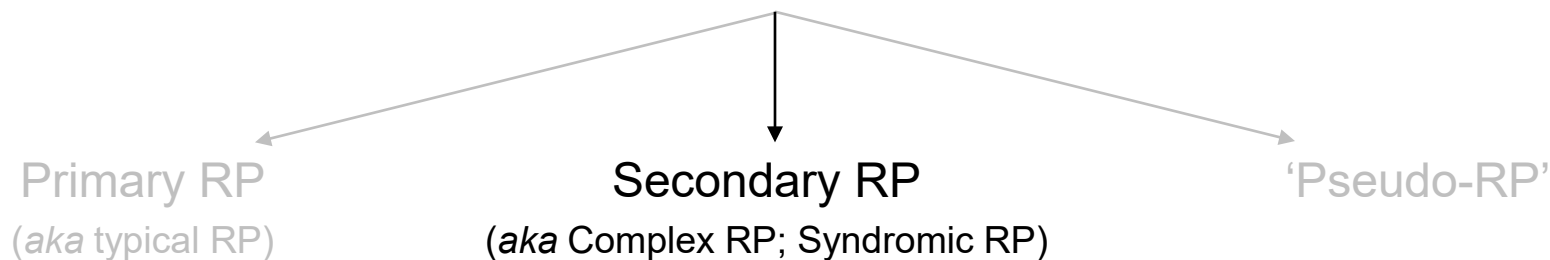


Peroxisomal disorders tl;dr

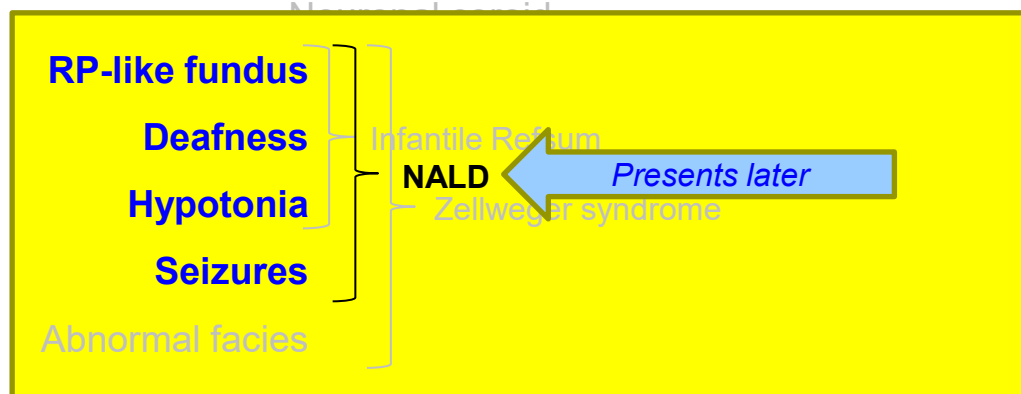
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DDx for an RP-like Fundus



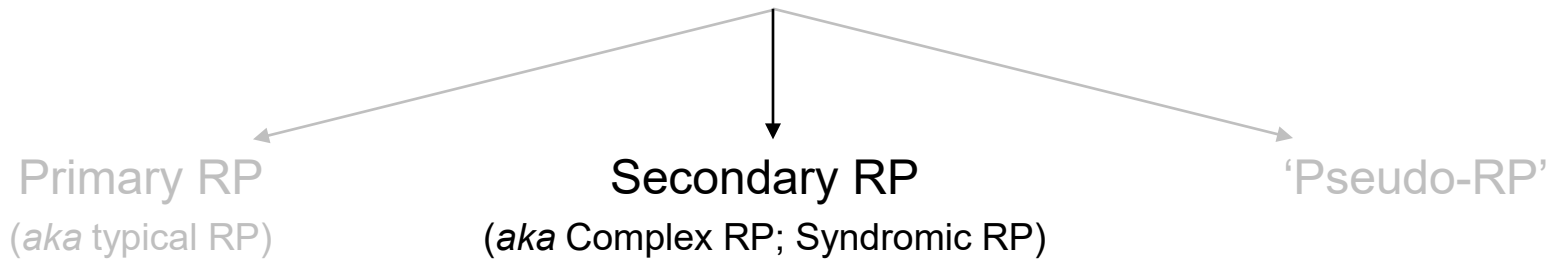
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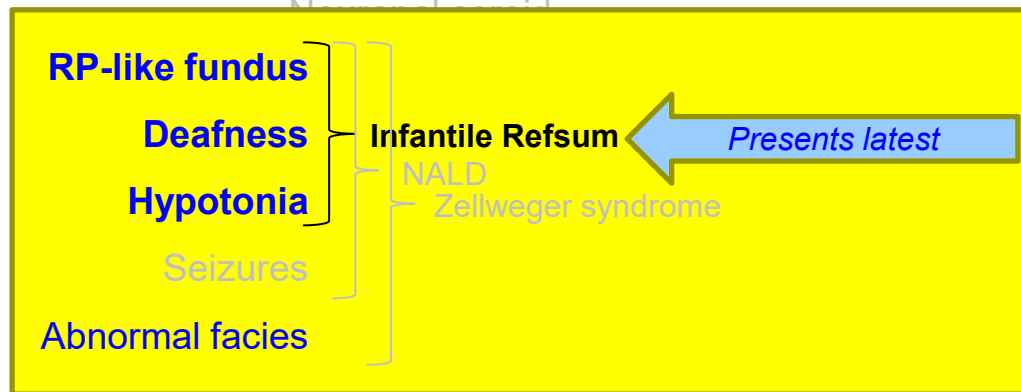
Peroxisomal disorders tl;dr

(Review slides—no questions)

DDx for an RP-like Fundus



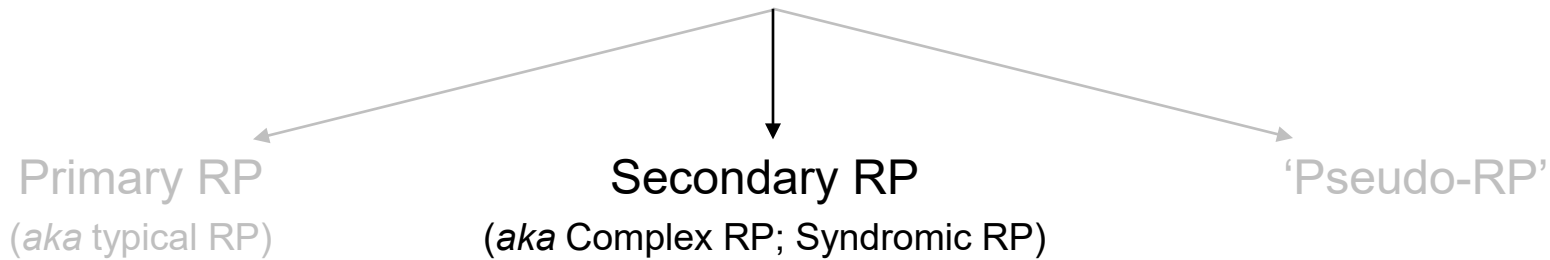
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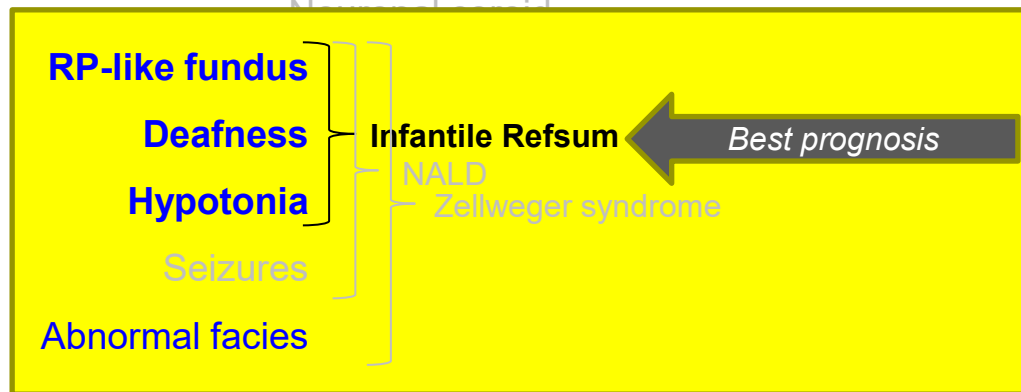
*Peroxisomal disorders **tl;dr***

(Review slides—no questions)

DDx for an RP-like Fundus



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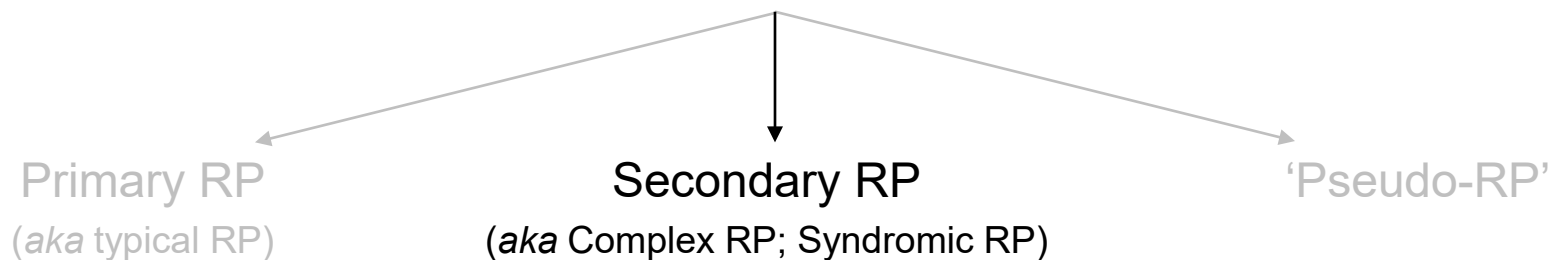


Peroxisomal disorders tl;dr

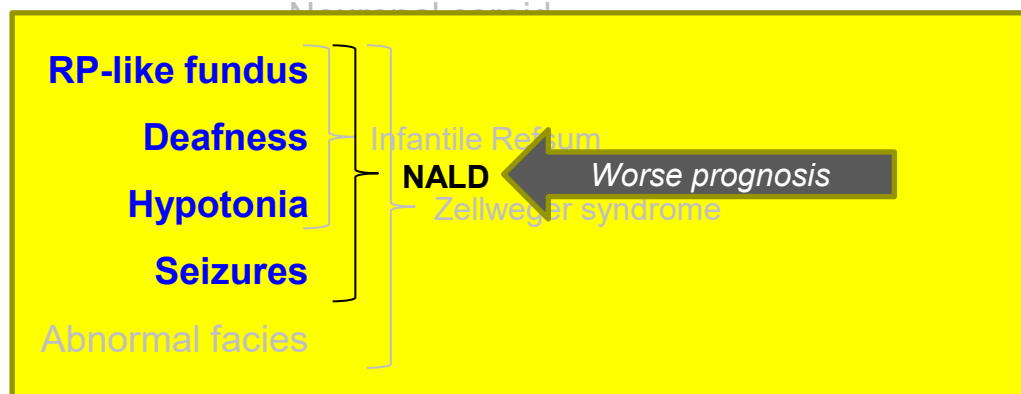
(Review slides—no questions)



DDx for an RP-like Fundus



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- **Peroxisomal disorders**
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy**
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Peroxisomal disorders tl;dr

(Review slides—no questions)



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Peroxisomal disorders tl;dr

(Review slides—no questions)



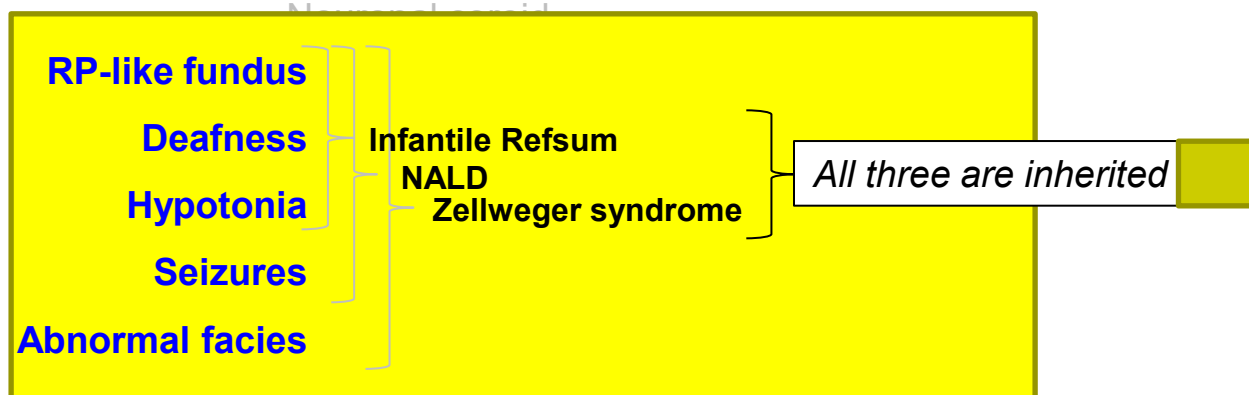
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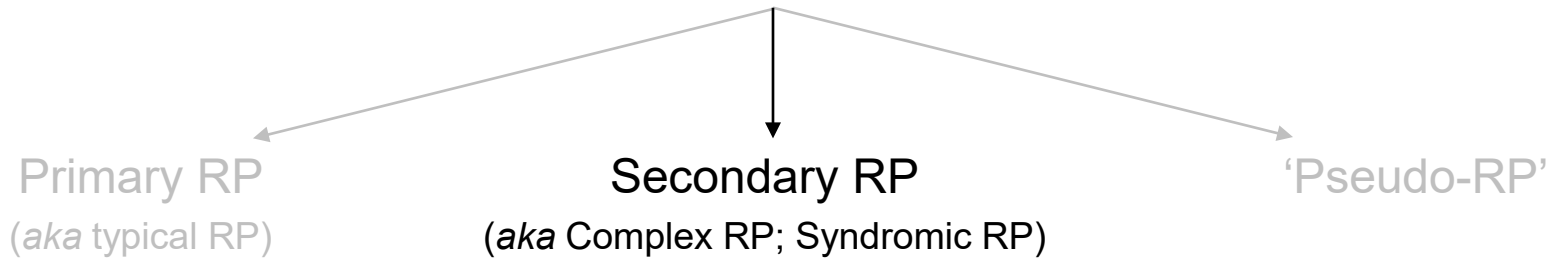
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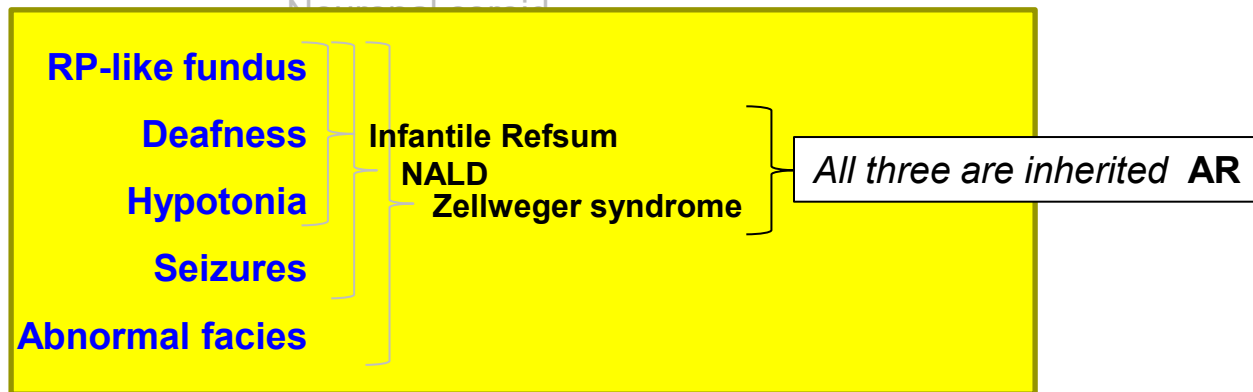


Peroxisomal disorders tl;dr

DDx for an RP-like Fundus



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Peroxisomal disorders tl;dr



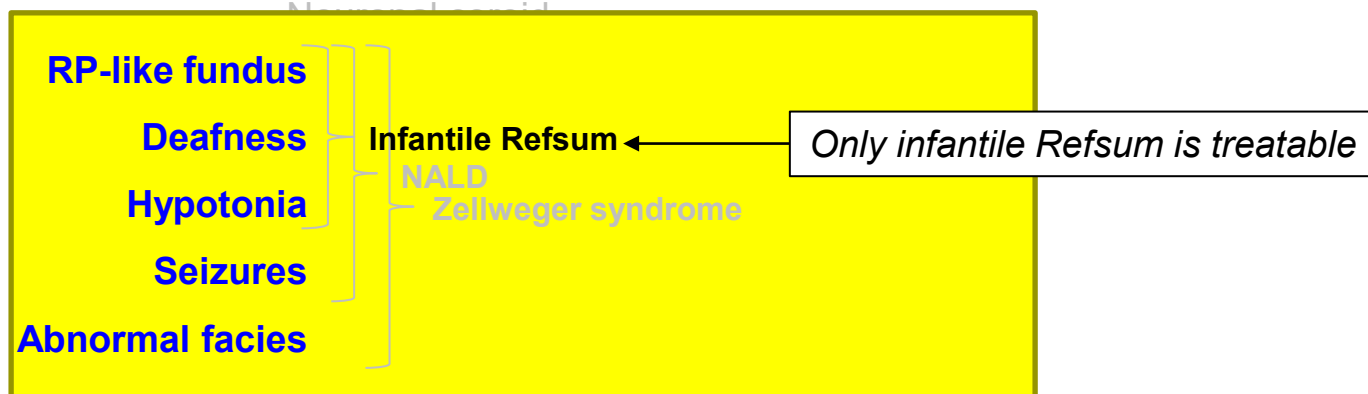
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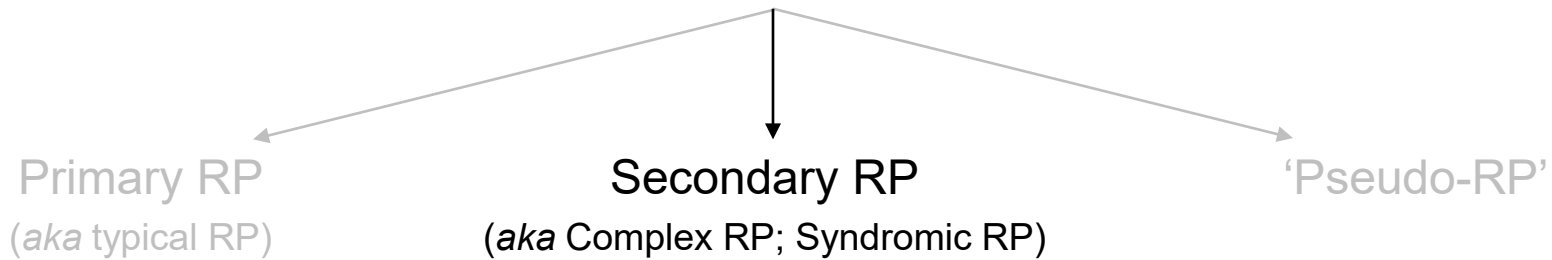
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Peroxisomal disorders tl;dr

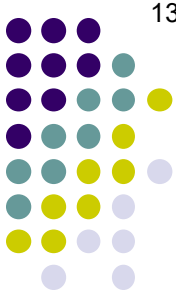
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DDx for an RP-like Fundus



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- **Neuronal ceroid lipofuscinoses**
 - aka 'Batten dz'
- Ciliopathies
- Abetalipoproteinemia
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What are the neuronal ceroid lipofuscinoses (NCLs; collectively referred to as Batten dz)?



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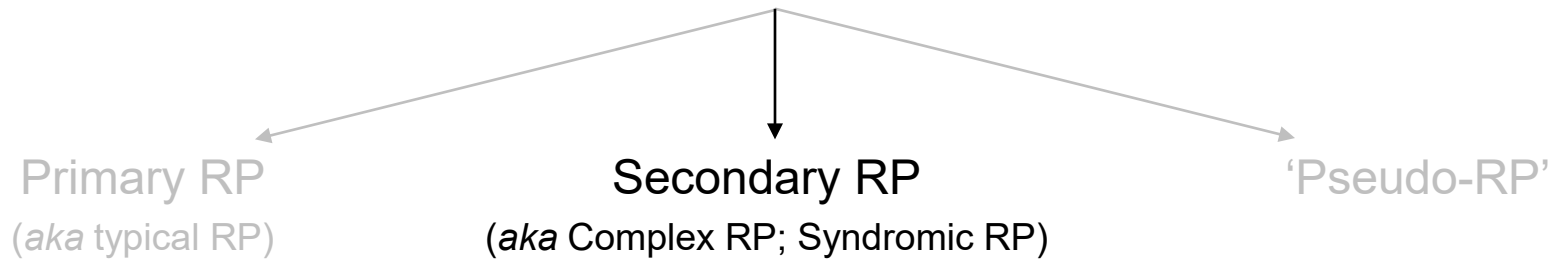
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What are the neuronal ceroid lipofuscinoses (NCLs; collectively referred to as Batten dz)?
Neurodegenerative conditions stemming from the buildup of **two substances** in cells



DDx for an RP-like Fundus

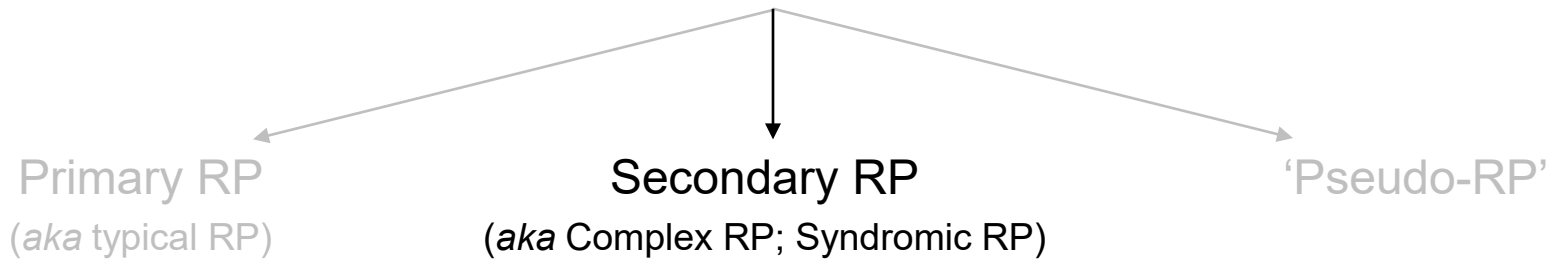


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DDx for an RP-like Fundus



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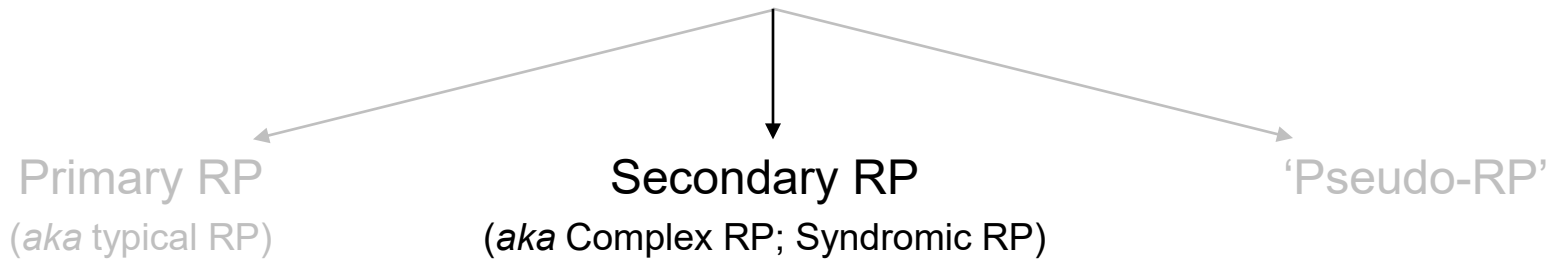
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What is the inheritance pattern?



DDx for an RP-like Fundus



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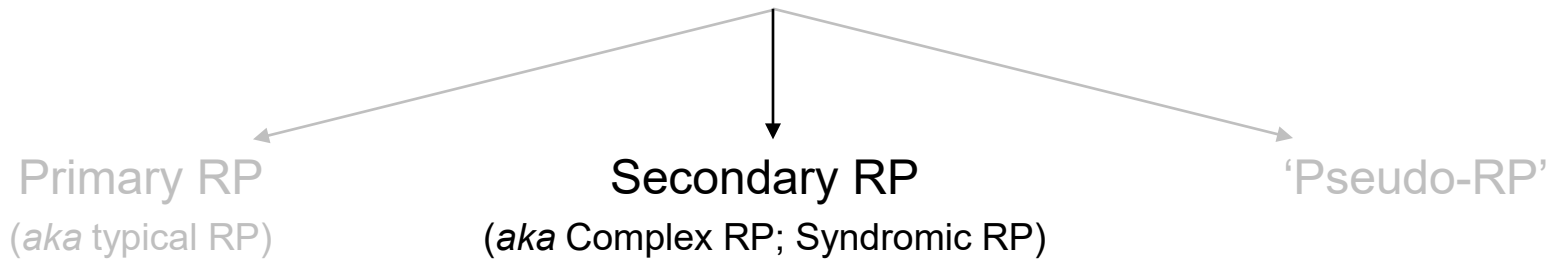
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 AR



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How do Batten dz pts present?

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How do Batten dz pts present?
In infancy to early childhood with:
--RP-like fundus

--?

--?

--?

--?



DDx for an RP-like Fundus

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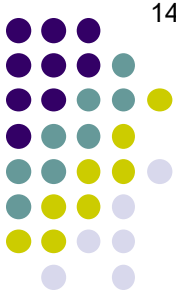
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What is the inheritance pattern?
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How do Batten dz pts present?
In infancy to early childhood with:
--RP-like fundus
--Seizures
--Myoclonus
--Microcephaly (in the infantile forms)
--Relentlessly progressive neurologic and cognitive decline



DDx for an RP-like Fundus

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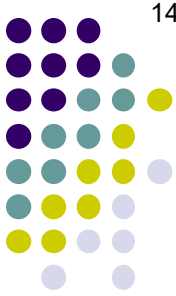
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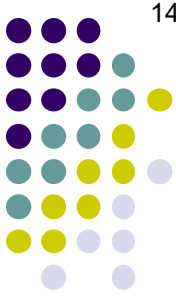
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What is the prognosis?
Depending on the form, it is fatal by **late childhood to early adulthood**



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How is Batten dz diagnosed?

What are the neuronal ceroid lipofuscinoses (NCLs; collectively referred to as Batten dz)?
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How do Batten dz pts present?

with:

(all forms)
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Neurodegenerative conditions stemming from the buildup of ceroid & lipofuscin in cells

What is the inheritance pattern?
AR

How do Batten dz pts present?

How is Batten dz diagnosed?

It is a mélange of imaging, genetic and other tests. If asked, punt to a geneticist.

with:

- Abetalipoproteinemia (rare, autosomal recessive, fat malabsorption, acanthocytosis, retinitis pigmentosa, cerebellar ataxia, and neurodegeneration)
 - aka 'Bassen-Kornzweig syndrome'

--Relentlessly progressive neurologic and cognitive decline

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It is a mélange of imaging, genetic and other tests. If asked, punt to a geneticist.

How is Batten dz managed?

with:

(several forms)
--Relentlessly progressive neurologic and cognitive decline

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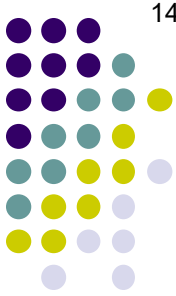
How is Batten dz managed?

Supportively

with:

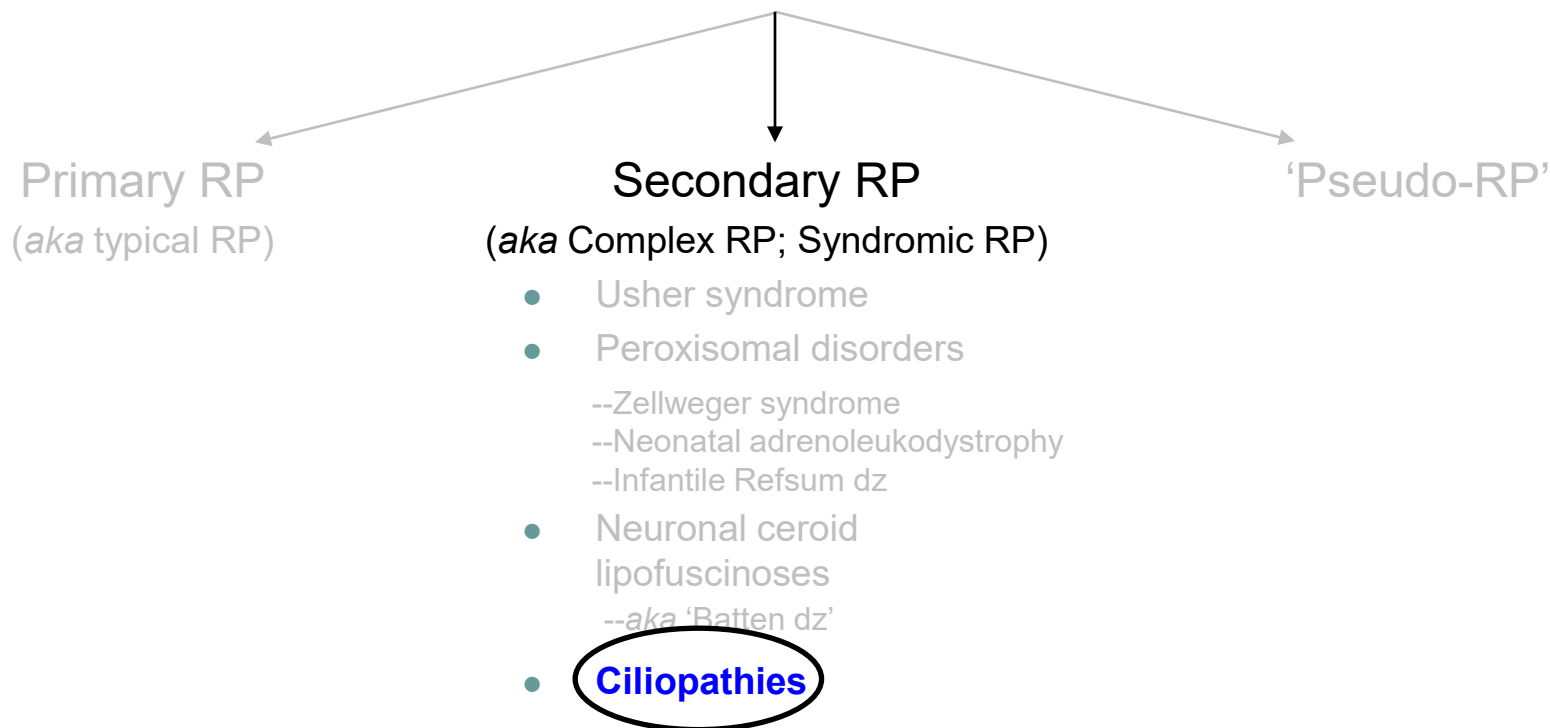
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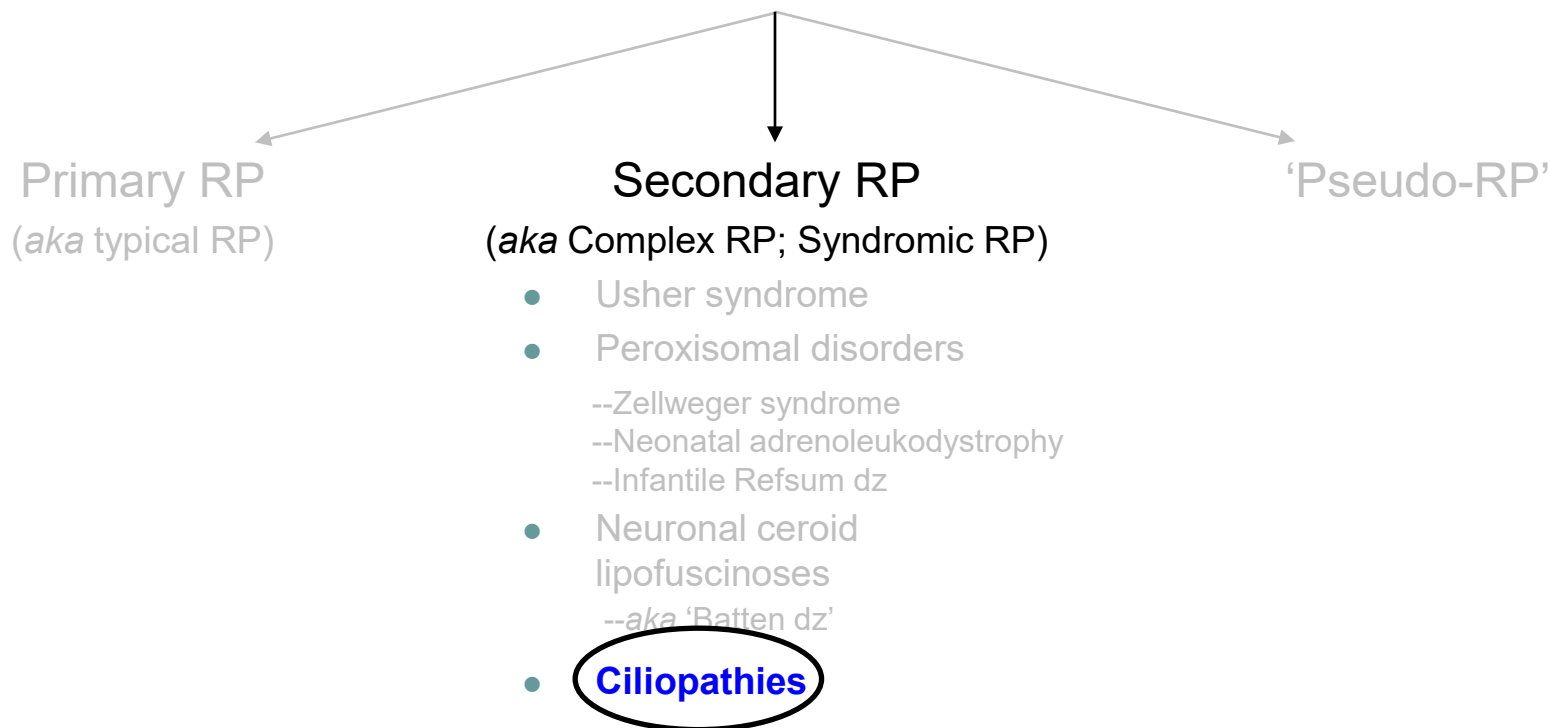
DDx for an RP-like Fundus



What is a ciliopathy?



DDx for an RP-like Fundus

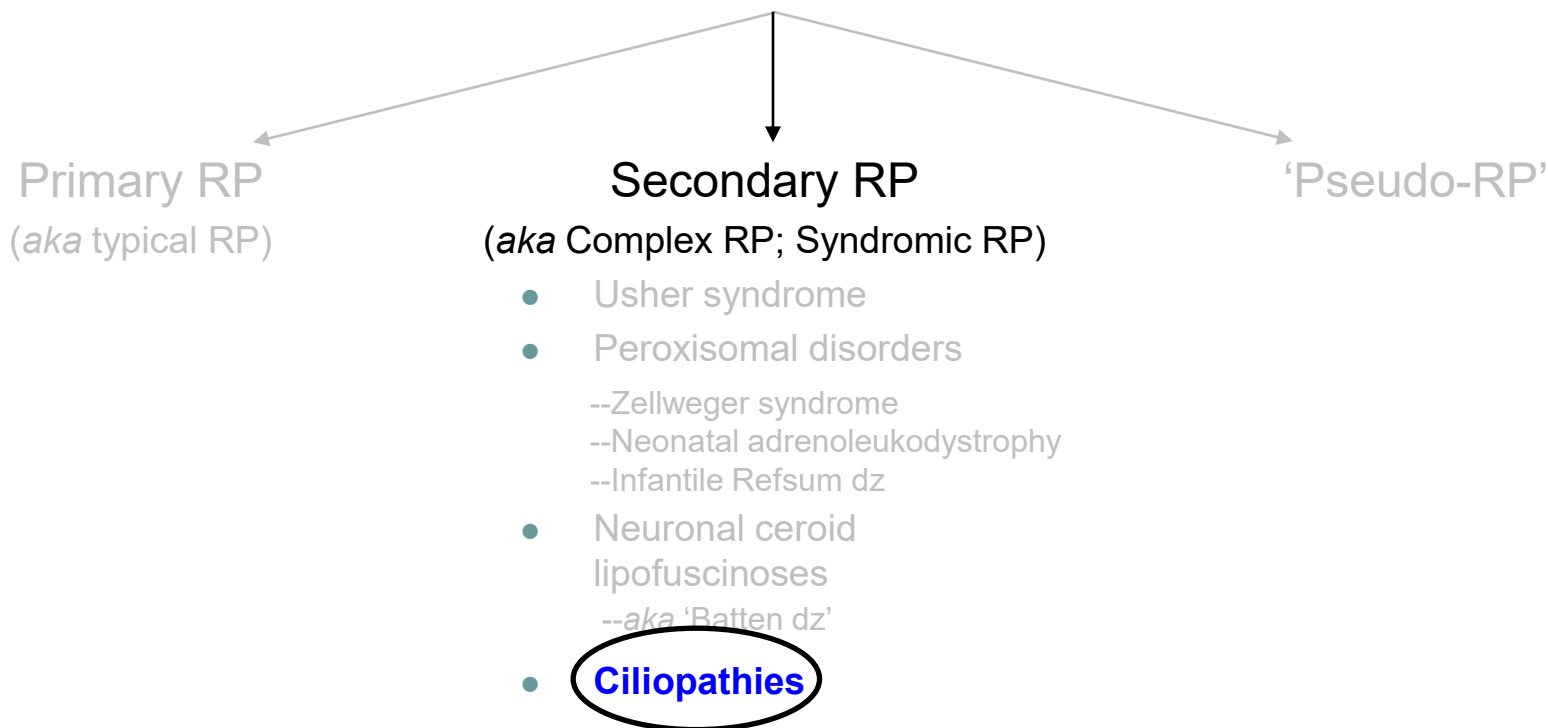


What is a ciliopathy?

An inherited condition marked by abnormal structure and/or function of cilia



DDx for an RP-like Fundus



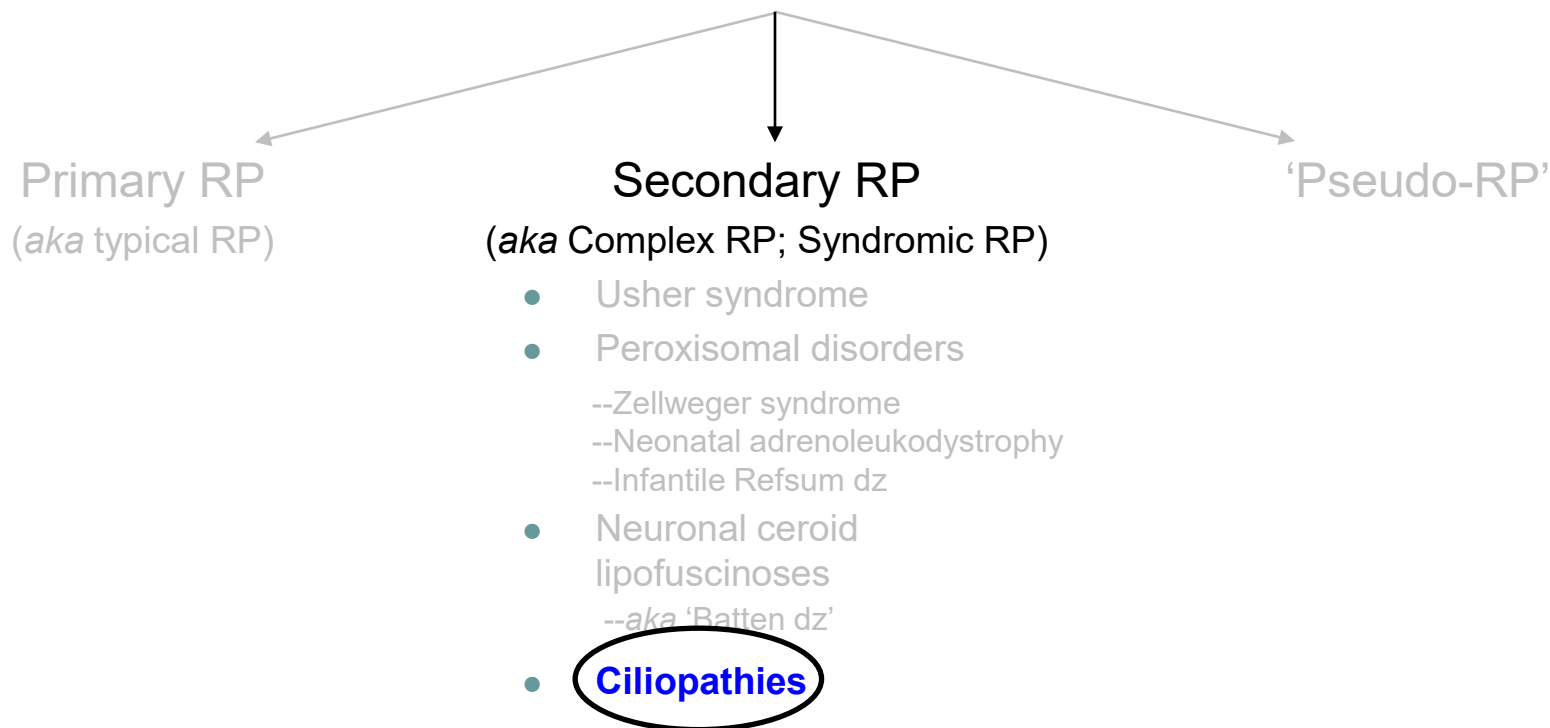
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Cilia are ubiquitous. That said, ciliopathies primarily affect three organs—what are they?



DDx for an RP-like Fundus



What is a ciliopathy?

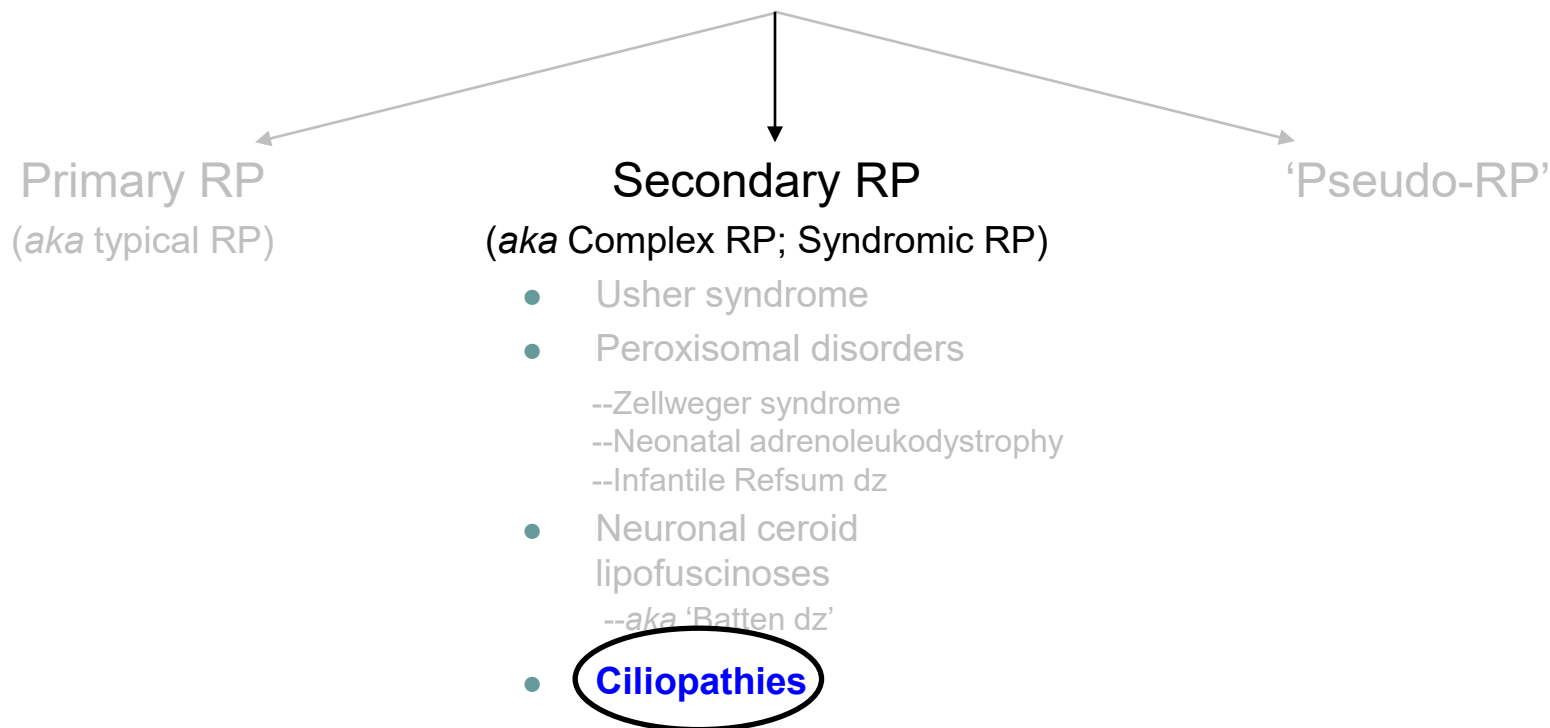
An inherited condition marked by abnormal structure and/or function of cilia

Cilia are ubiquitous. That said, ciliopathies primarily affect three organs—what are they?

The eyes, brain and kidneys



DDx for an RP-like Fundus



What is a ciliopathy?

An inherited condition marked by abnormal structure and/**function of cilia**

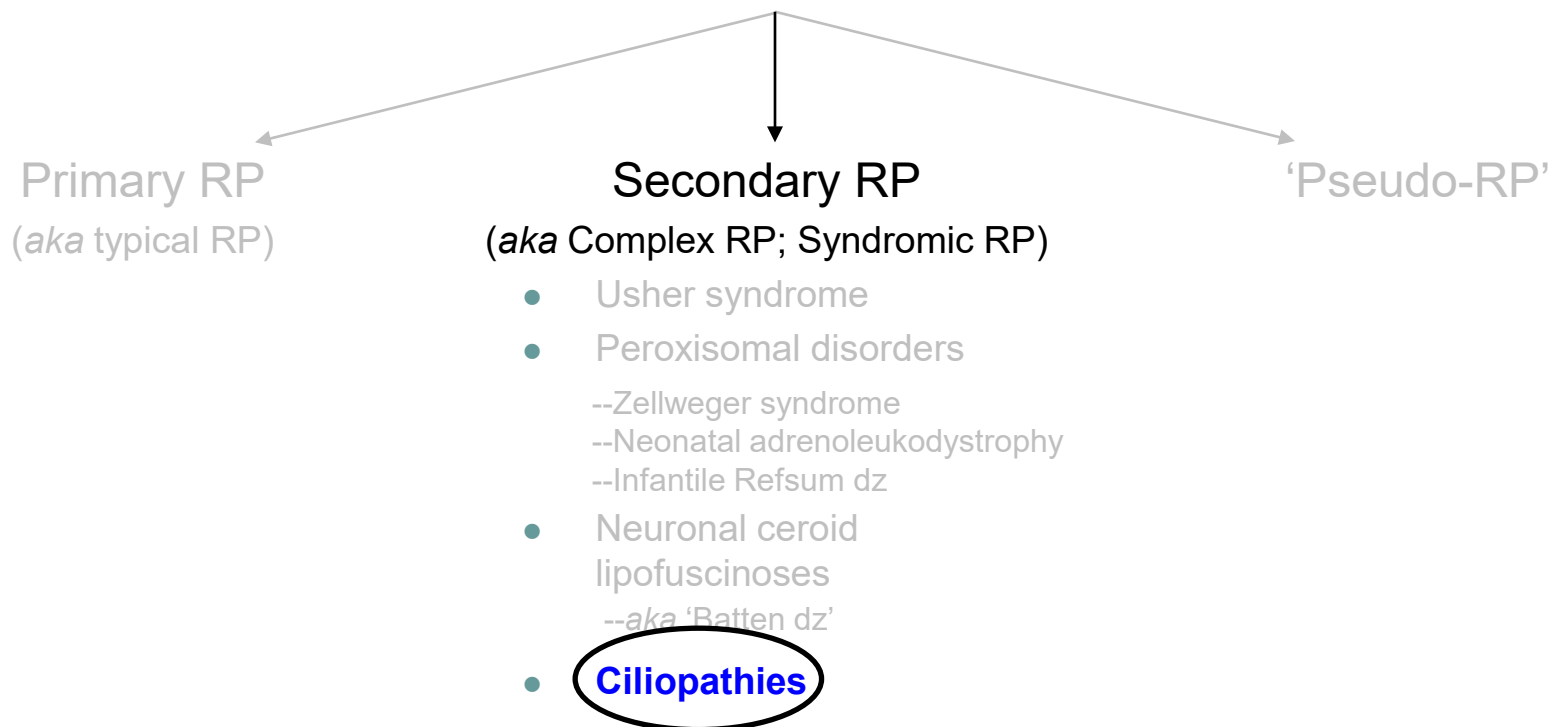
Cilia are organelles found in many cells of the body, including the eyes and brain.

The eyes

The eyes??!! Which part of the eye contains cilia wiggling about?



DDx for an RP-like Fundus



What is a ciliopathy?

An inherited condition marked by abnormal structure and/or **function of cilia**

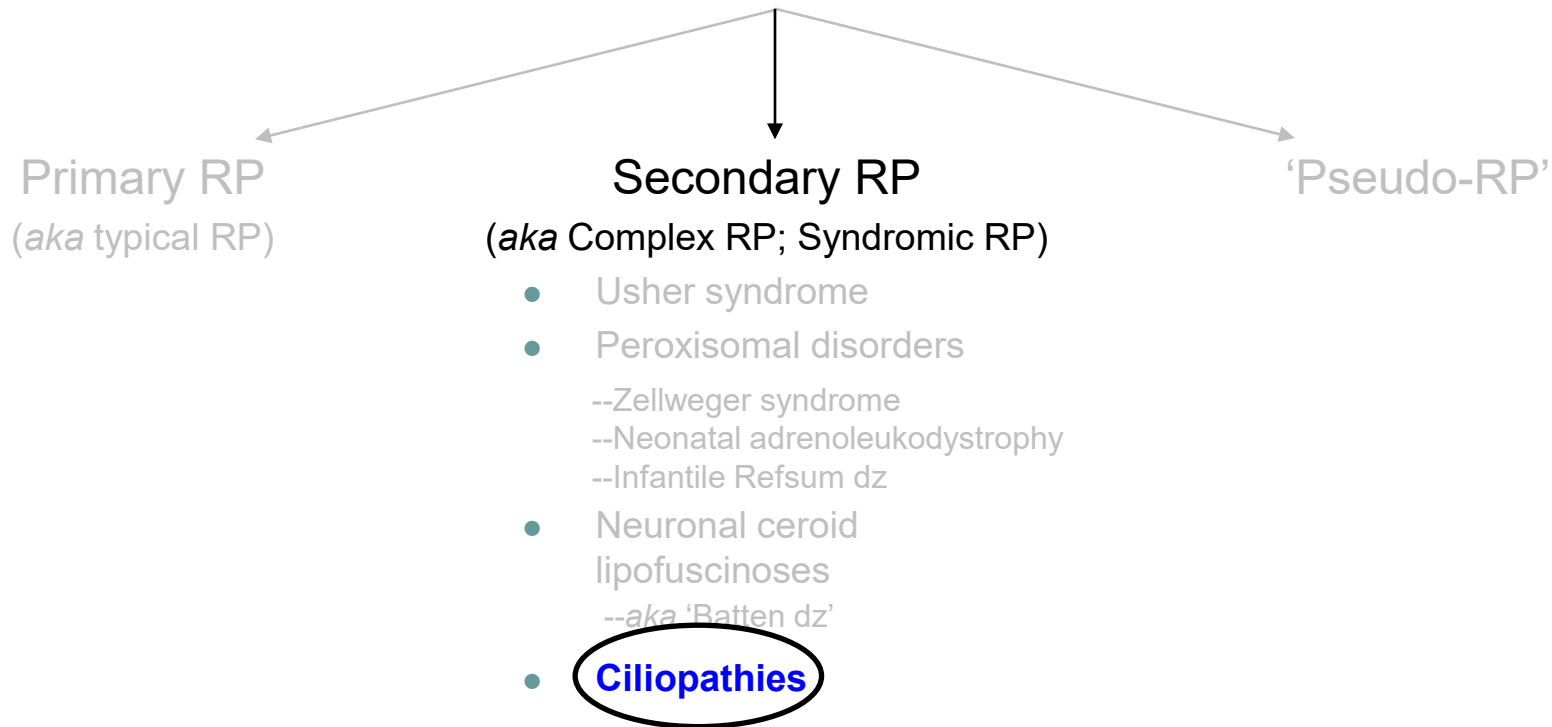
Cilia are organelles found in many types of cells, including those in the brain.

The eyes

The eyes??!! Which part of the eye contains cilia wiggling about?

None. Remember, cilia come in two basic flavors: Motile, and nonmotile. It is the **nonmotile** type which is ubiquitous in the eye.

DDx for an RP-like Fundus



OK then, where in the eye are the nonmotile cilia, dysfunction of which leads to an RP-like fundus?

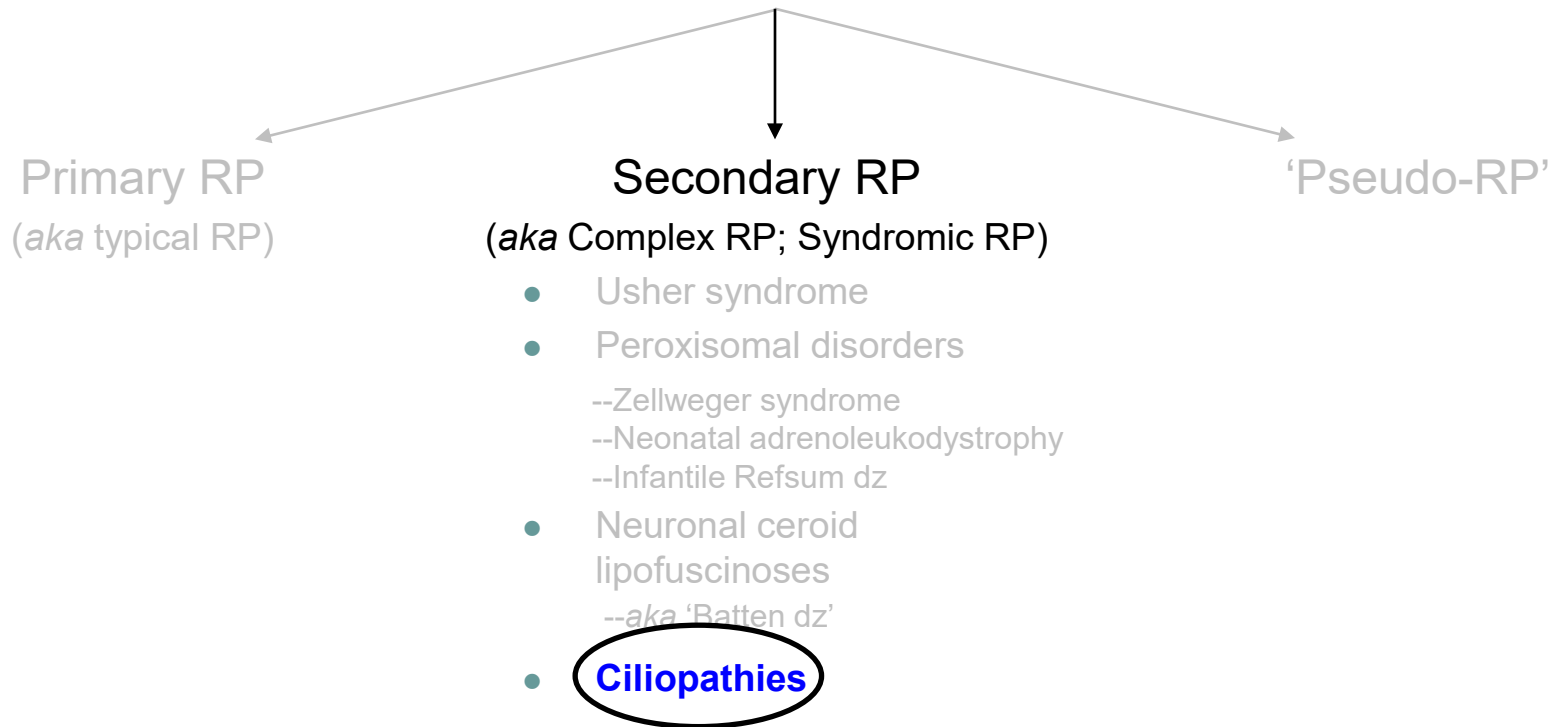
Cilia are organelles found in the brain

The eyes

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DDx for an RP-like Fundus



OK then, where in the eye are the nonmotile cilia, dysfunction of which leads to an RP-like fundus?
Recall that, fundamentally, RP is a one word disorder

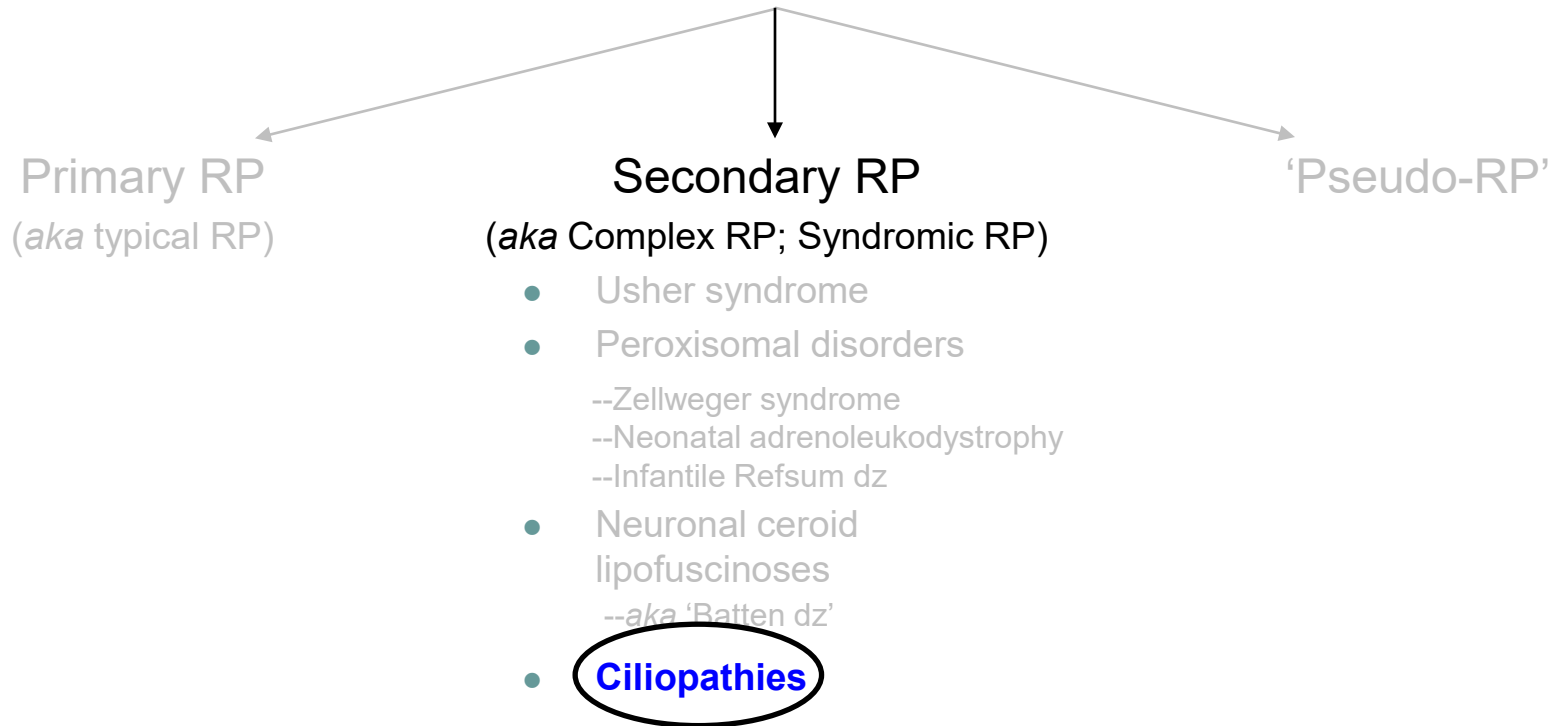
Cilia are organelles

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DDx for an RP-like Fundus



OK then, where in the eye are the nonmotile cilia, dysfunction of which leads to an RP-like fundus?
Recall that, fundamentally, RP is a photoreceptor disorder

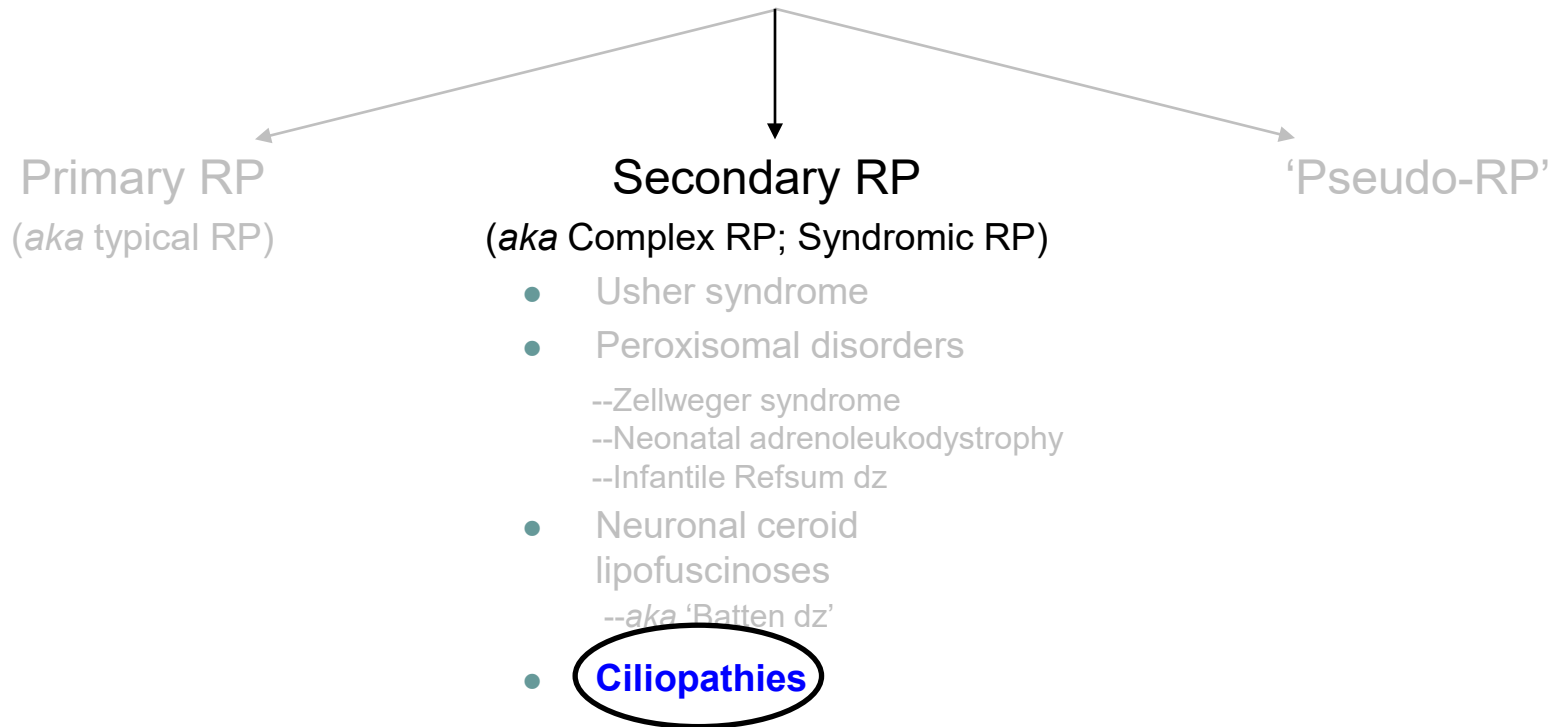
Cilia are organelles

The eyes

The eyes??!! Which part of the eye contains cilia wiggling about?

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OK then, where in the eye are the nonmotile cilia, dysfunction of which leads to an RP-like fundus? Recall that, fundamentally, RP is a photoreceptor disorder. Given this, it should come as no surprise that nonmotile cilia comprise a portion of the photoreceptors themselves.

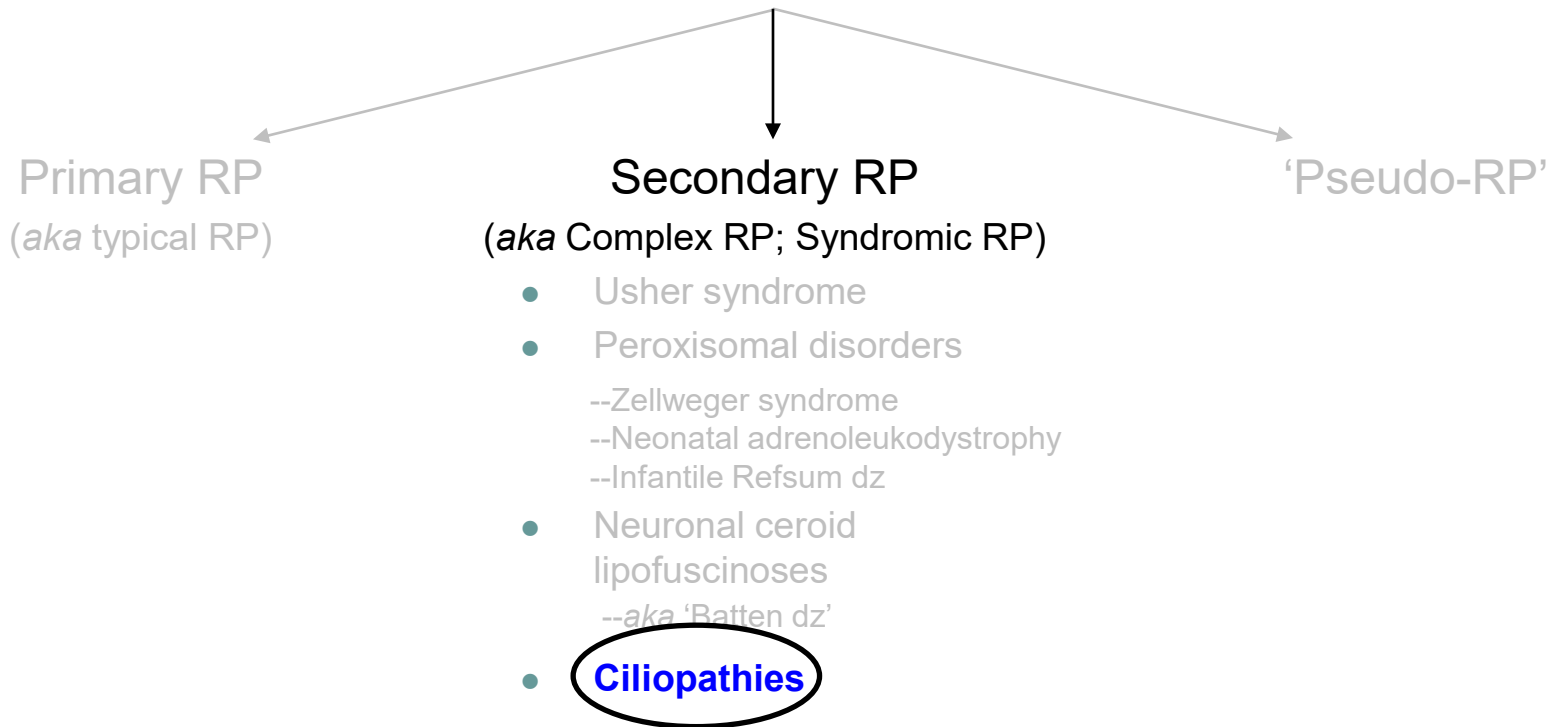
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DDx for an RP-like Fundus



As for where in the PR complex the cilia is located: Let's review PR structure

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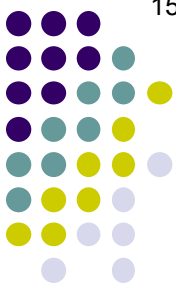
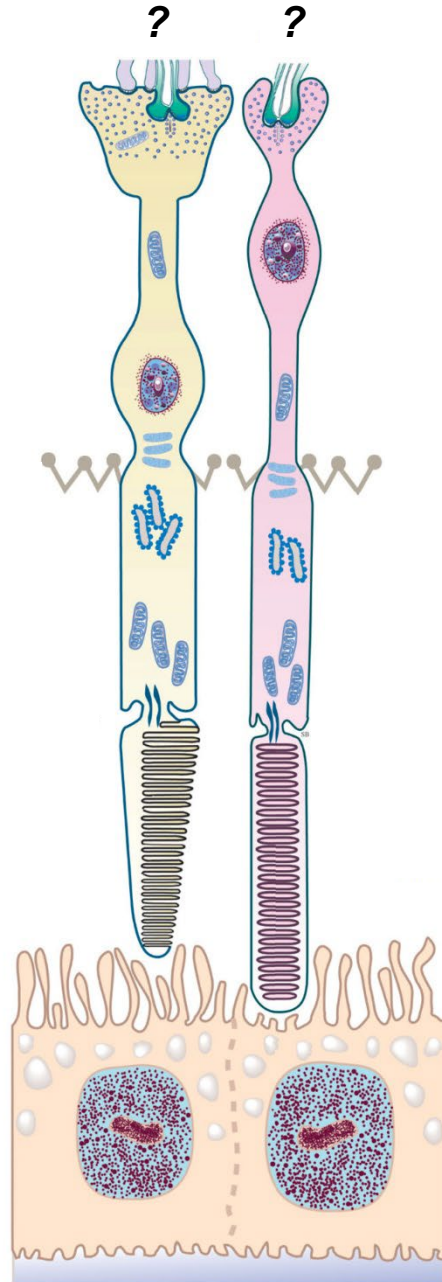
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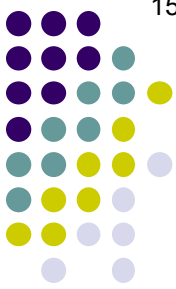
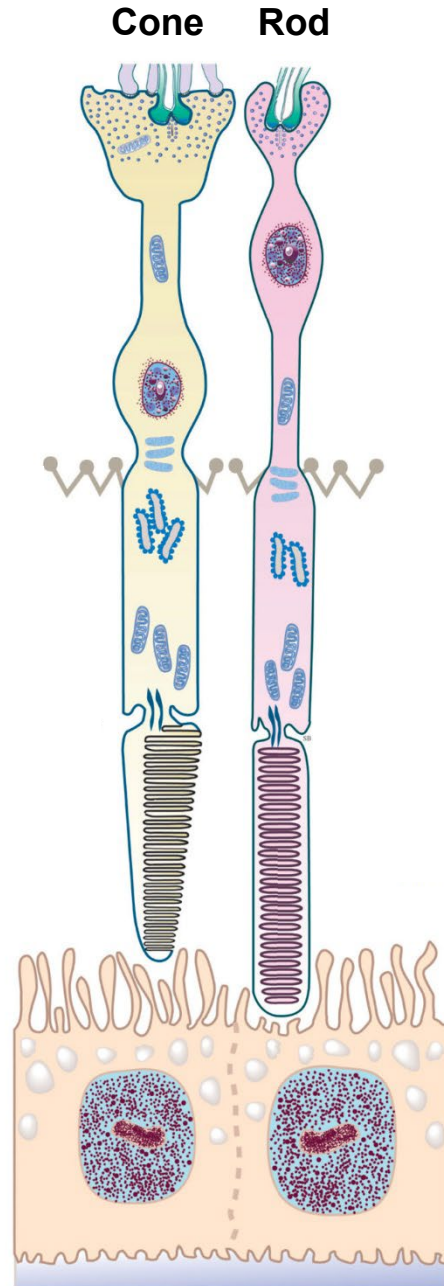
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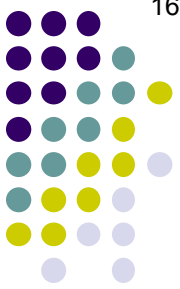
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First things first: Which is a cone, and which a rod?



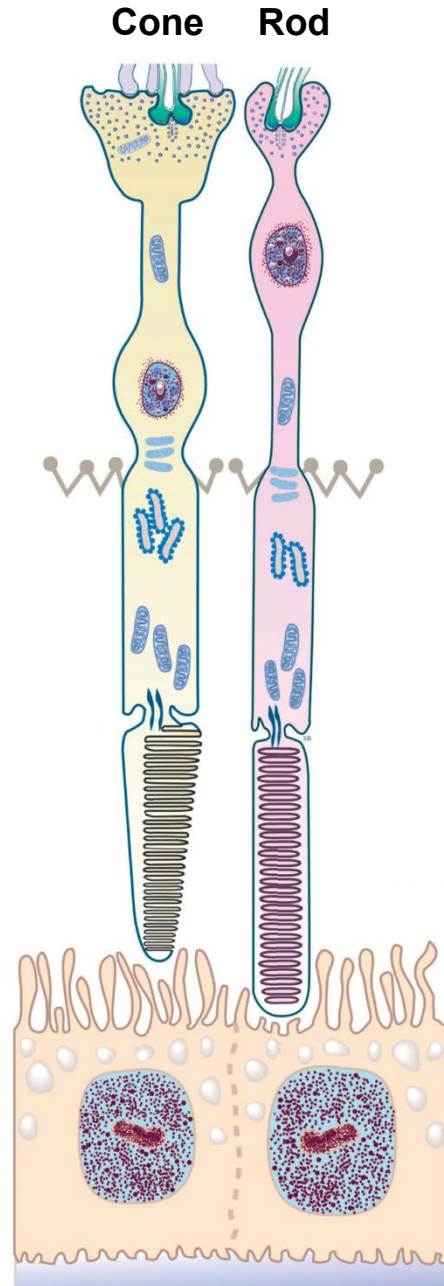
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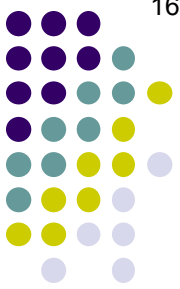




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How can you tell?



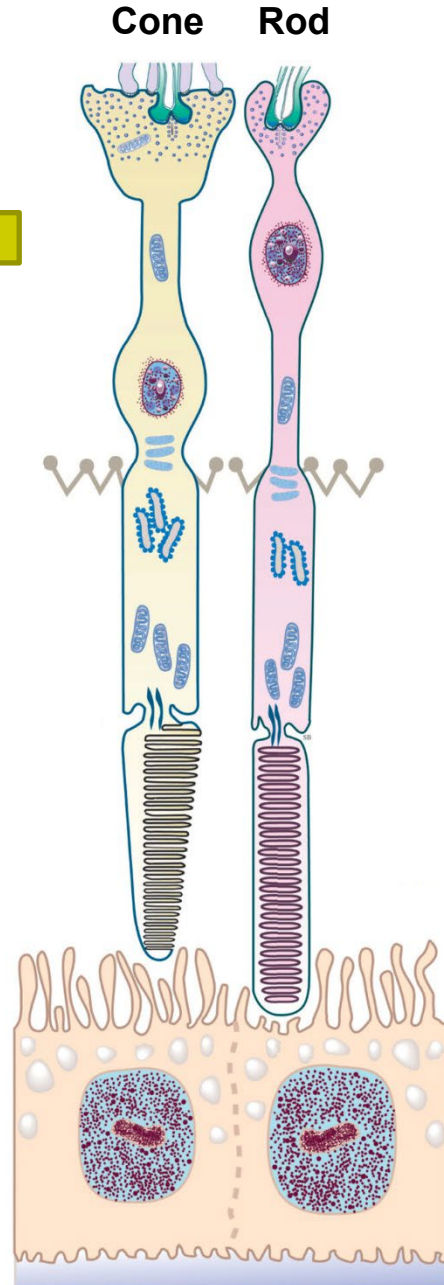


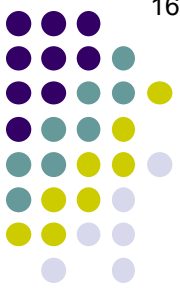
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How can you tell?

By the shape of their

two words

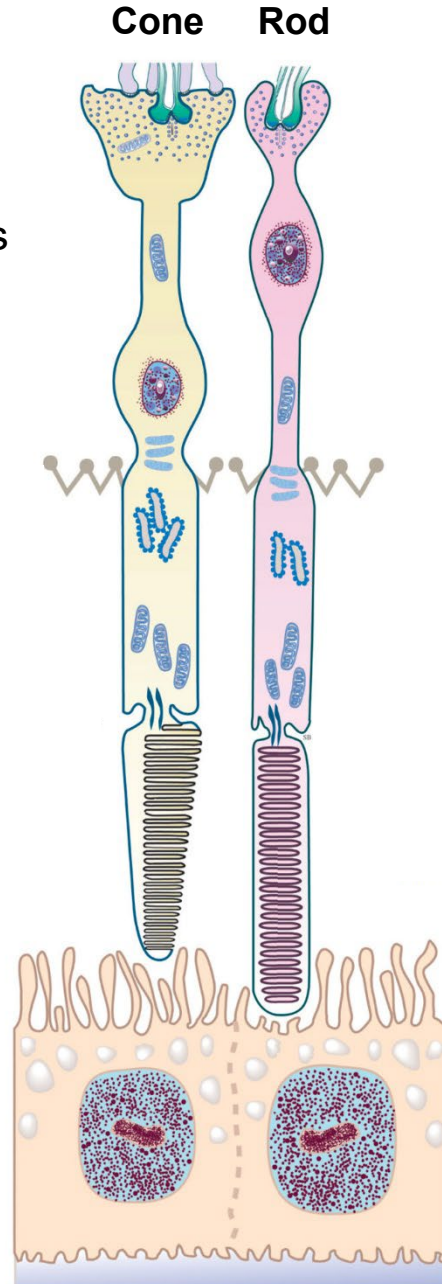


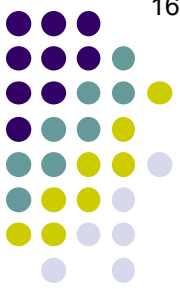


First things first: Which is a cone, and which a rod?

How can you tell?

By the shape of their outer segments



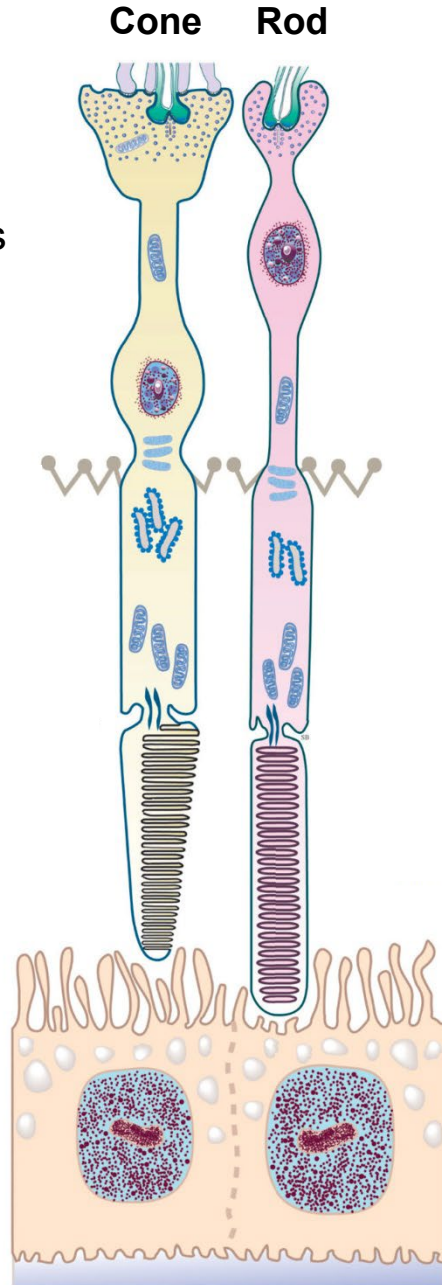


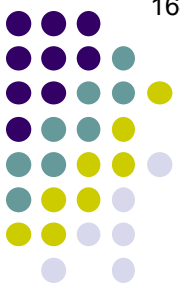
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Which portion constitutes their outer segments?





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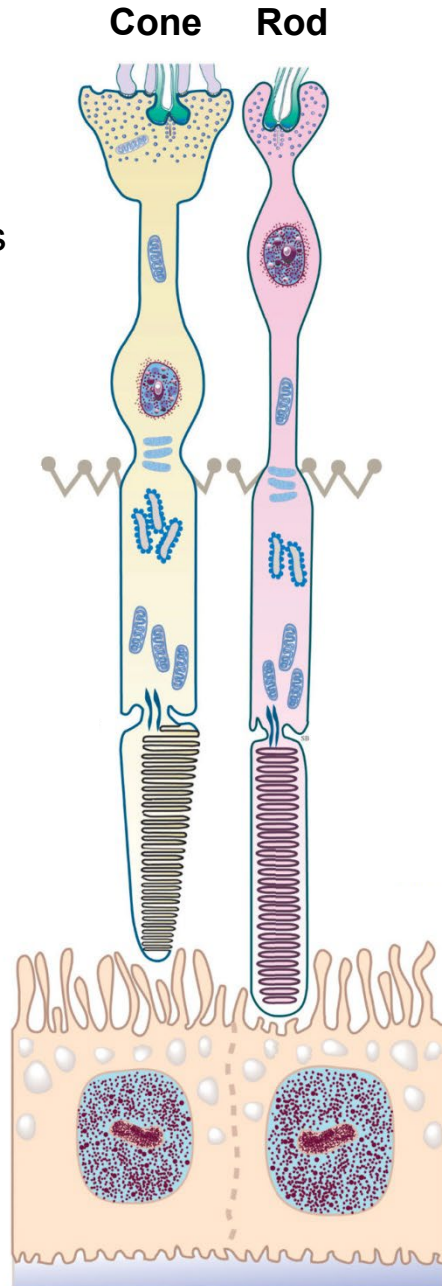
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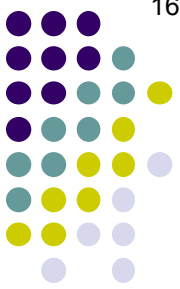
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Outer segment





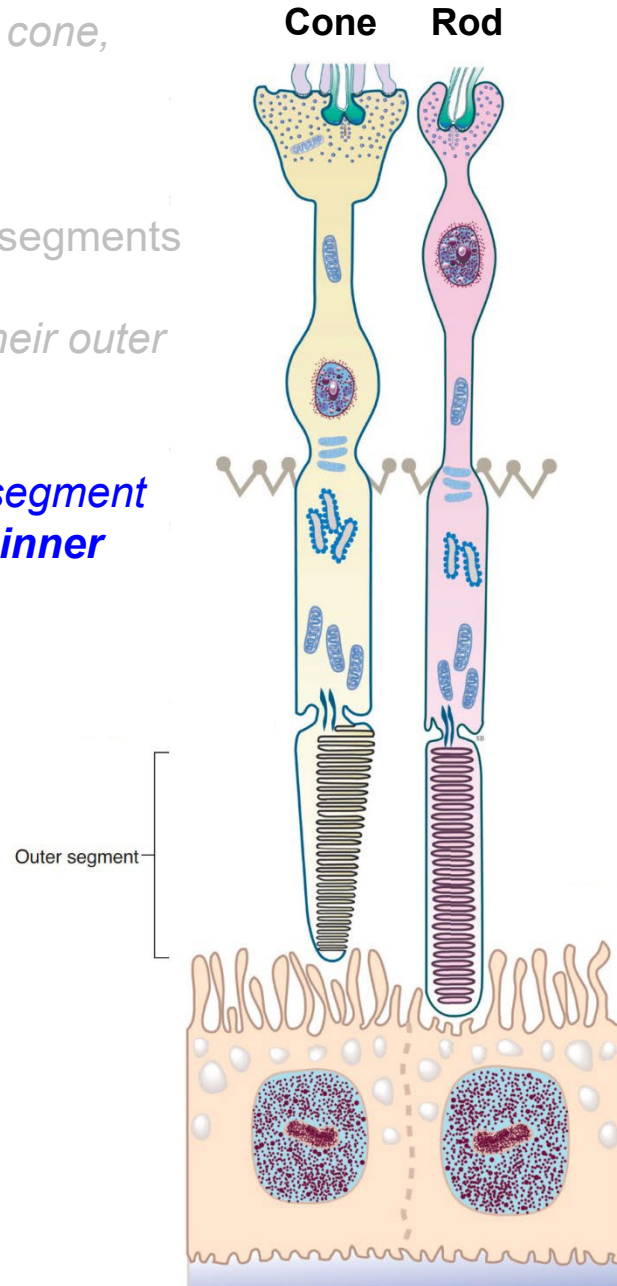
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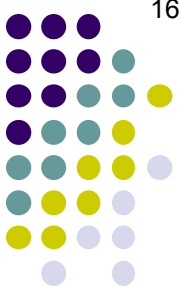
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By the shape of their outer segments

Which portion constitutes their outer segments?

*The presence of an **outer** segment implies the existence of an **inner** segment. Is this the case?*





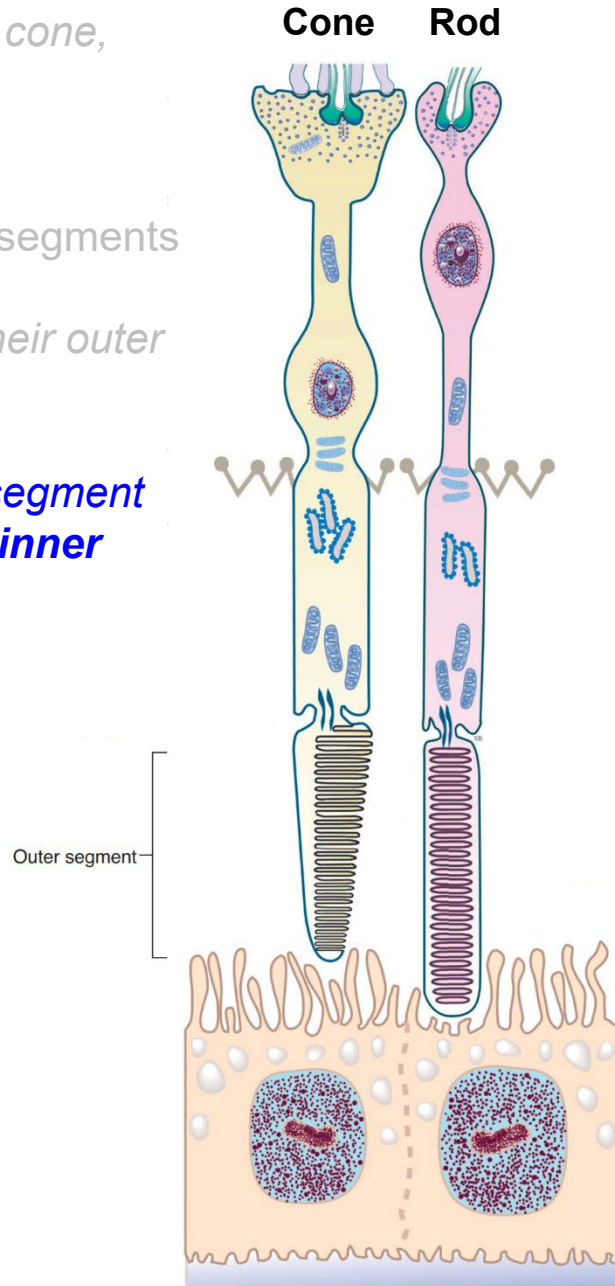
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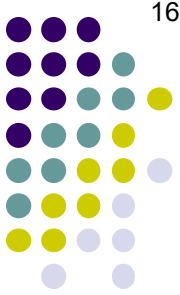
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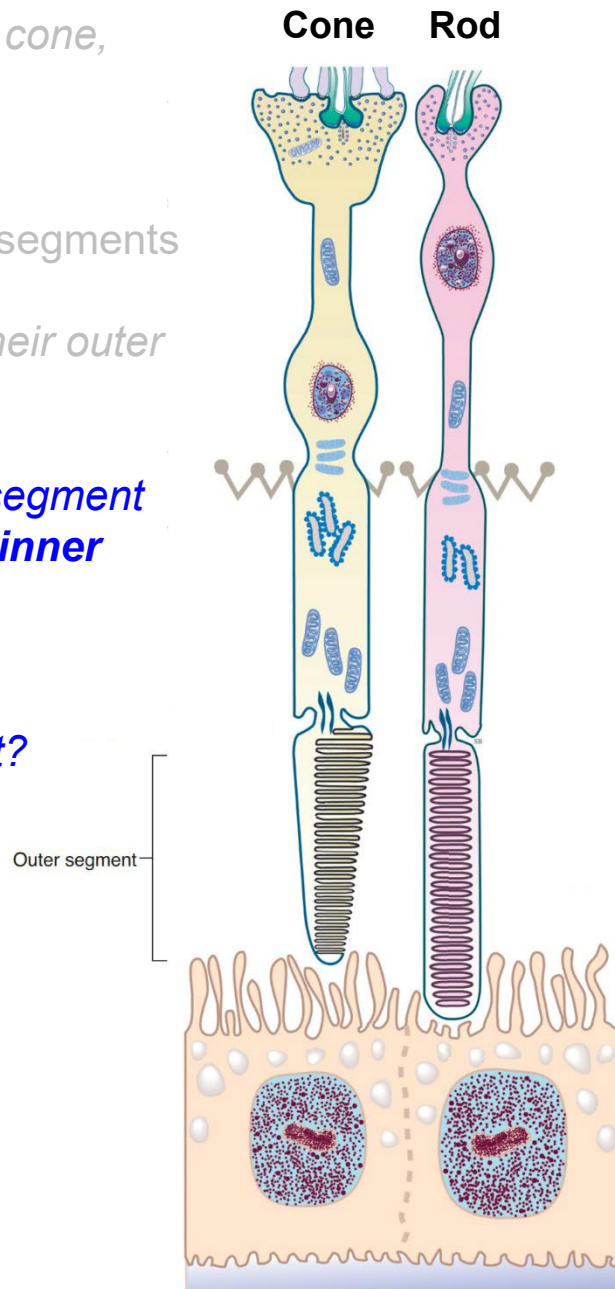
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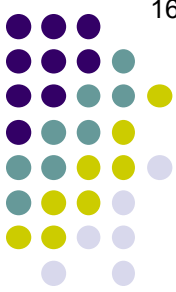
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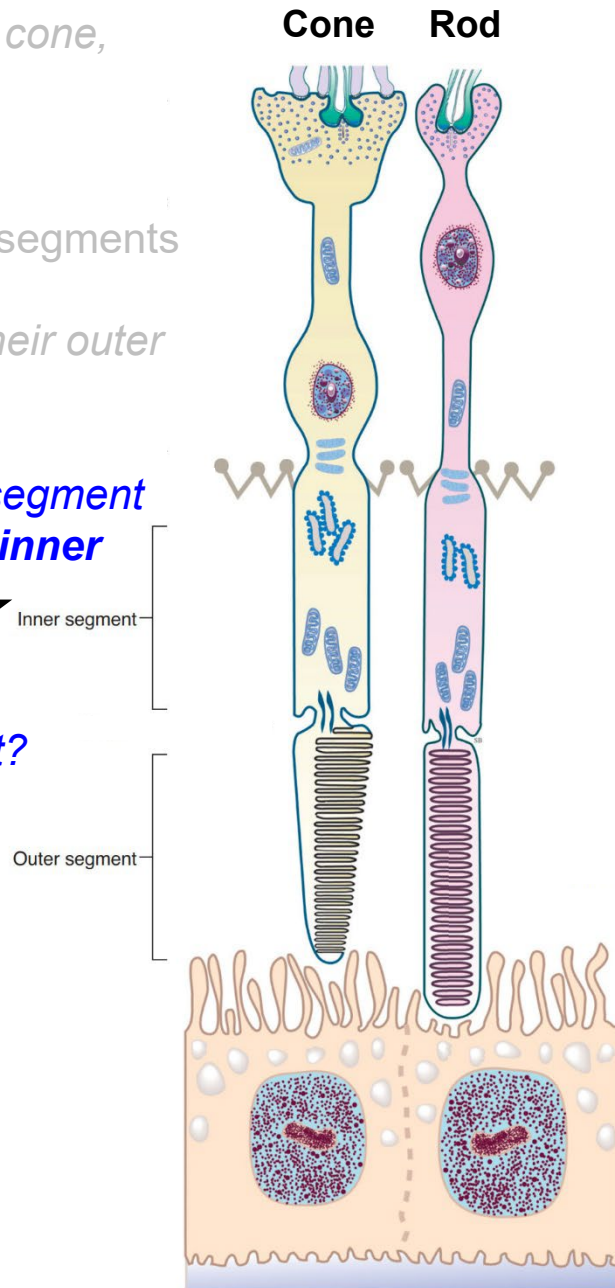
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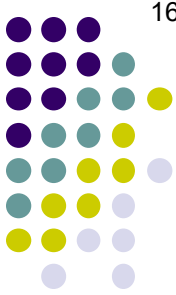
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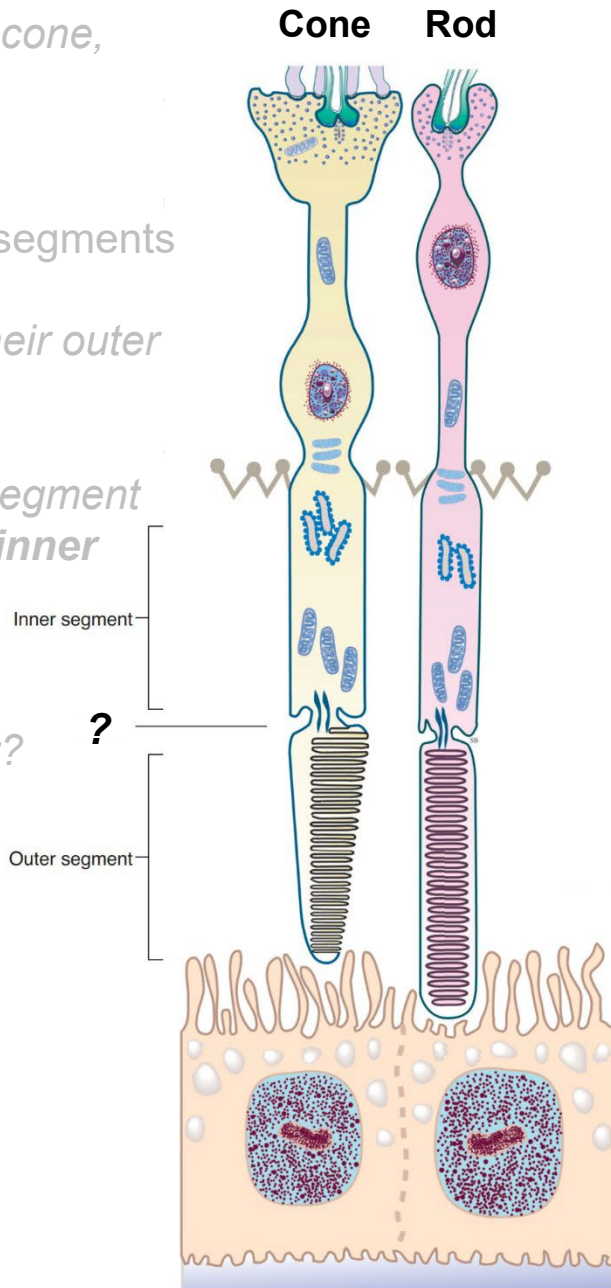
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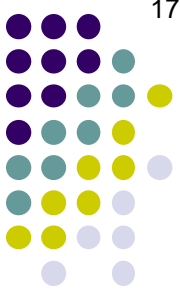
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Where is the inner segment?

What connects the inner and outer segments?





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How can you tell?

By the shape of their outer segments

Which portion constitutes their outer segments?

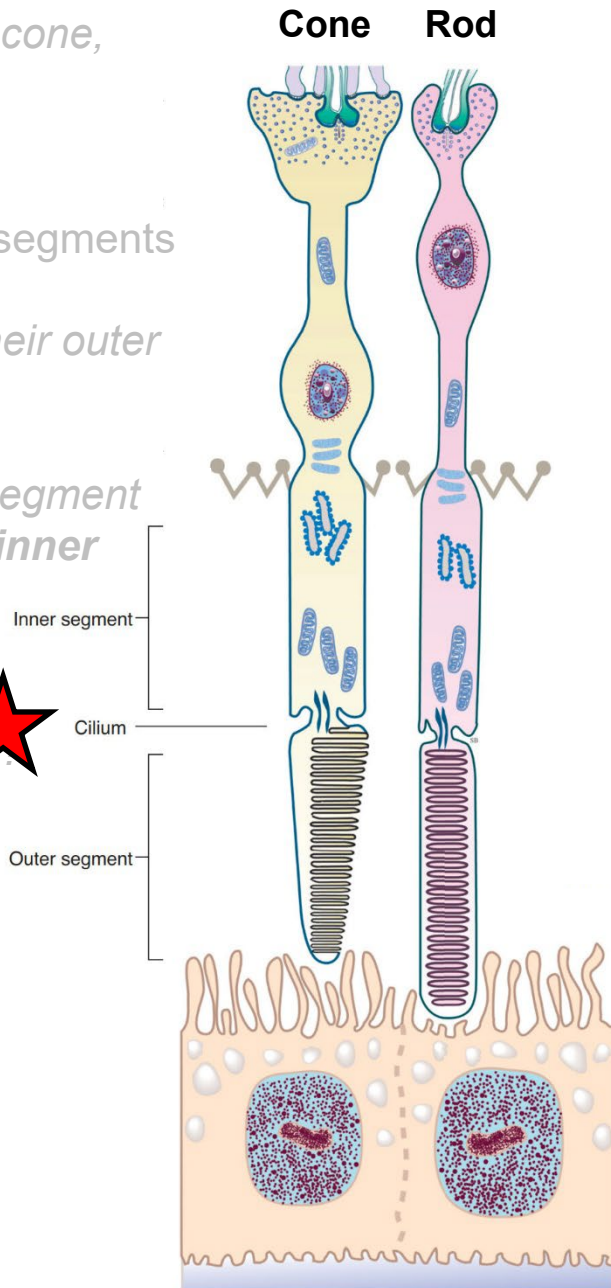
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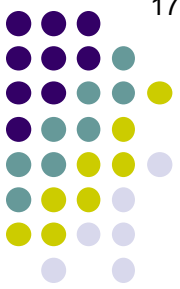
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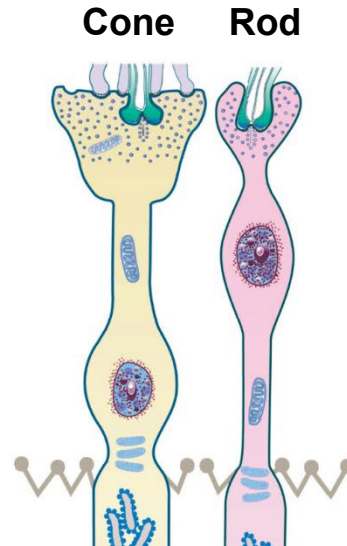
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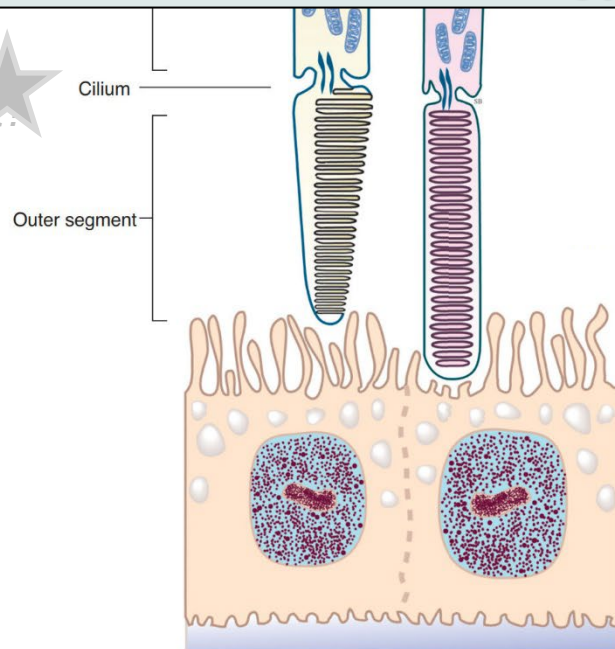
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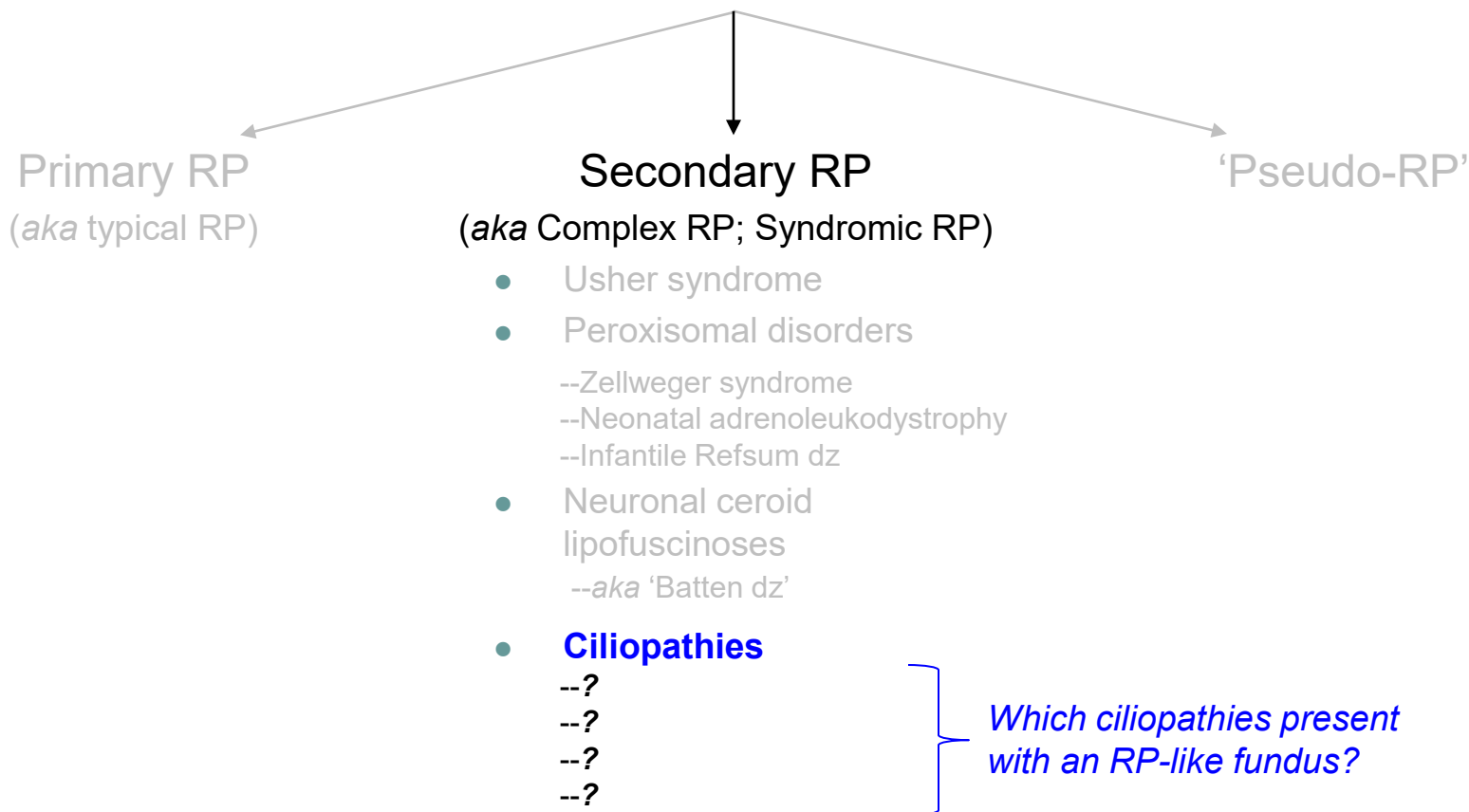


For more on PR and retinal histology, see slide-set R17





DDx for an RP-like Fundus



What is a ciliopathy?

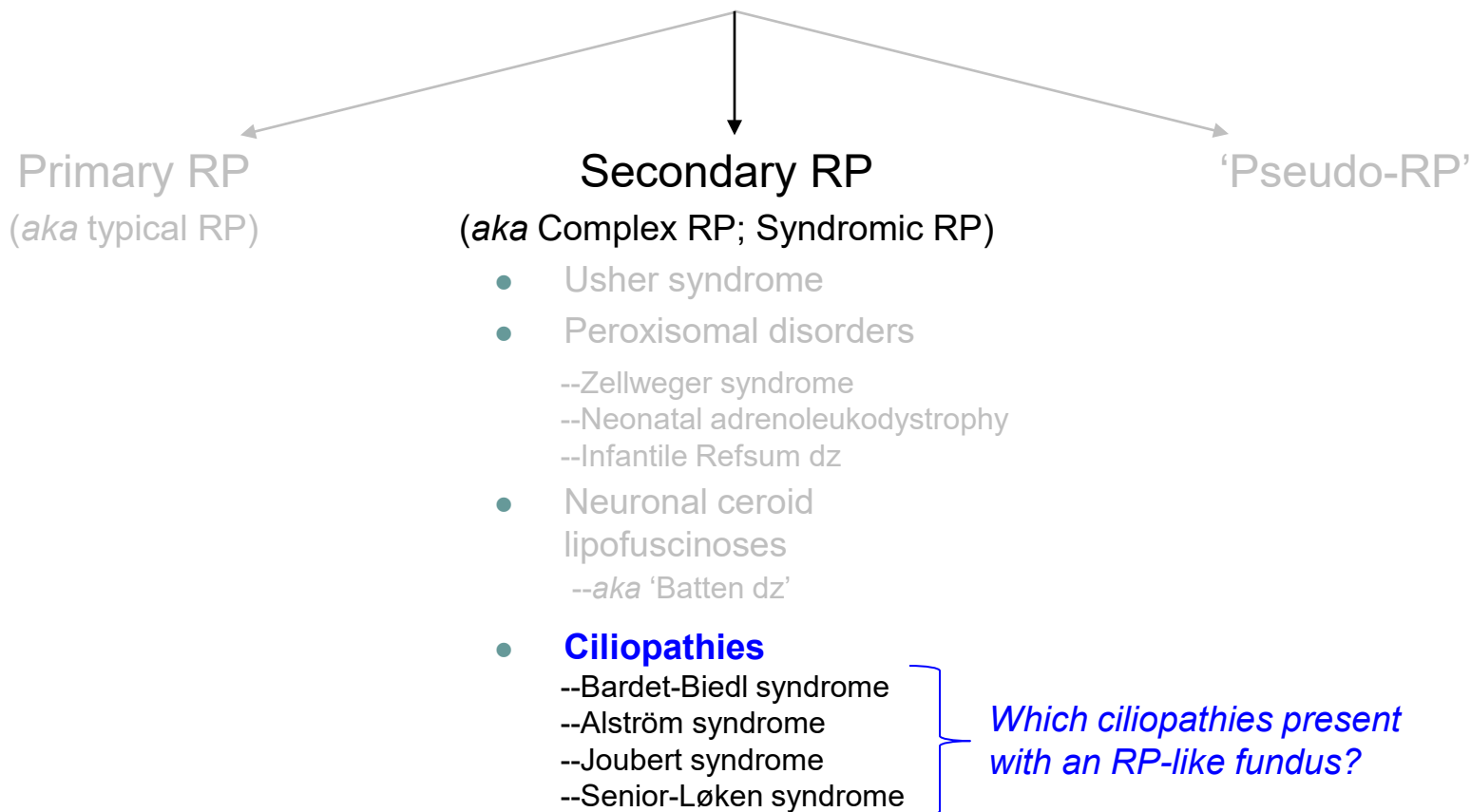
An inherited condition marked by abnormal structure and/or function of cilia

Cilia are ubiquitous. That said, ciliopathies primarily affect three organs--what are they?

The eyes, brain and kidneys



DDx for an RP-like Fundus



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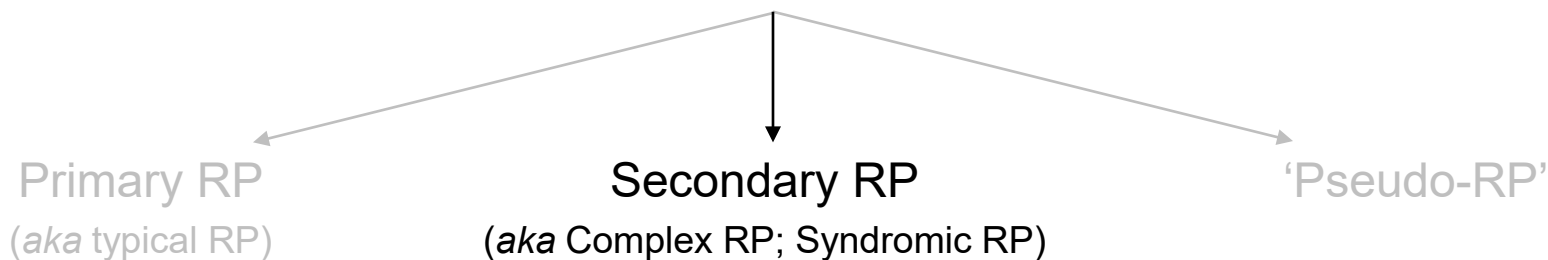
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 - Zellweger syndrome
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 - Infantile Refsum dz
- Neuronal ceroid lipofuscinoses
 - aka 'Batten dz'
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 - Joubert syndrome
 - Senior-Løken syndrome

Note that ***all of the ciliopathies are marked by relentlessly progressive renal failure*** resulting in ESRD early in life!

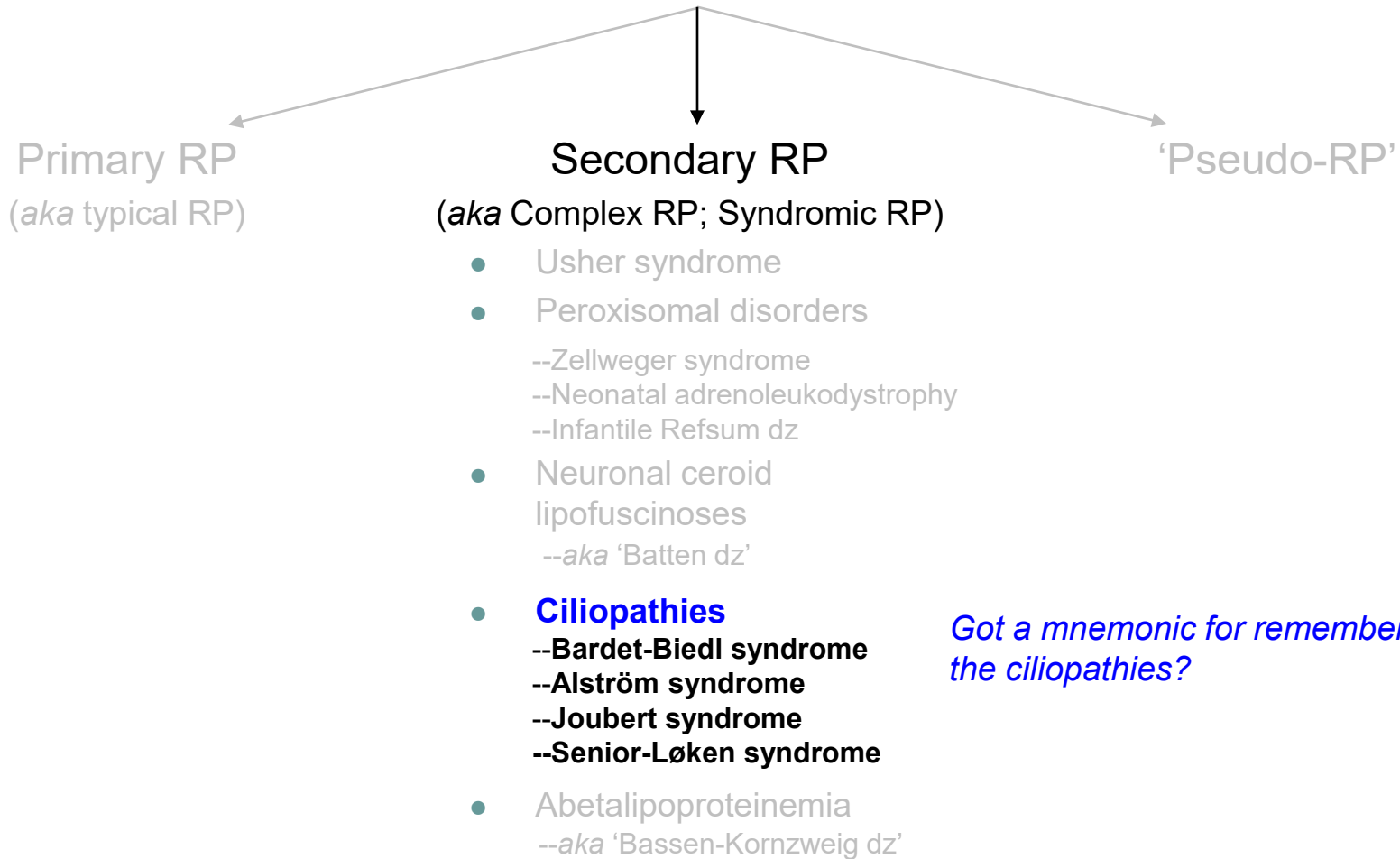
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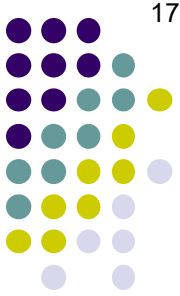
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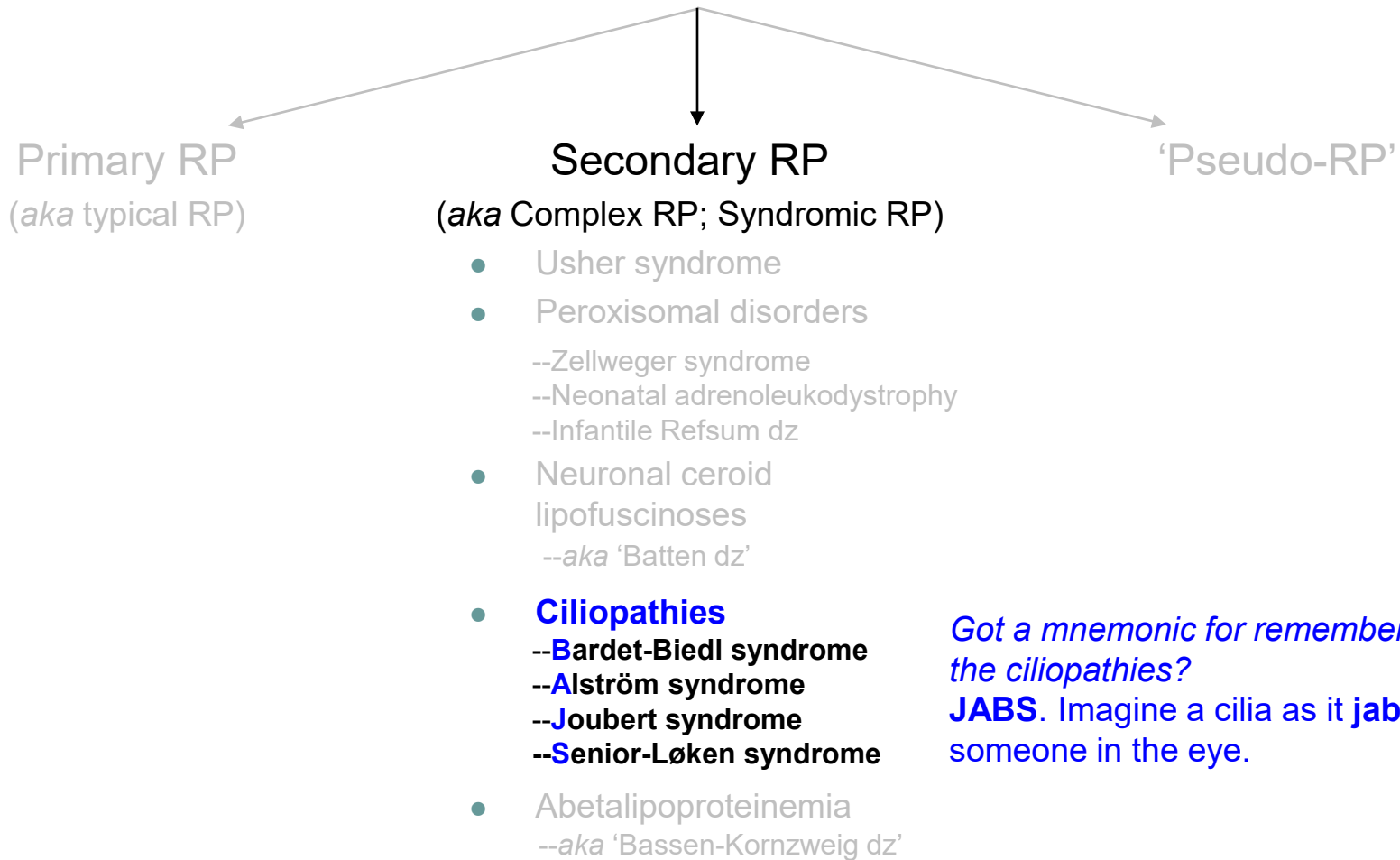
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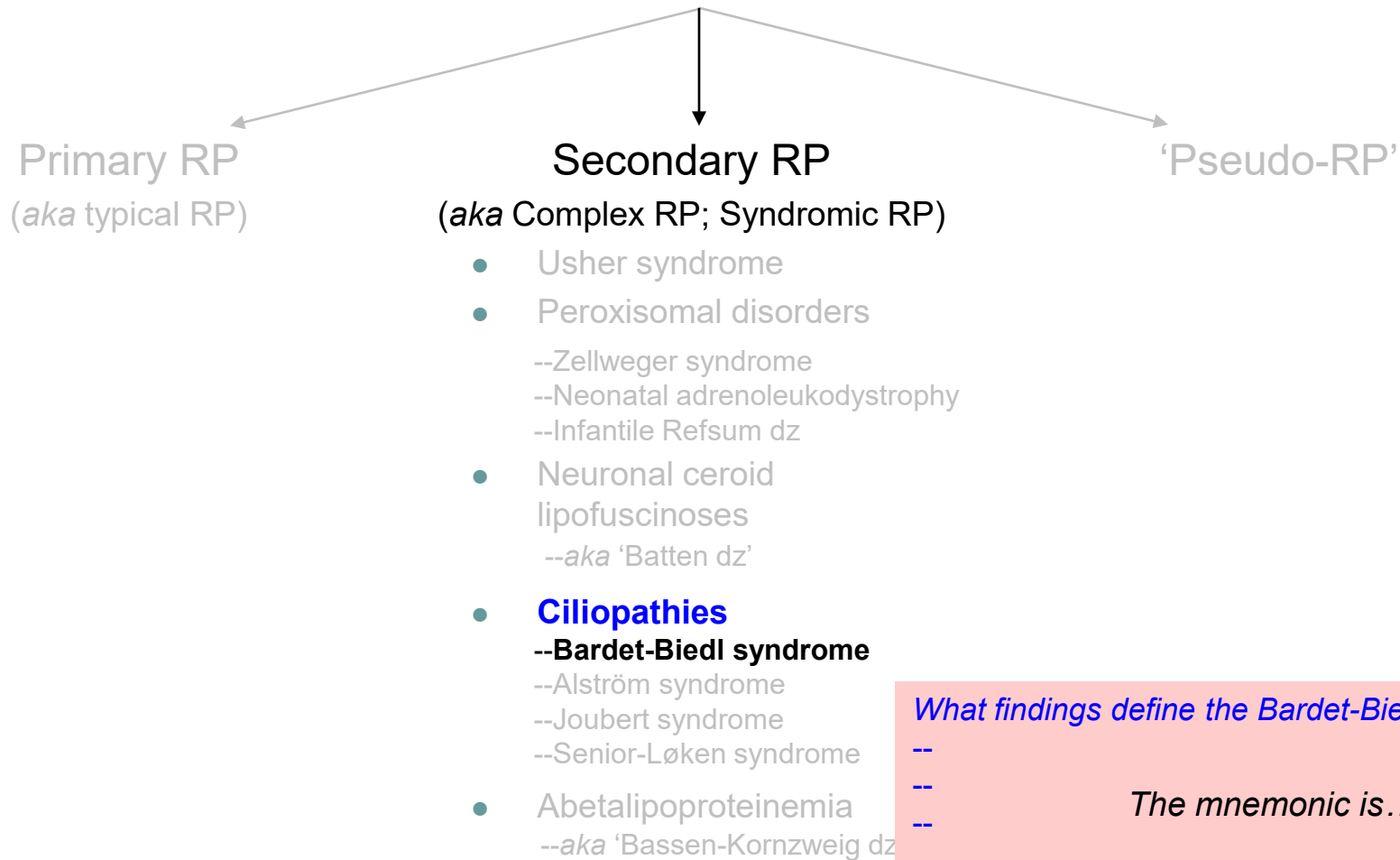
Got a mnemonic for remembering the ciliopathies?



DDx for an RP-like Fundus



DDx for an RP-like Fundus

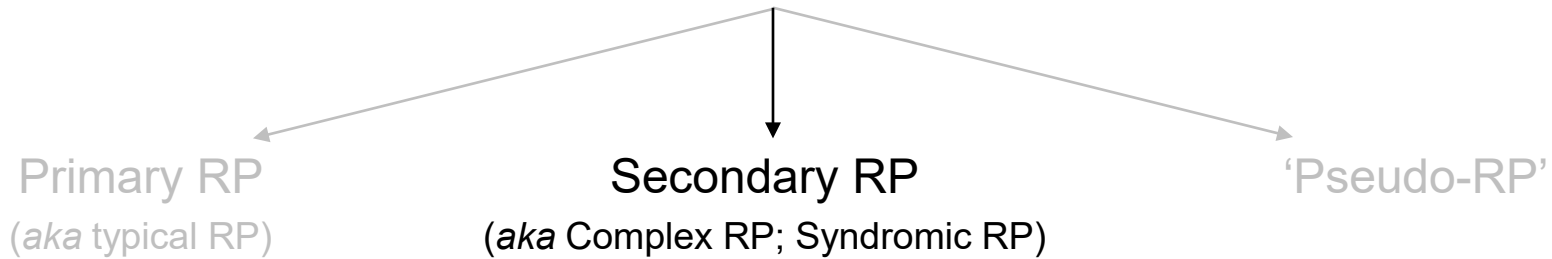


What findings define the Bardet-Biedl complex?

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The mnemonic is...

DDx for an RP-like Fundus



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What findings define the Bardet-Biedl complex?

--H
--O
--M
--E
--R

(as in Simpson)

DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP
(aka Complex RP; Syndromic RP)

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What findings define the Bardet-Biedl complex?

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--RP-like fundus

*Not surprisingly, the 'R' stands for RP-like fundus.
As for the rest...*

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What findings define the Bardet-Biedl complex?

- Hypogonadism
- Obesity
- Mental retardation
- Extra fingers (polydactyly)
- RP-like fundus

*Not surprisingly, the 'R' stands for RP-like fundus.
As for the rest...*

DDx for an RP-like Fundus

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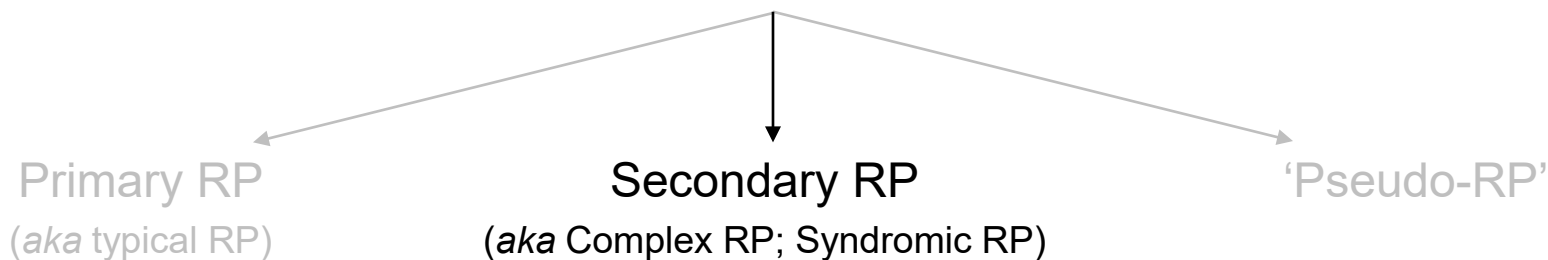
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- H**ypogonadism
- O**besity
- M**ental retardation
- E**xtra fingers (polydactyly)
- R**P-like fundus

And yeah, I know, Homer only has four digits per hand--paucidactyly, not polydactyly. But the rest fits him pretty well.



DDx for an RP-like Fundus



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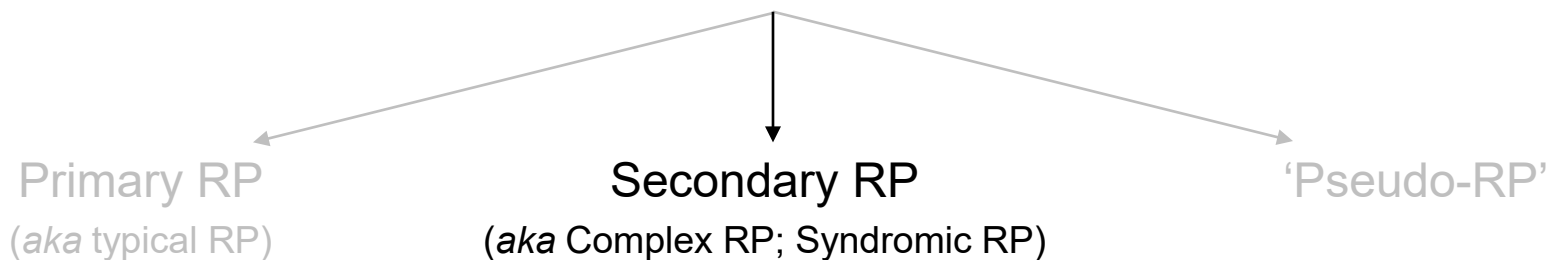
Alström syndrome includes an RP-like fundus (duh), but shares only one other finding with the B-B complex— which one?

What findings define the Bardet-Biedl complex?

- Hypogonadism?**
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DDx for an RP-like Fundus



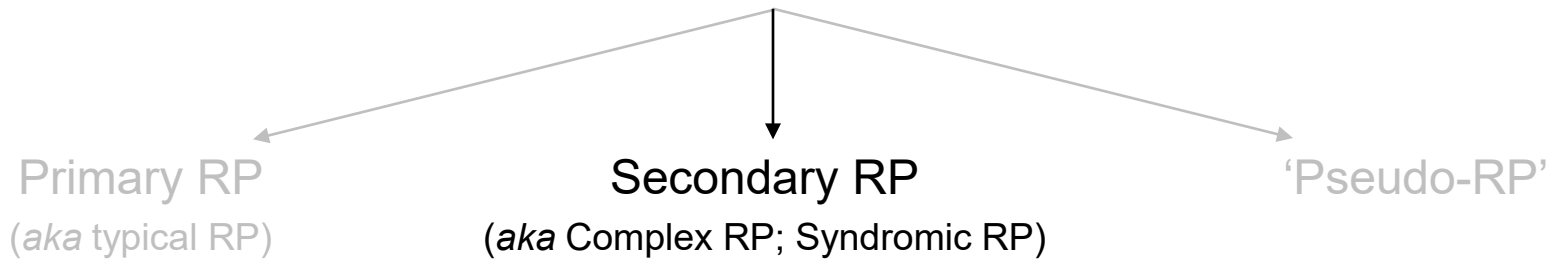
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DDx for an RP-like Fundus



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It has two features not found in B-B:
What are they?

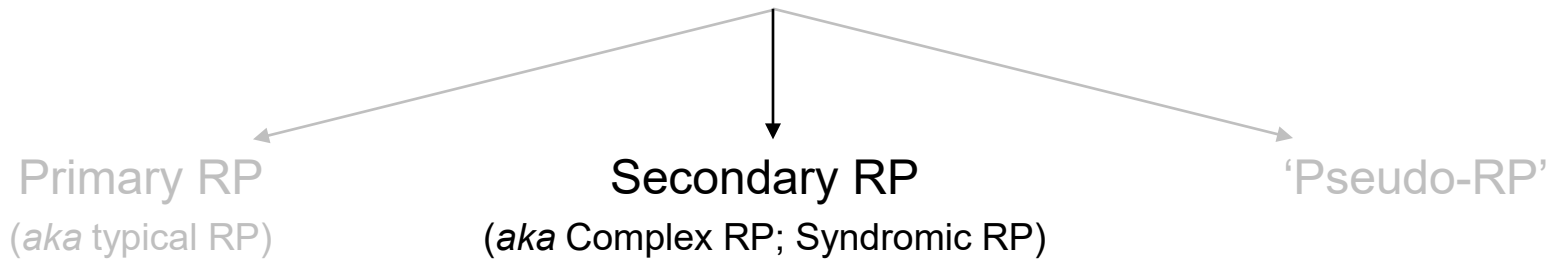
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--?
--?

Both occur in
childhood to teens

DDx for an RP-like Fundus



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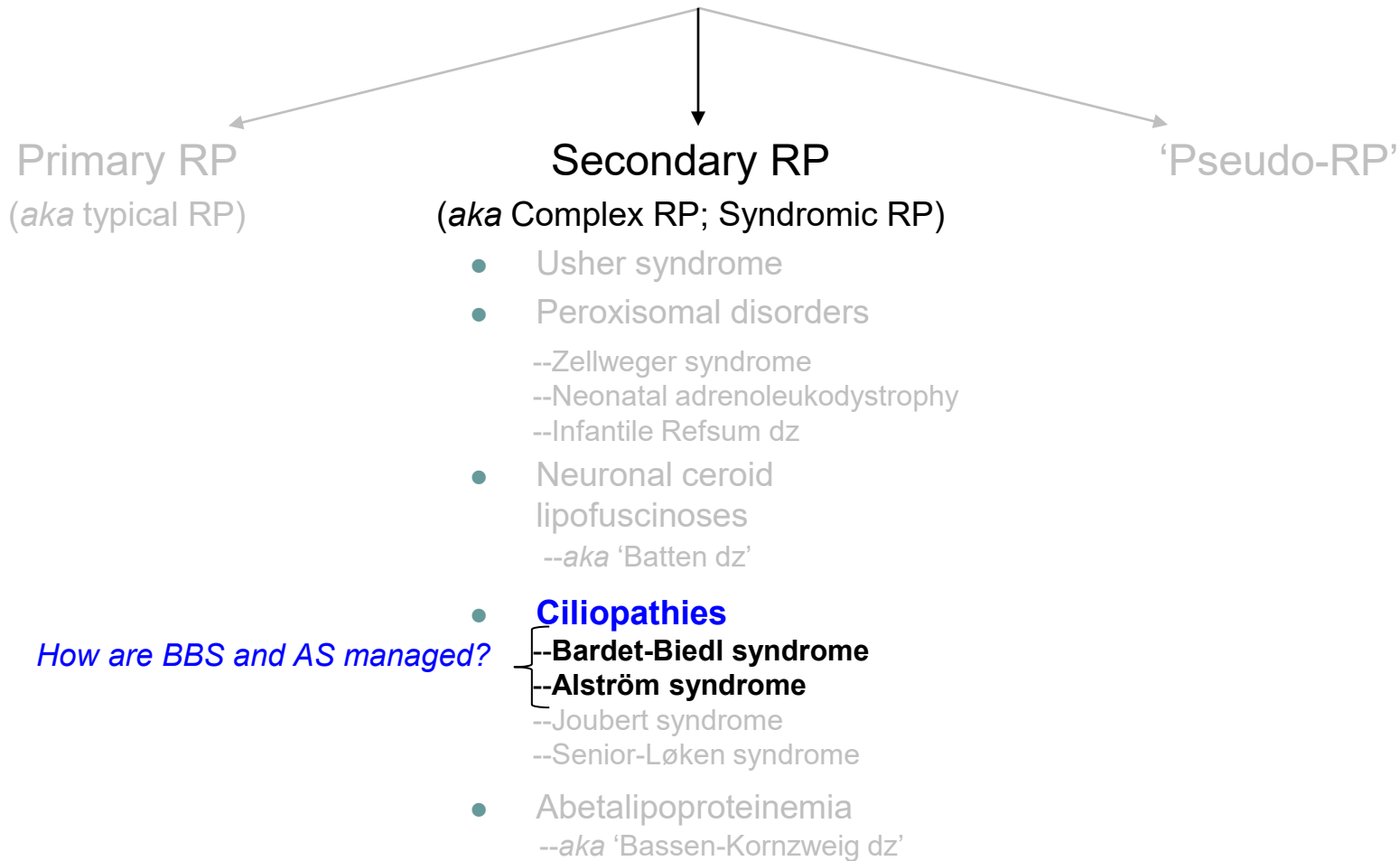
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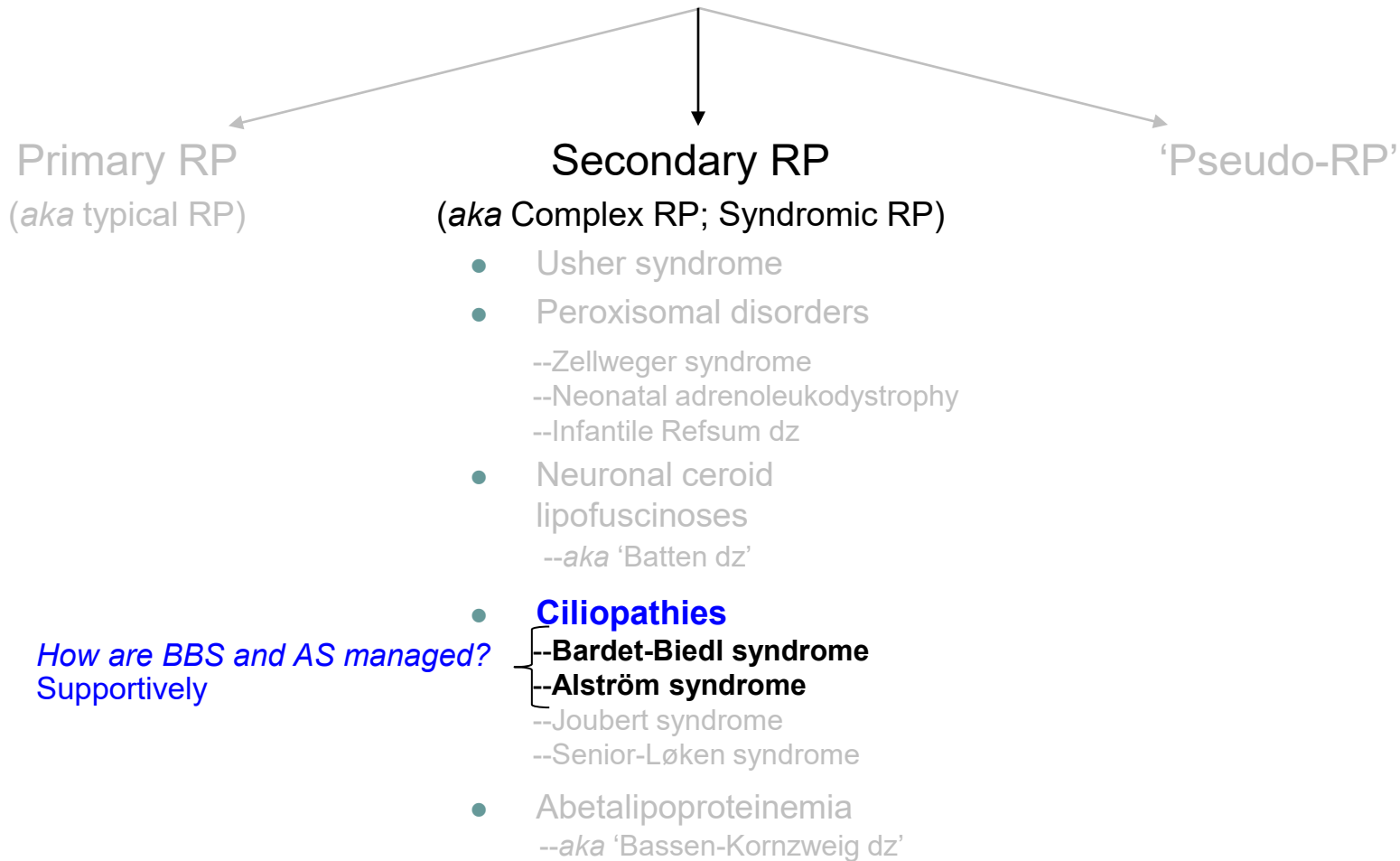
- Cardiomyopathy**
- Early-onset type 2 DM**

Both occur in childhood to teens

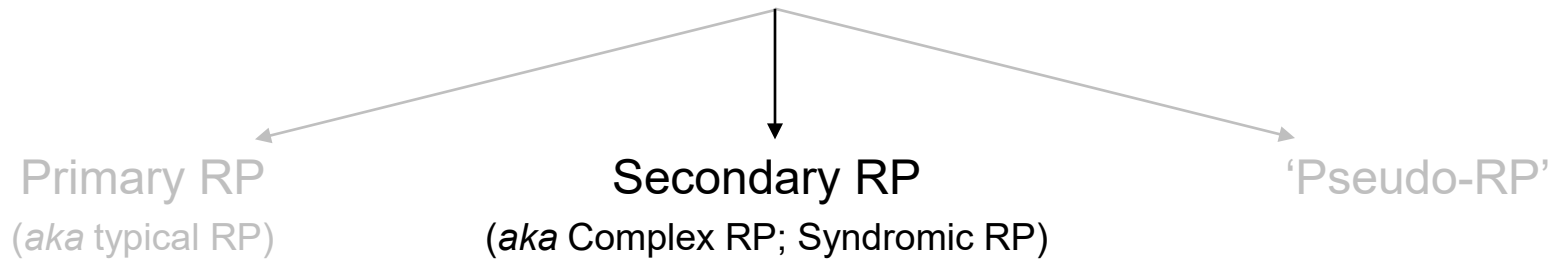
DDx for an RP-like Fundus



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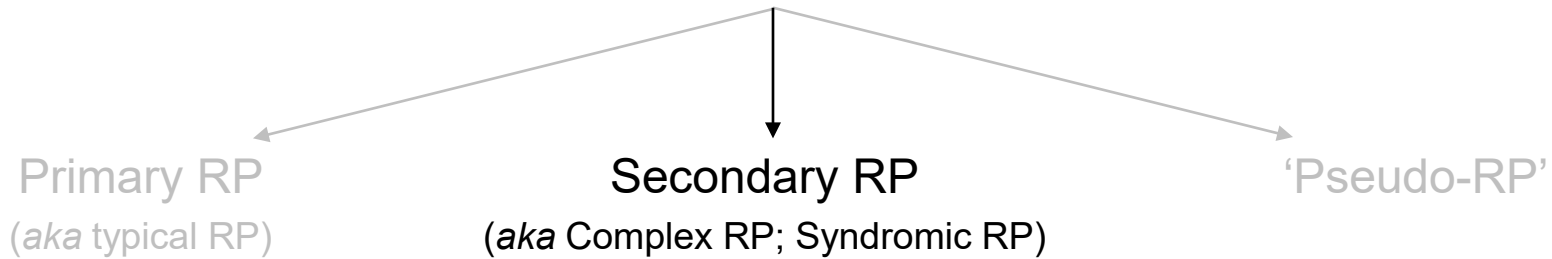


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What are the main nonocular structures affected in JS?



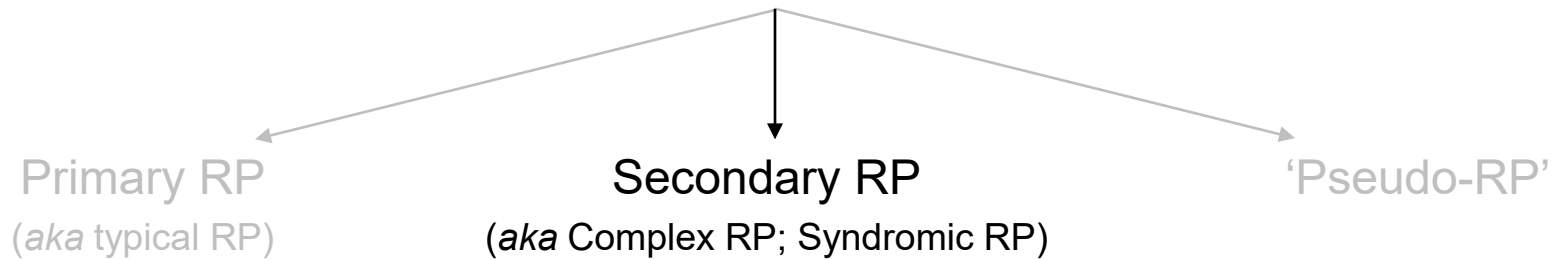
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What are the main nonocular structures affected in JS?
The brainstem and cerebellum

DDx for an RP-like Fundus

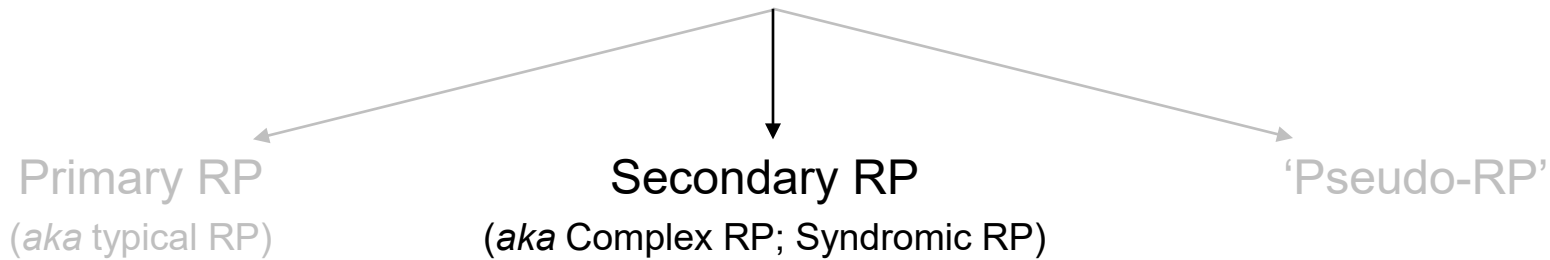


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What classic MRI finding is the hallmark of JS?

DDx for an RP-like Fundus

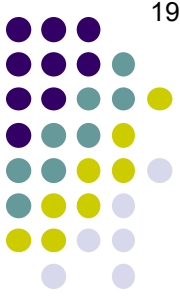


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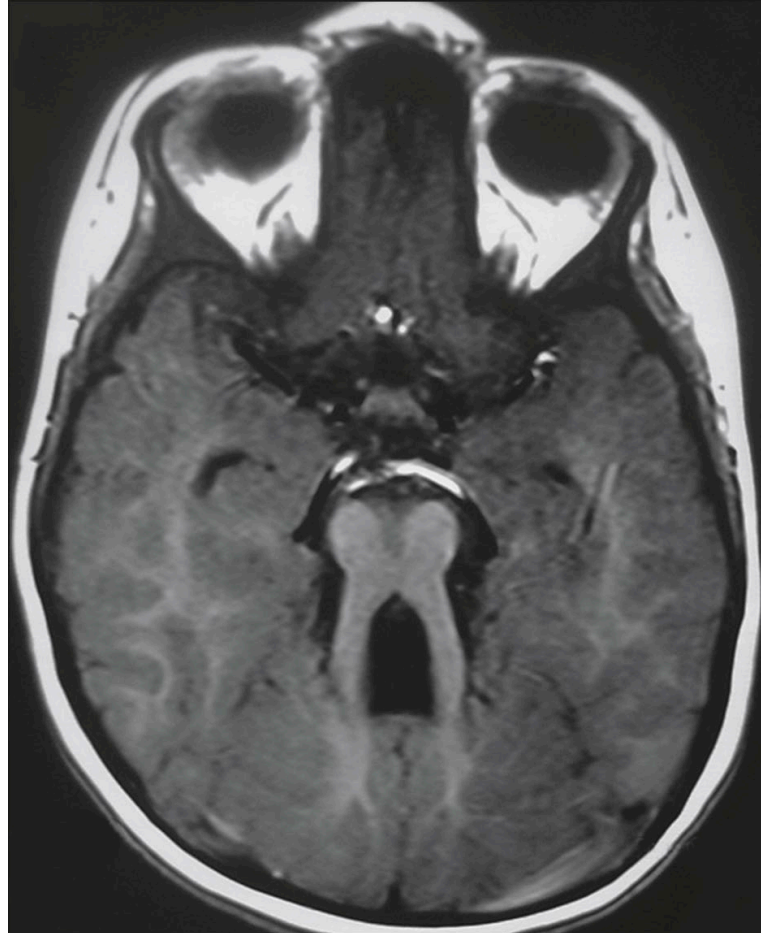
What are the main nonocular structures affected in JS?
The brainstem and cerebellum

What classic MRI finding is the hallmark of JS?
'Molar tooth sign'



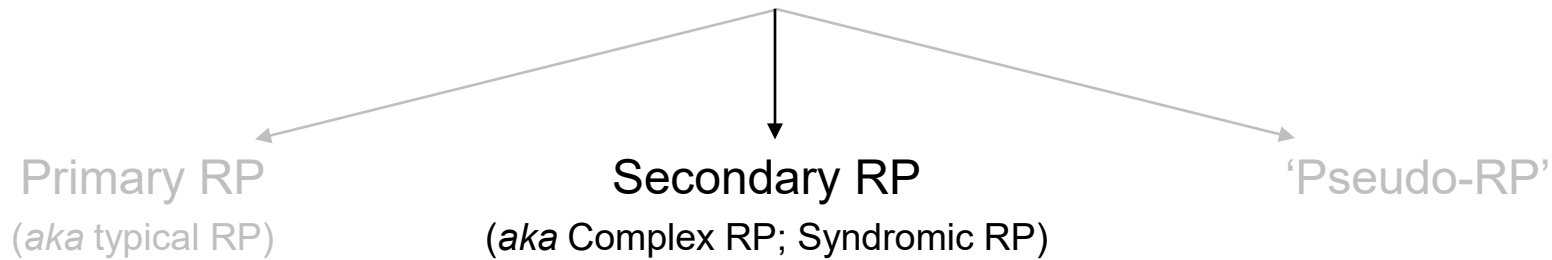


DDx for an RP-like Fundus



Joubert syndrome: Molar-tooth sign (look at the brainstem)

DDx for an RP-like Fundus



- Usher syndrome
- Peroxisomal disorders
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
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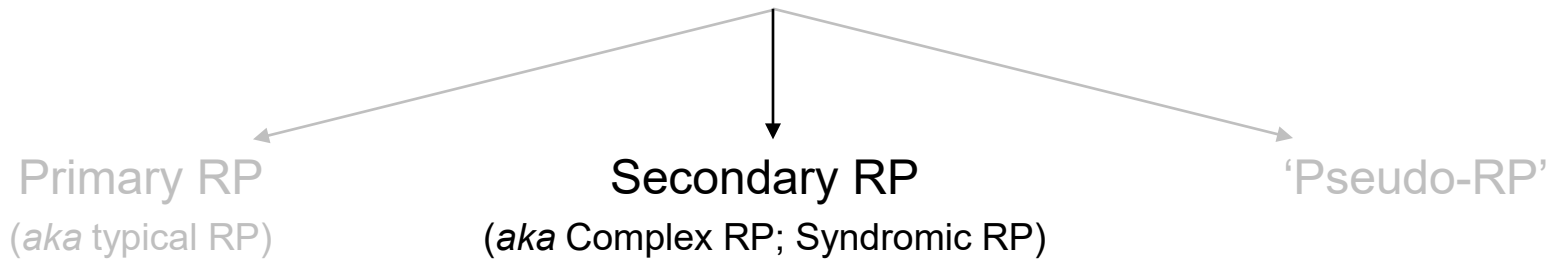
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DDx for an RP-like Fundus



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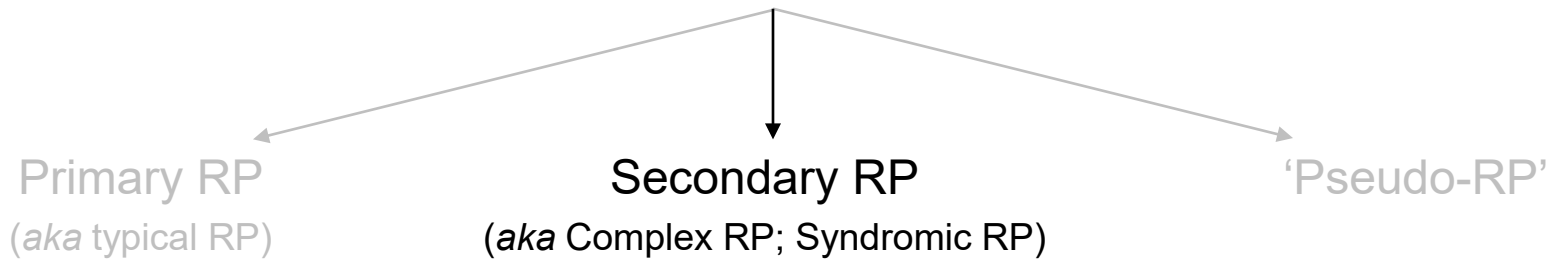
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--RP-like fundus

--?
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DDx for an RP-like Fundus



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- Intellectual and motor deficits
- Seizures
- Abnormal facies

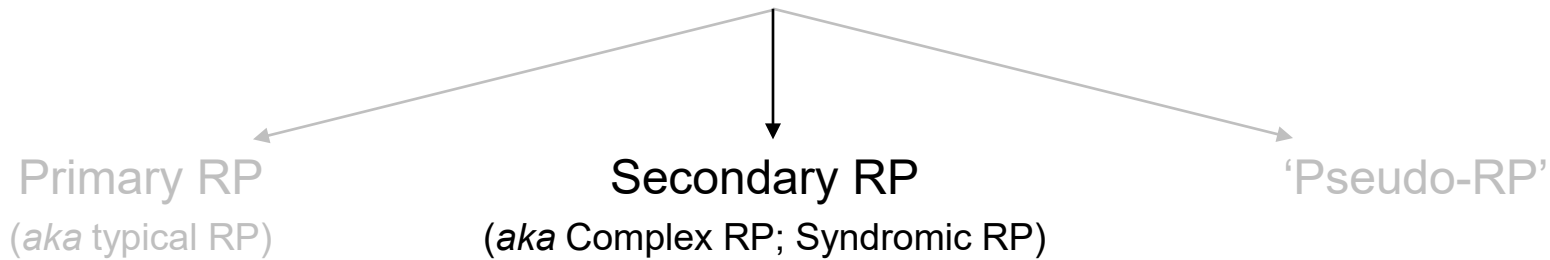


DDx for an RP-like Fundus



Joubert syndrome: Facies. Note the large head, broad forehead

DDx for an RP-like Fundus



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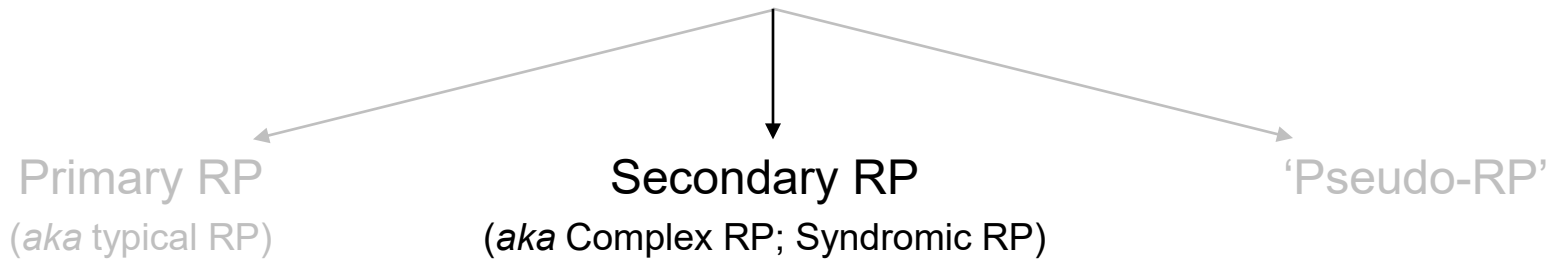
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DDx for an RP-like Fundus



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What is the prognosis?

It is highly variable

DDx for an RP-like Fundus

Primary RP
(aka typical RP)

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(aka Complex RP; Syndromic RP)

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'Pseudo-RP'

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How do JS pts present?

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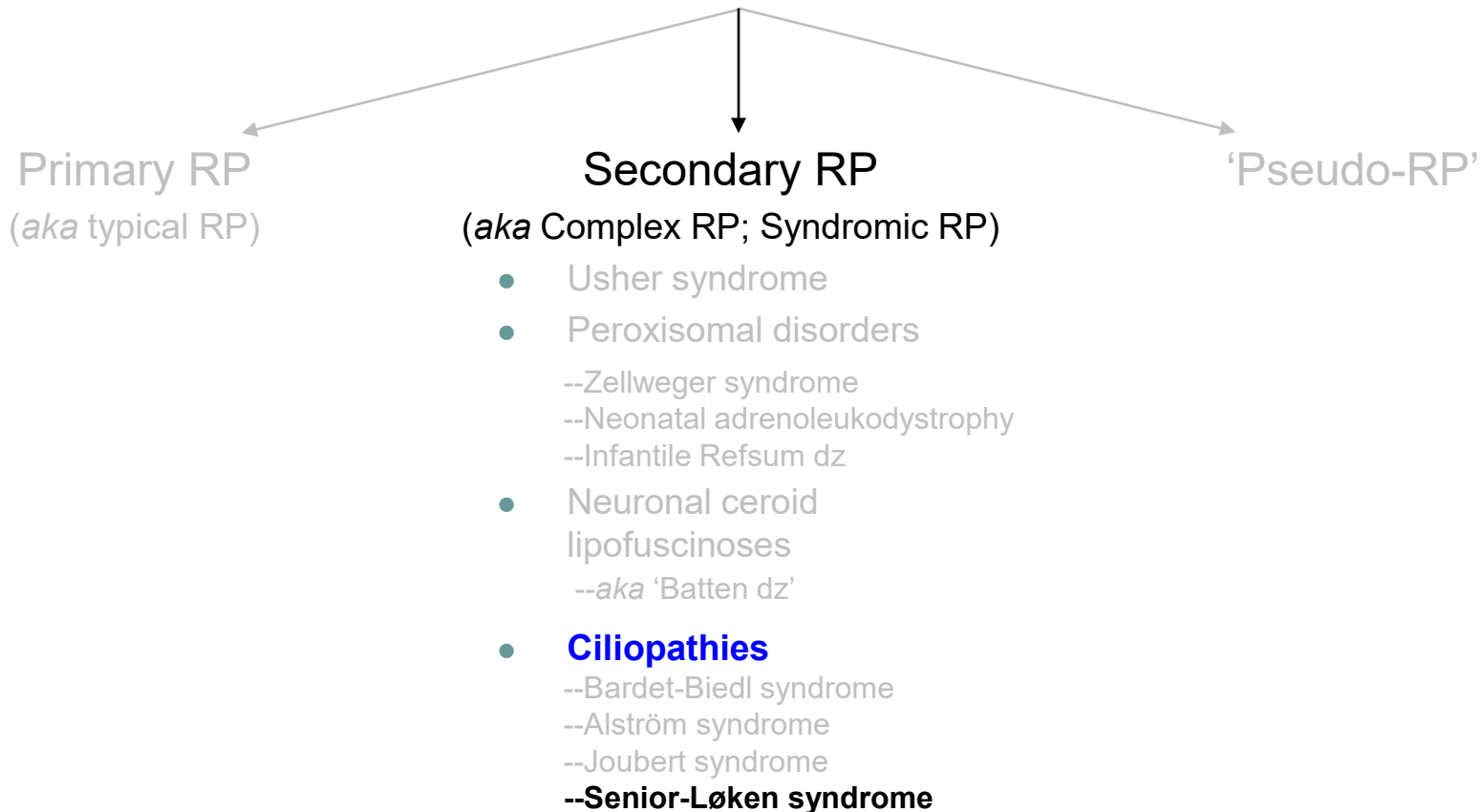
How is JS managed? Supportively

- RP-like fundus
- Hypotonia
- Disordered breathing (hyperpnea or apnea)
- Intellectual and motor deficits
- Seizures
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What is the prognosis?
It is highly variable

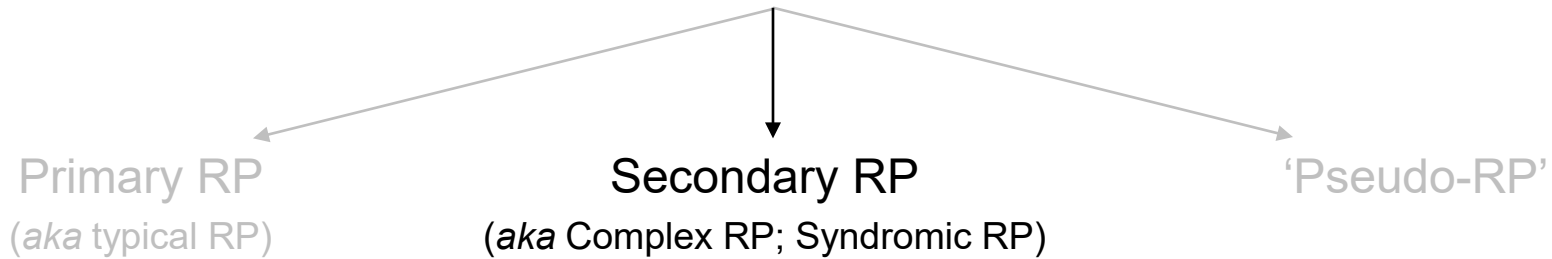


DDx for an RP-like Fundus



Senior-Løken syndrome is not listed with the other ciliopathies in the Retina book; rather, it is discussed in the Peds book, and only briefly. All you need to know about it is that, like all the ciliopathies mentioned, it involves retinal degeneration (with an LCA or RP-like fundus appearance) and **relentlessly progressive renal failure**.

DDx for an RP-like Fundus



- Usher syndrome
- Peroxisomal disorders
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy

For completeness' sake:

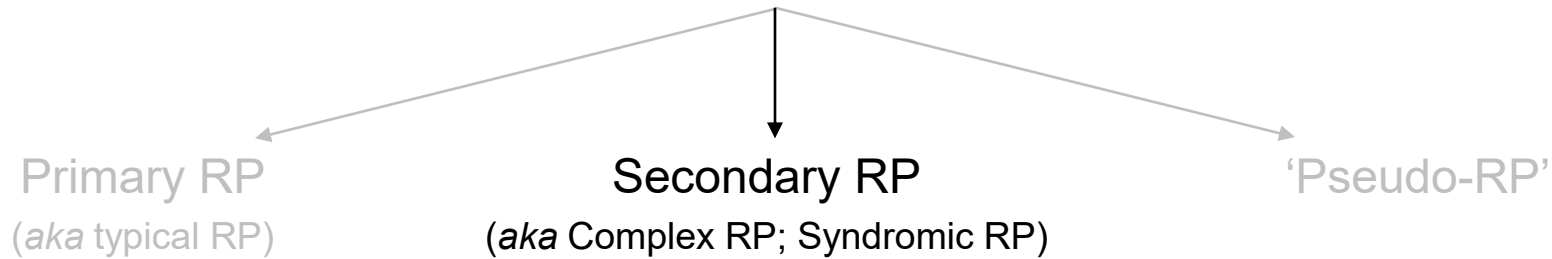
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They are two words syndromes

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DDx for an RP-like Fundus



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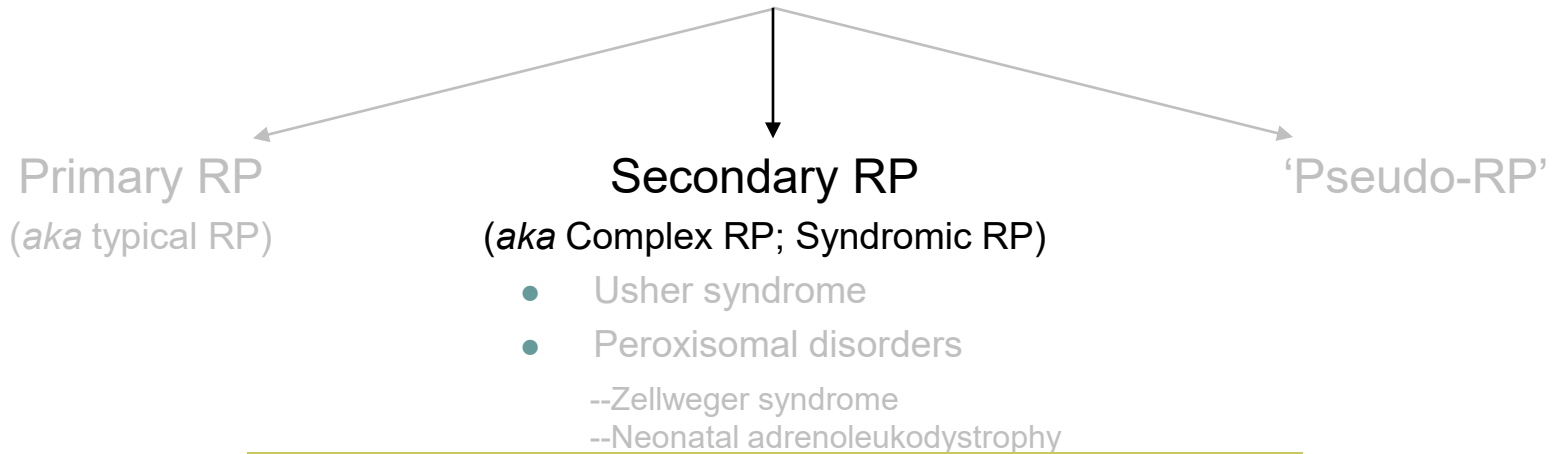
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DDx for an RP-like Fundus



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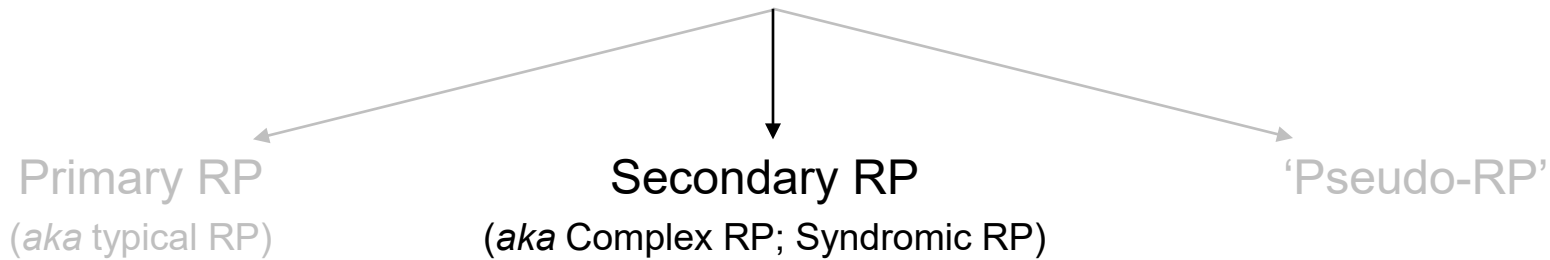
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DDx for an RP-like Fundus



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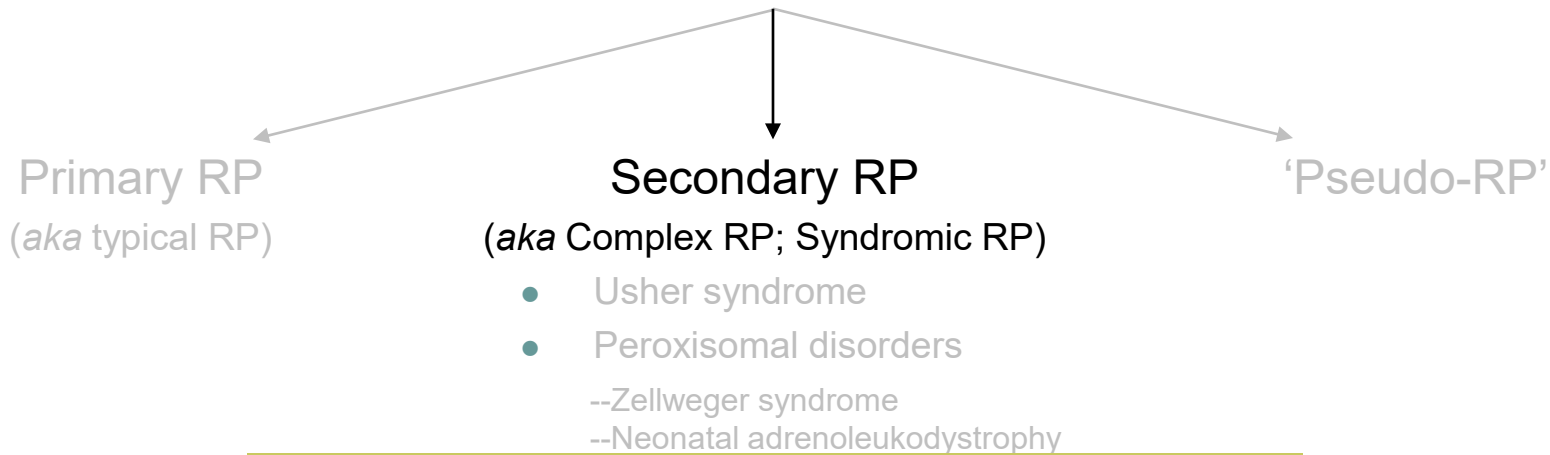
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*How many familial oculorenal syndromes are there?
Including the four ciliopathies—six*

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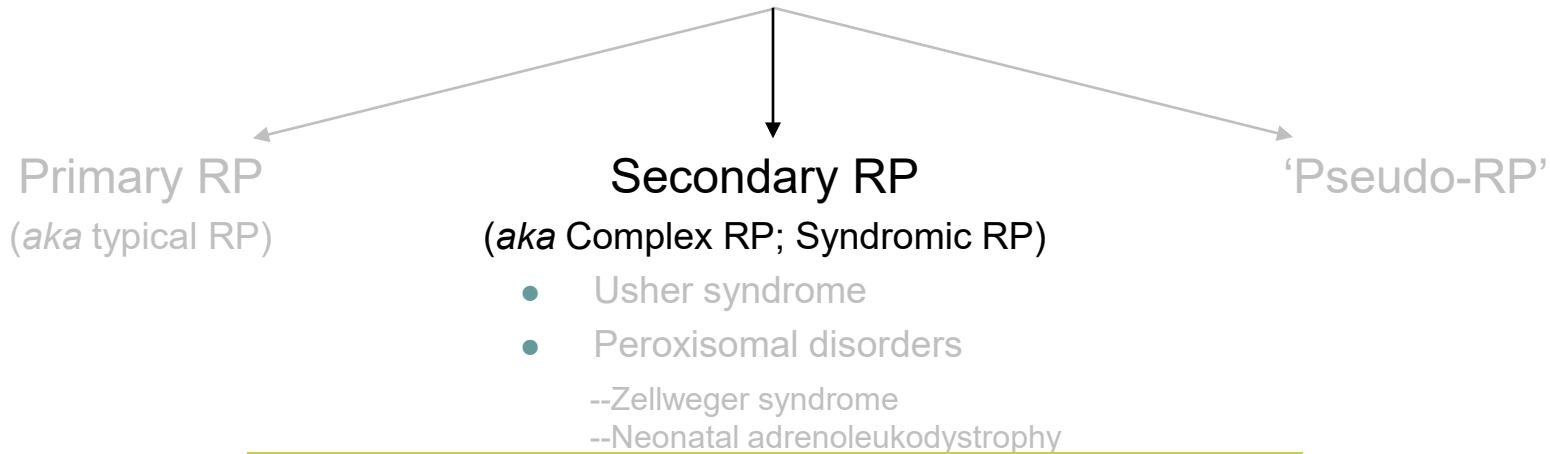
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What are the other two?

DDx for an RP-like Fundus



For completeness' sake:

In three words (including syndromes), what are these ciliopathies?

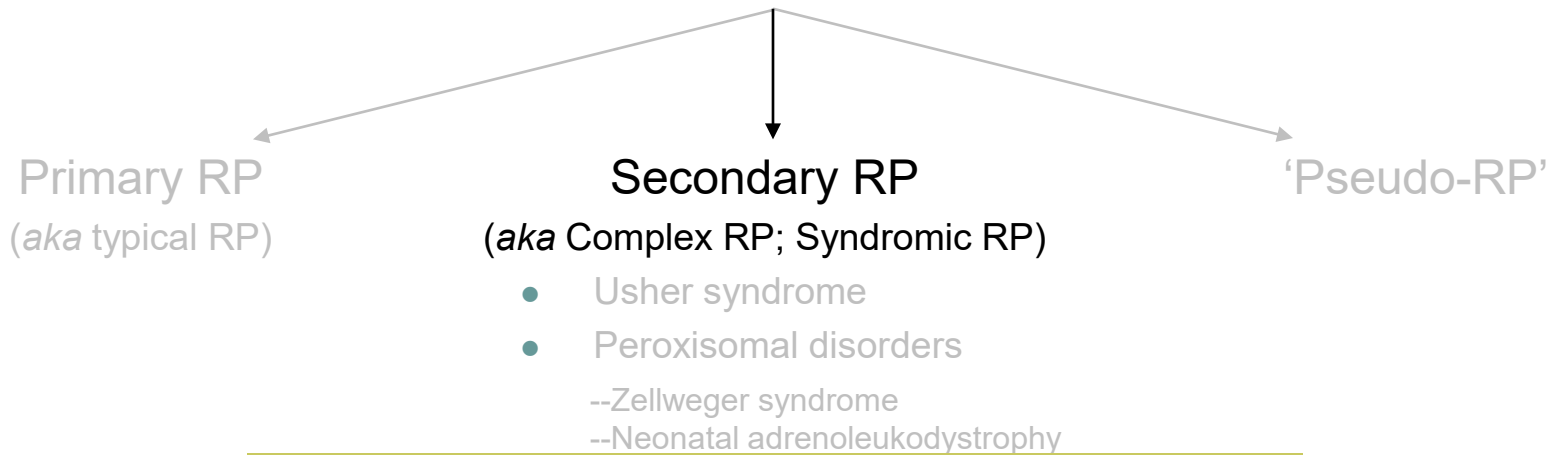
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Alport syndrome and Lowe syndrome

DDx for an RP-like Fundus



For completeness' sake:

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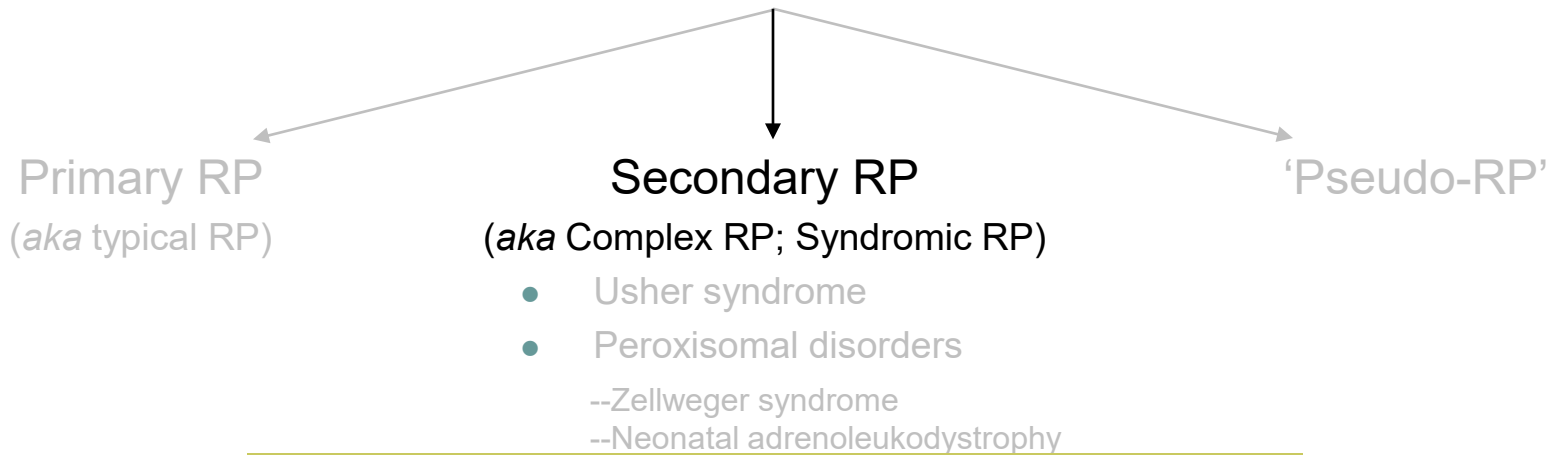
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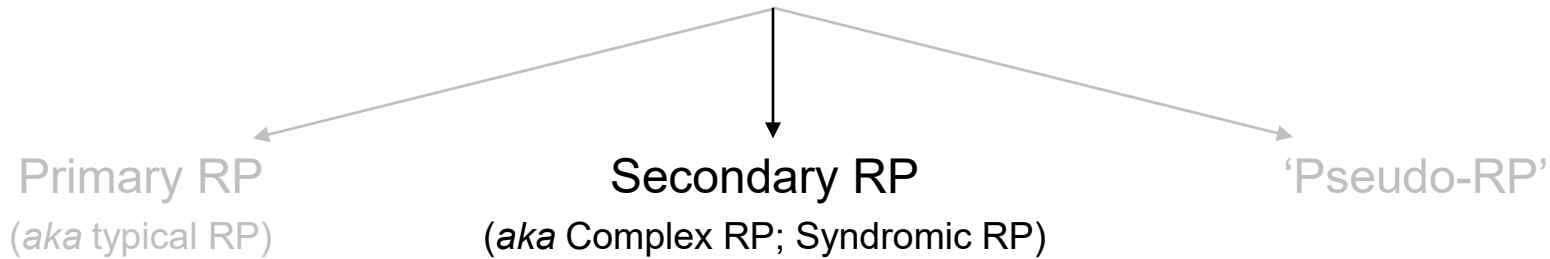
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Are Alport and Lowe syndromes ciliopathies? No

DDx for an RP-like Fundus



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How many familial oculorenal syndromes are there? Including the four ciliopathies—six

What are the other two?

Alport syndrome and Lowe syndrome

Are Alport and Lowe syndromes ciliopathies? No

Note: The latest (at the time I'm writing this—August 2023) copy of the *Peds* book asserts that Lowe syndrome **is** a ciliopathy. However, I'm pretty certain it's wrong on this score. FWIW, Dr Google seems to agree with me. Still, caveat emptor.

DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP
(aka Complex RP; Syndromic)

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Are Alport and Lowe syndrome in the DDx for an RP-like fundus?

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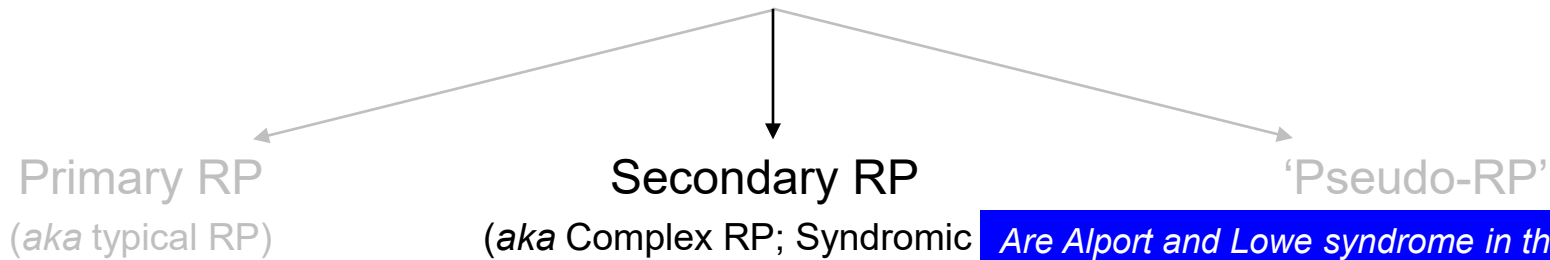
Lowe syndrome does not manifest retinal changes, so it is not. Alport syndrome is associated with what the *Peds* book describes as a "fleck retinopathy" and the *Retina* book as a "pigmentary retinopathy;" for this reason the *Retina* book considers it to be in the DDx.

What are the other two?

Alport syndrome and Lowe syndrome



DDx for an RP-like Fundus



- Usher syndrome
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(Note also that Alport syndrome is associated with hearing loss, so it is in the DDx for a pt with suspected **Alport** syndrome.)

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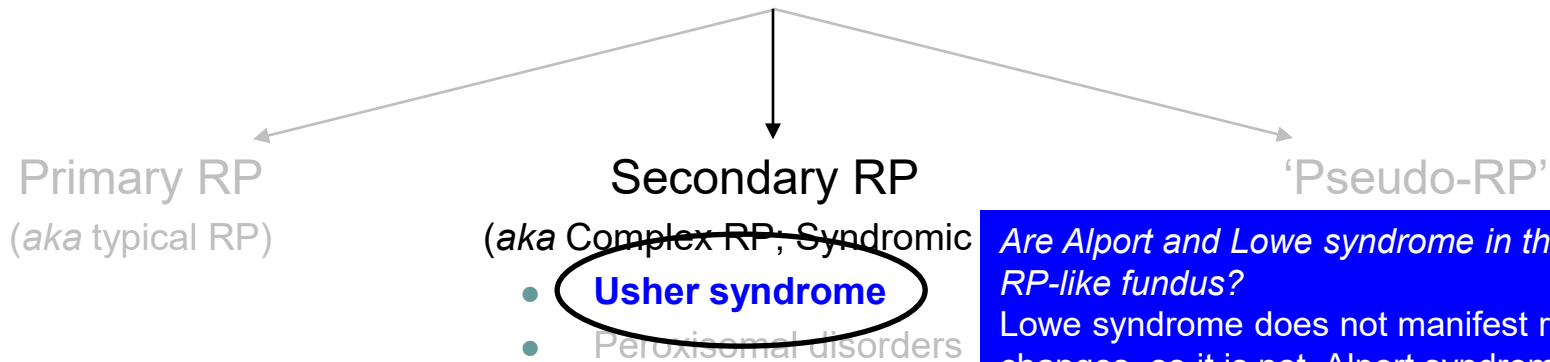
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The lens



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What lens pathologies occur with Alport and Lowe syndromes?

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Alport syndrome and Lowe syndrome

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The lens

What lens pathologies occur with Alport and Lowe syndromes?

- Lenticonus?
- Cataracts?
- Microspherophakia?

Which is the classic association with Alport and Lowe syndromes, ie, which should come first to mind?

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The lens

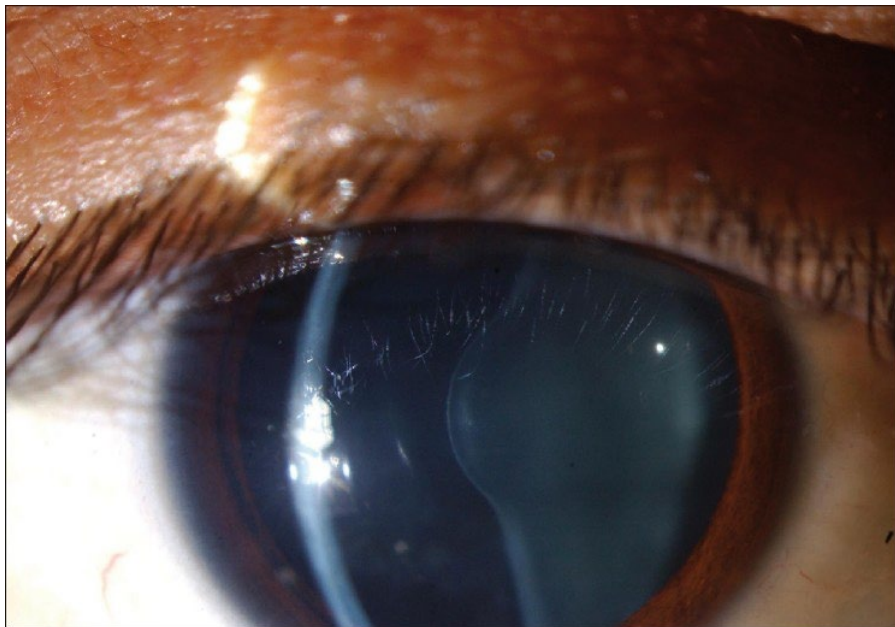
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--Lenticonus!

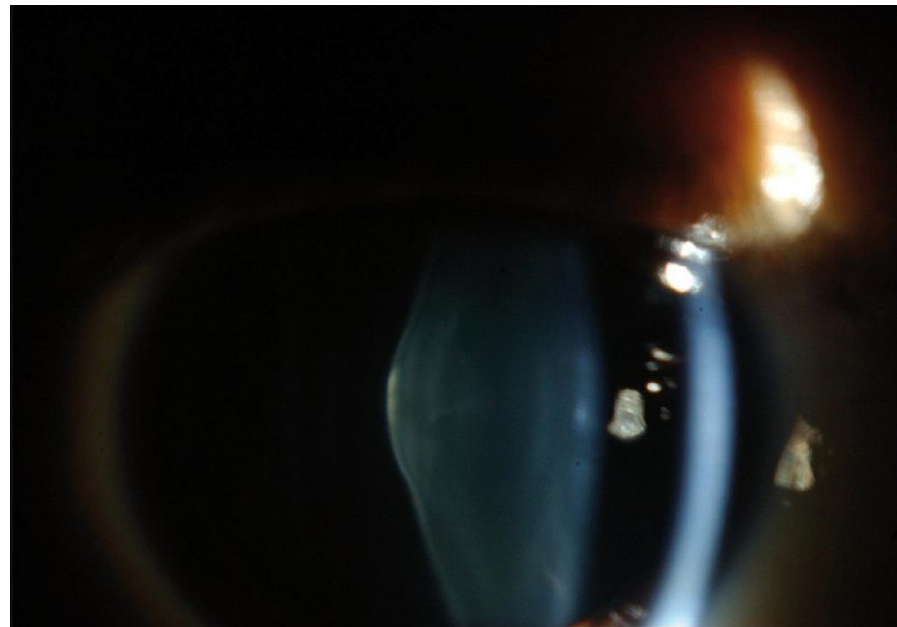
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Which is the classic association with Alport and Lowe syndromes, ie, which should come first to mind?
Lenticonus



Anterior lenticonus



Posterior lenticonus

DDx for an RP-like Fundus

Primary RP
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For completeness' sake:

In three words (including syndromes), what are these ciliopathies?

They are **familial oculorenal syndromes**

- **Ciliopathies**
 - Bardet-Biedl syndrome
 - Alström syndrome
 - Joubert syndrome
 - Senior-Løken syndrome
- Abetalipoproteinemia
 - aka 'Bassen-Kornzweig dz'

Are Alport and Lowe syndrome in the DDx for an RP-like fundus?

Lowe syndrome does not manifest retinal changes, so it is not. Alport syndrome is associated with what the *Peds* book describes as a "fleck retinopathy" and the *Retina* book as a "pigmentary retinopathy;" for this reason the *Retina* book considers it to be in the DDx.

What are the other two?

Alport syndrome and Lowe syndrome

Abnormalities of what intraocular structure are associated with Alport and Lowe syndromes?

The lens

What lens pathologies occur with Alport and Lowe syndromes?

- Lenticonus?**
- Cataracts?**
- Microspherophakia?**

Are these associated with the ciliopathies?

DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP

(aka Complex RP; Syndromic)

- Usher syndrome
- Peroxisomal disorders
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy

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What lens pathologies occur with Alport and Lowe syndromes?

- Lens dislocation
- Cataracts
- Microphthalmia

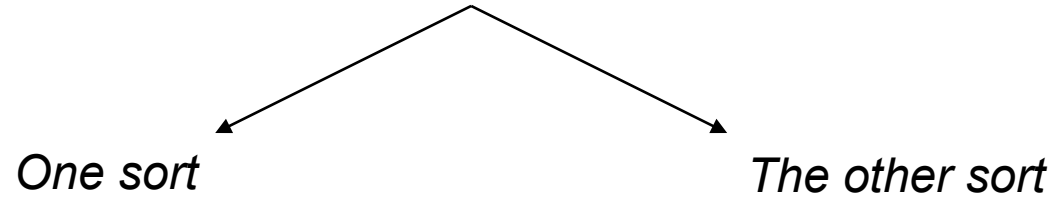
Are these associated with the ciliopathies?

No



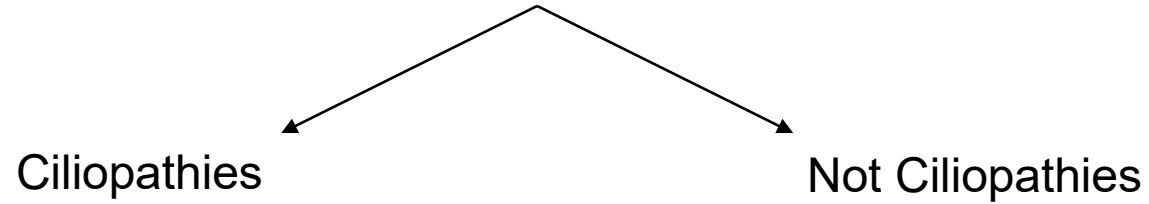
Q

Familial Oculorenal Syndromes *tl;dr*

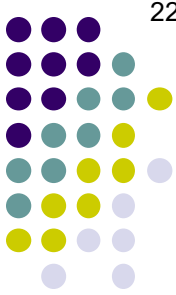
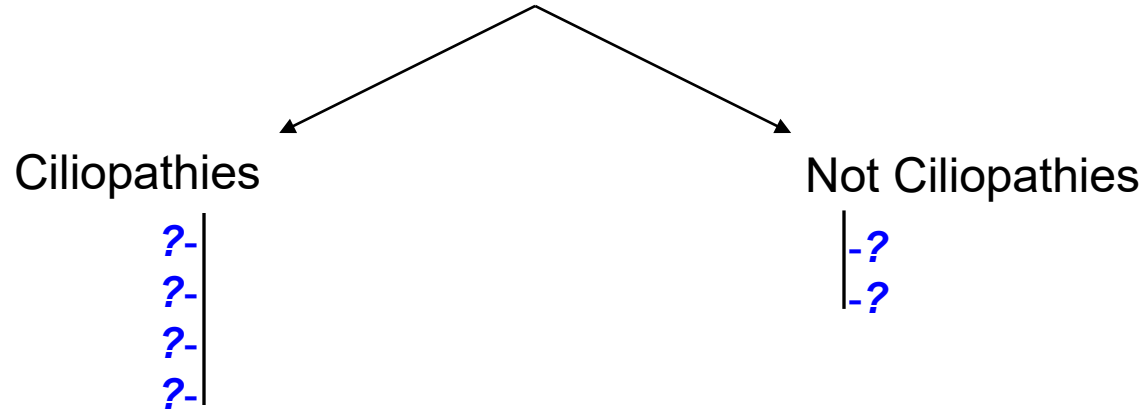


A

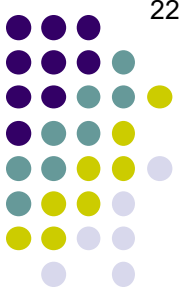
Familial Oculorenal Syndromes *tl;dr*



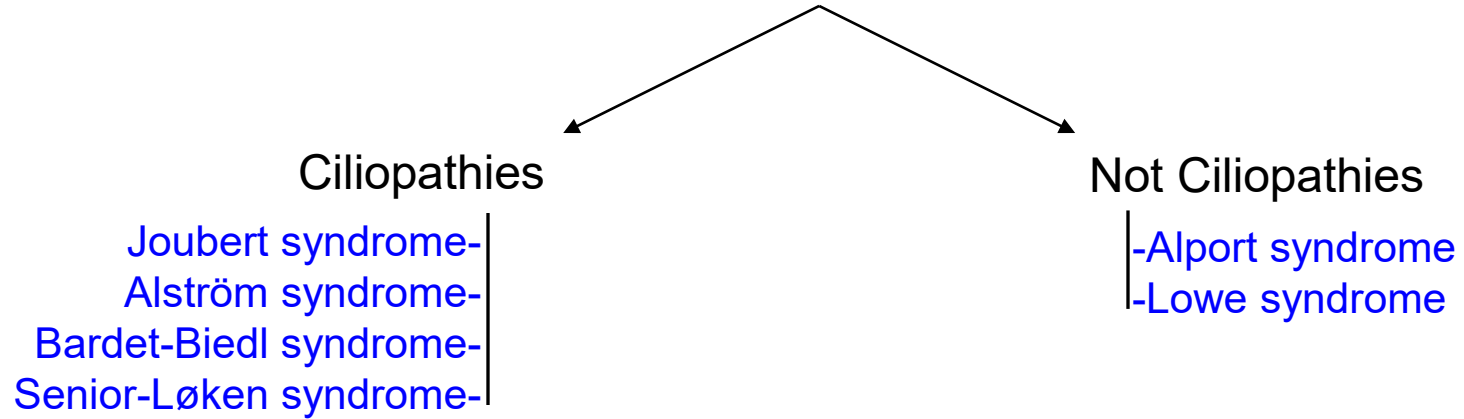
Familial Oculorenal Syndromes *tl;dr*



A



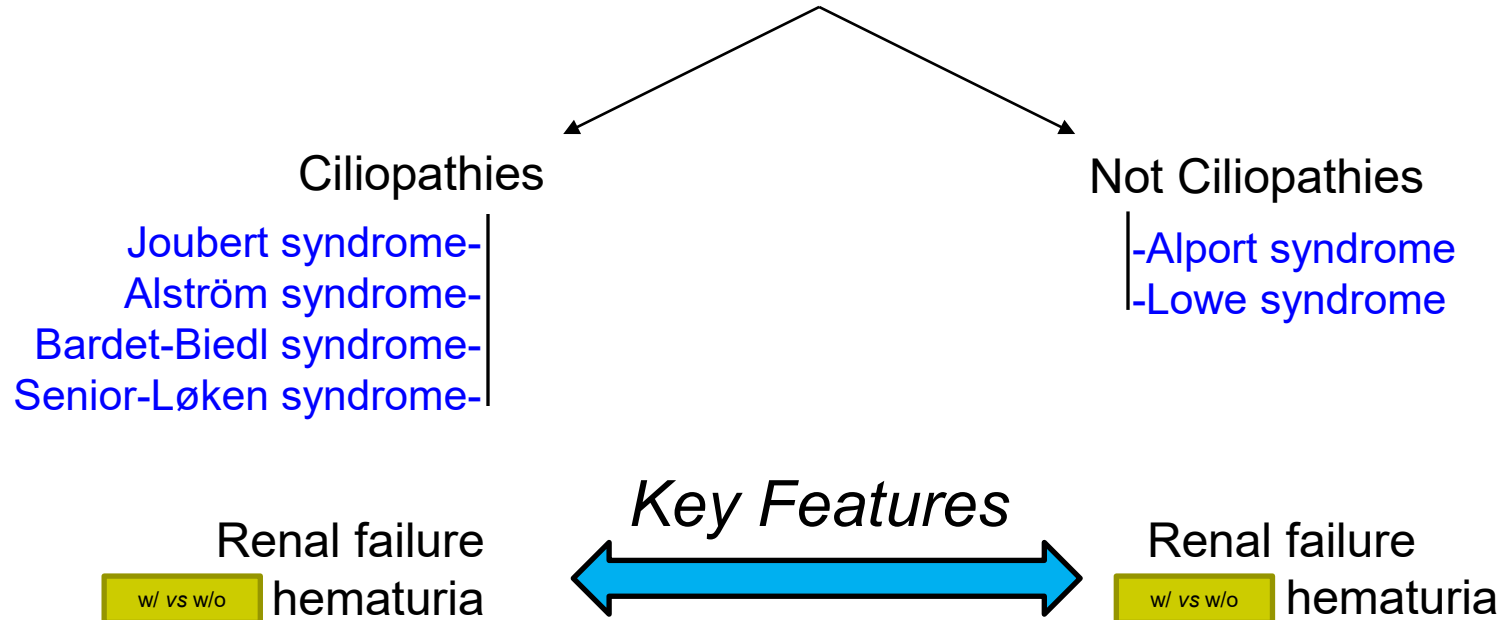
Familial Oculorenal Syndromes *tl;dr*

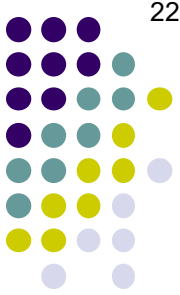




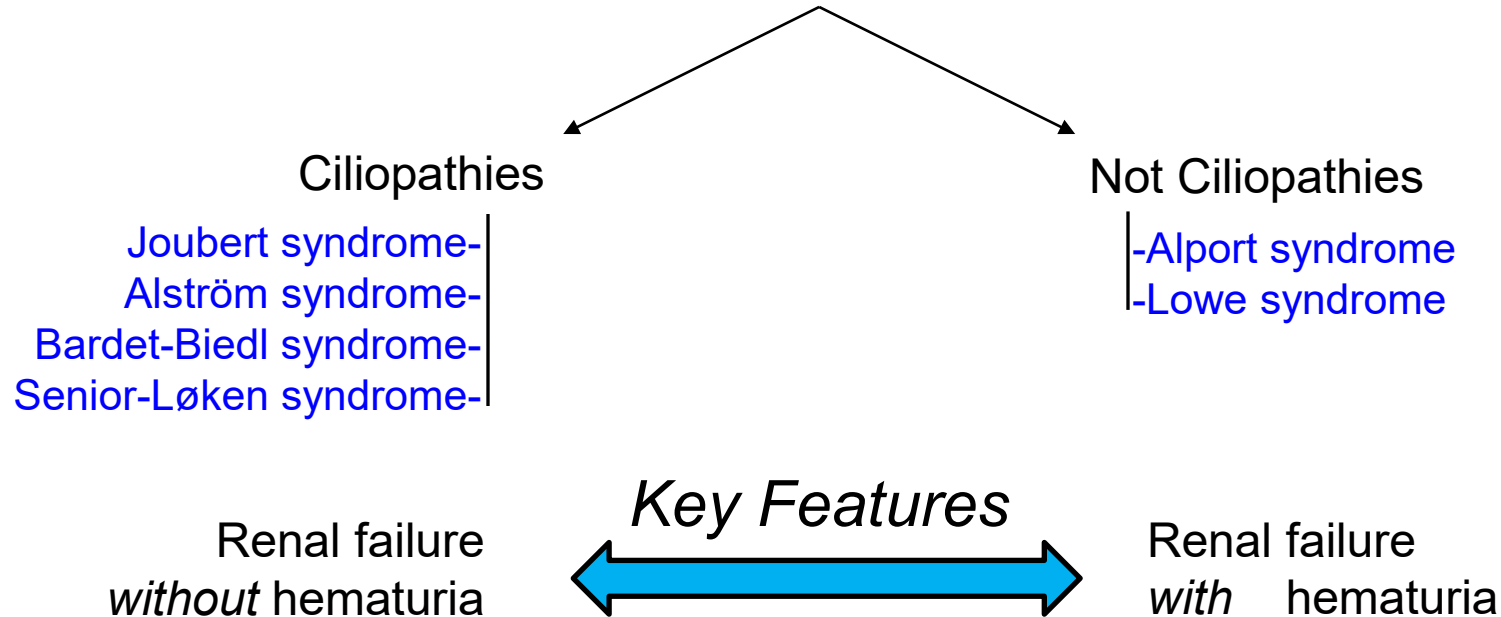
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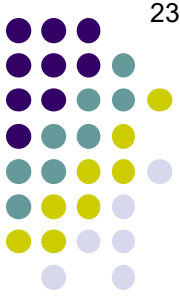
Familial Oculorenal Syndromes *tl;dr*



**A**

Familial Oculorenal Syndromes *tl;dr*





Q

Familial Oculorenal Syndromes *tl;dr*

Ciliopathies

Joubert syndrome-
Alström syndrome-
Bardet-Biedl syndrome-
Senior-Løken syndrome-

Not Ciliopathies

-Alport syndrome
-Lowe syndrome

Key Features

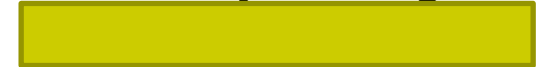
Renal failure
without hematuria

Classic eye finding:



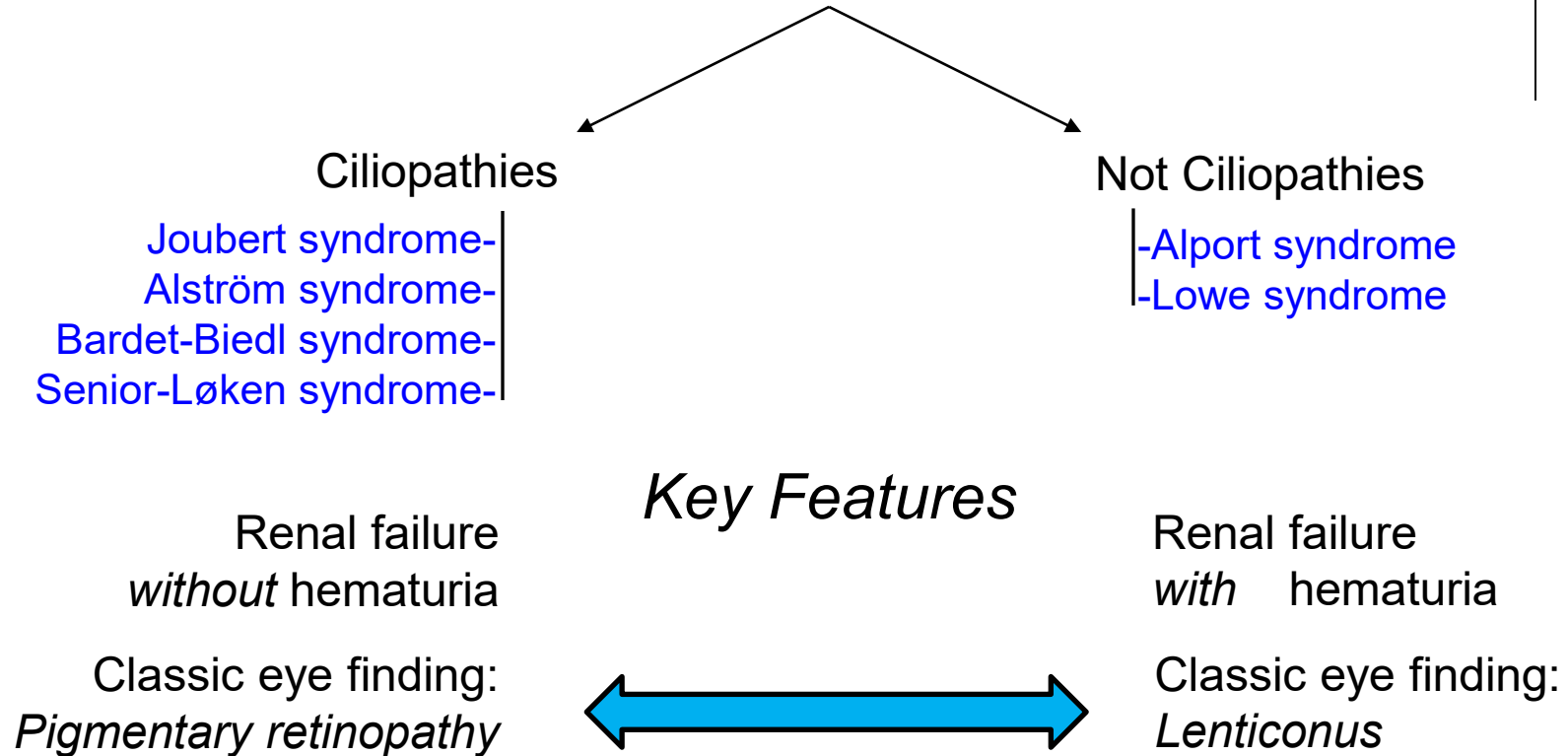
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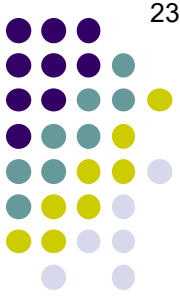
Classic eye finding:





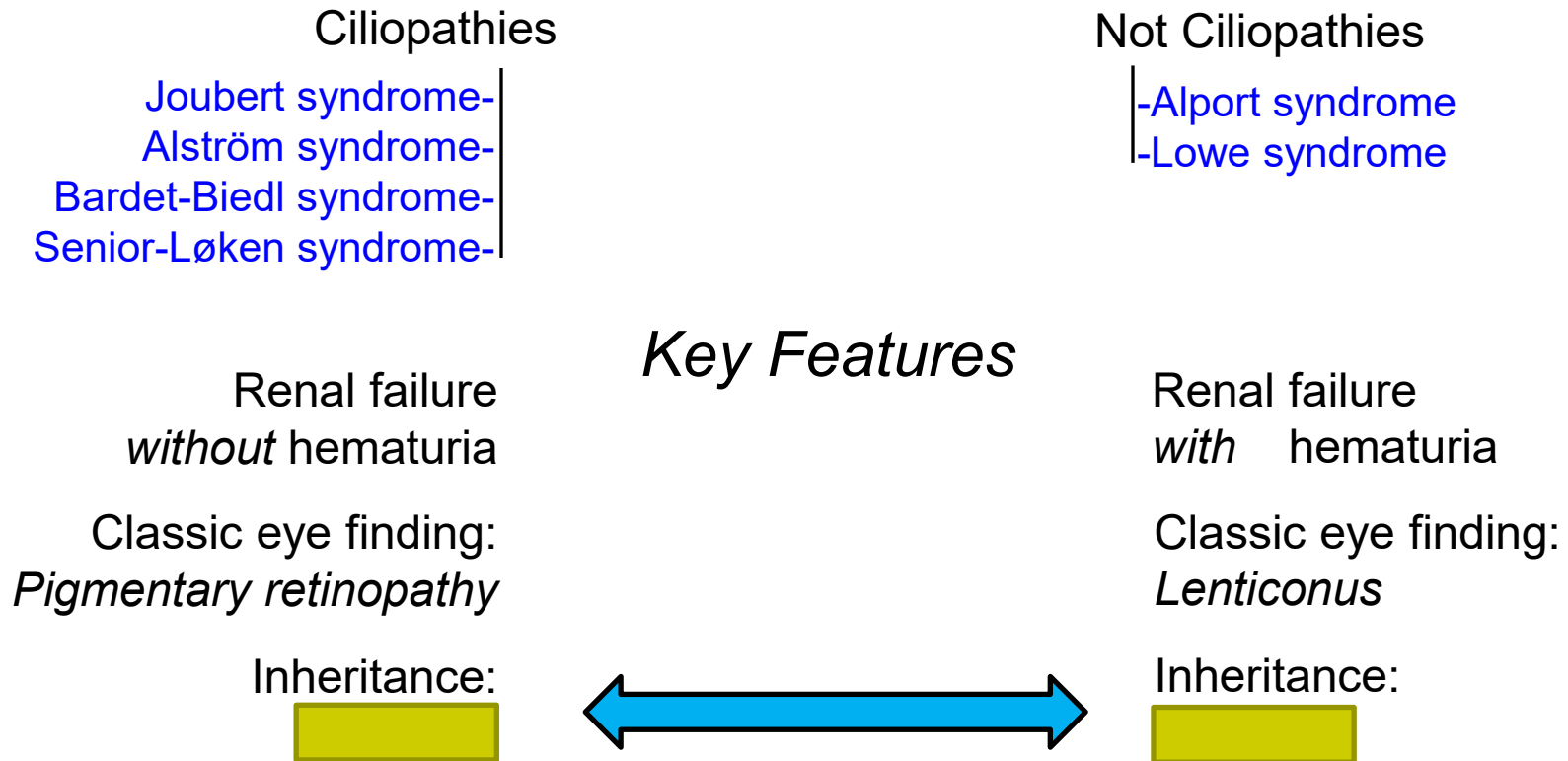
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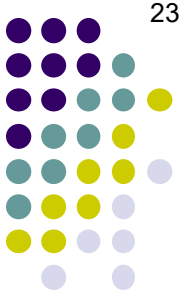




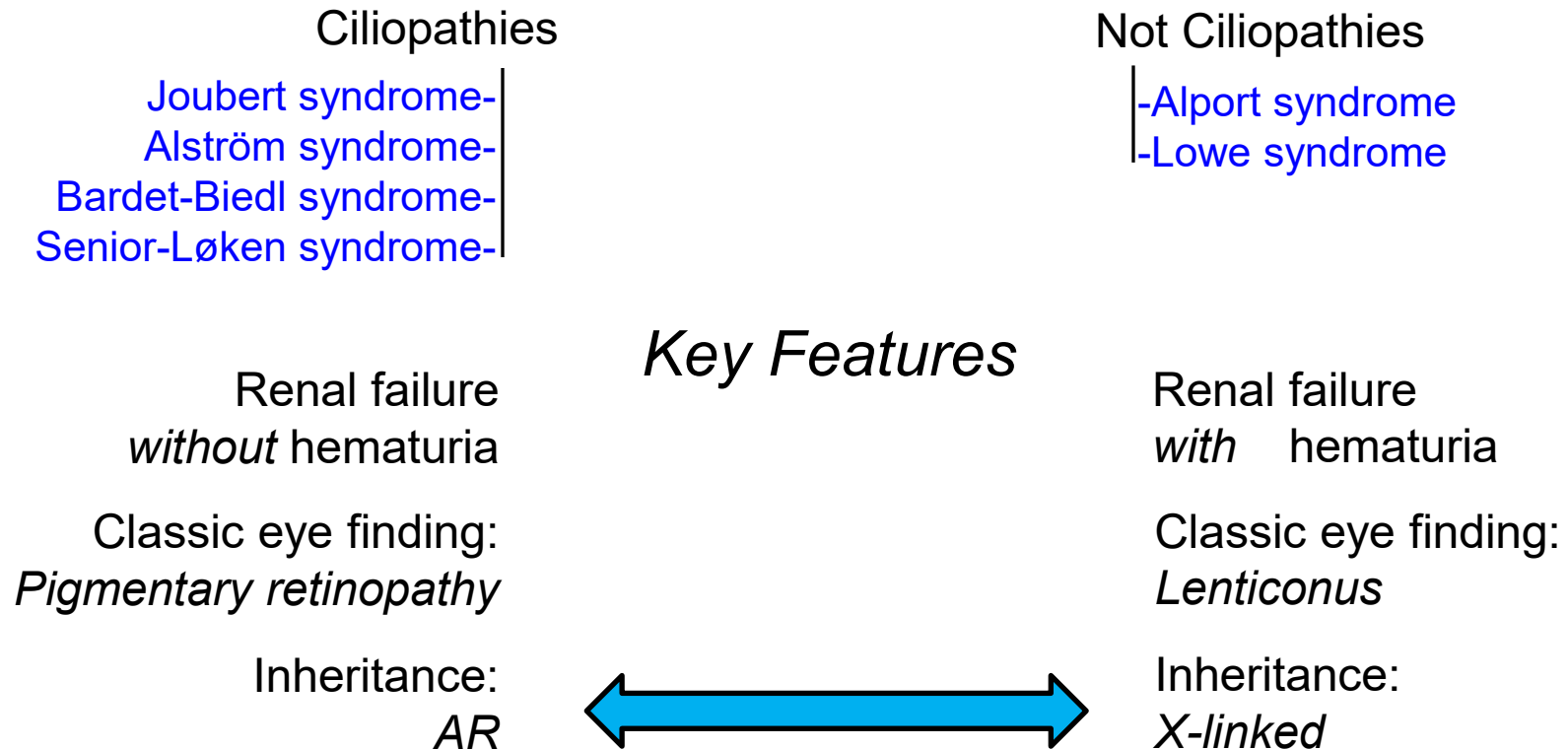
Q

Familial Oculorenal Syndromes *tl;dr*





Familial Oculorenal Syndromes *tl;dr*





Familial Oculorenal Syndromes *tl;dr*

Ciliopathies

Joubert syndrome-
Alström syndrome-
Bardet-Biedl syndrome-
Senior-Løken syndrome-

Renal failure
without hematuria

Classic eye finding:
Pigmentary retinopathy

Inheritance:
AR

Not Ciliopathies

-Alport syndrome
-Lowe syndrome

***For more info on Alport and Lowe syndromes,
see slide-set L4***

Key features

Renal failure
with hematuria

Classic eye finding:
Lenticonus

Inheritance:
X-linked



DDx for an RP-like Fundus

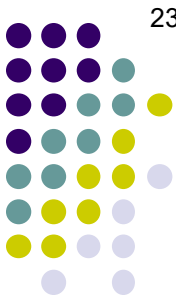
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'Pseudo-RP'

- Usher syndrome
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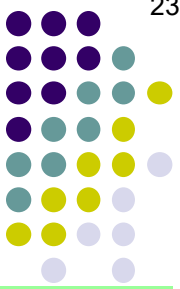
Worth stating explicitly that, in addition to being in the DDx for an RP-like fundus, these conditions are in the DDx for LCA. Once you get that connection locked down, learning this portion of the slide-set will constitute a twofer.





(This is a good point in the set to take a break)

DDx for an RP-like Fundus



What is the underlying problem in abetalipoproteinemia?

--Senior-Løken syndrome

- **Abetalipoproteinemia**
--aka 'Bassen-Kornzweig dz'

DDx for an RP-like Fundus

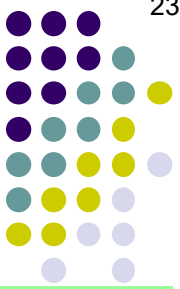


What is the underlying problem in abetalipoproteinemia?
One of the lipoproteins (ApoB) is not synthesized by the body

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DDx for an RP-like Fundus



What is the underlying problem in abetalipoproteinemia?

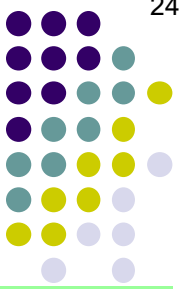
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DDx for an RP-like Fundus



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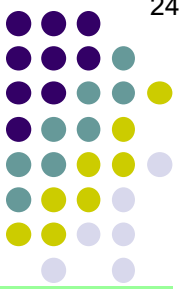
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DDx for an RP-like Fundus



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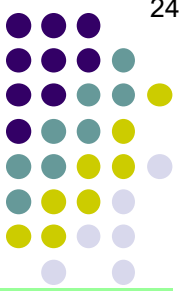
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How does the absence of ApoB lead to secondary RP?

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DDx for an RP-like Fundus

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How does the absence of ApoB lead to secondary RP?

Without ApoB, fat cannot be properly absorbed. Without proper fat absorption, adequate vitamin A (a fat-soluble vitamin) levels cannot be maintained. And absent adequate vitamin A levels, the retina will cease functioning (as will other aspects of the CNS).

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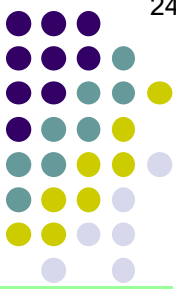
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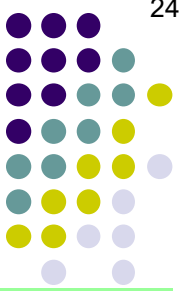
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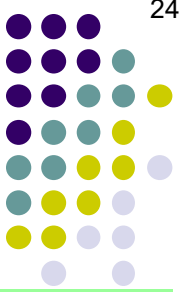
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In addition to low vitamin A levels, there is a classic finding on peripheral blood smear—what is it?

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What does acanthocytosis mean?

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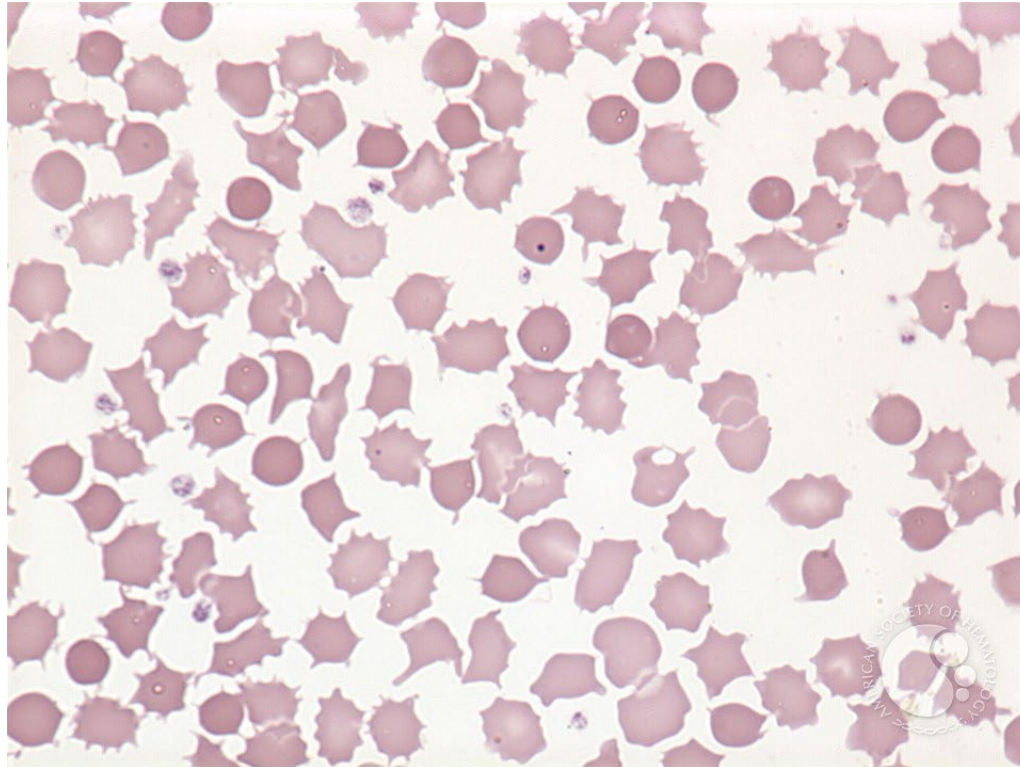
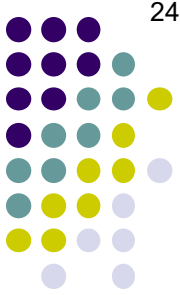
What does acanthocytosis mean?

It means the RBCs have a 'thorny' appearance

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--aka 'Bassen-Kornzweig dz'

DDx for an RP-like Fundus



Acanthocytosis



DDx for an RP-like Fundus

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With supplementary vitamins A & E

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How does the absence of ApoB lead to secondary RP?

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What is the most common cause of hypovitaminosis A? (It's not abetalipoproteinemia)

How is it diagnosed?

Checking vitamin A levels is a good start

How is it treated?

With supplementary vitamins A & E

--Senior-Løken syndrome

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DDx for an RP-like Fundus

What is the underlying problem in abetalipoproteinemia?

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How is abetalipoproteinemia inherited?

AR

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Without ApoB, fat cannot be properly absorbed. Without proper fat absorption, adequate vitamin A (a fat-soluble vitamin) levels are not maintained. This leads to retinopathy (as will other aspects of the disease).

What is the most common cause of hypovitaminosis A? (It's not abetalipoproteinemia)

Malabsorption secondary to GI surgery (eg, gastric bypass; small-bowel resection)

How is it diagnosed?

Checking vitamin A levels is a good start

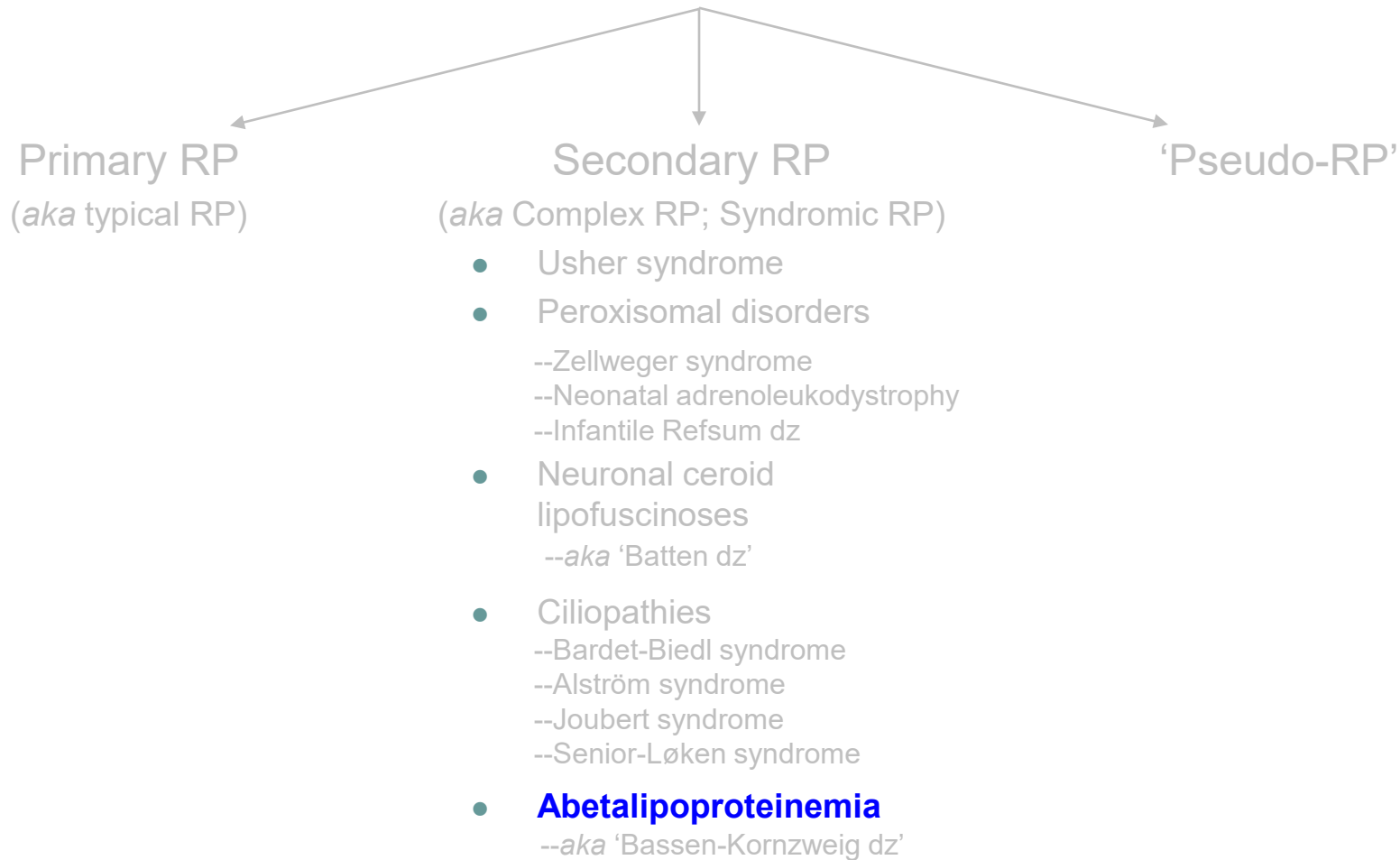
How is it treated?

With supplementary vitamins A & E

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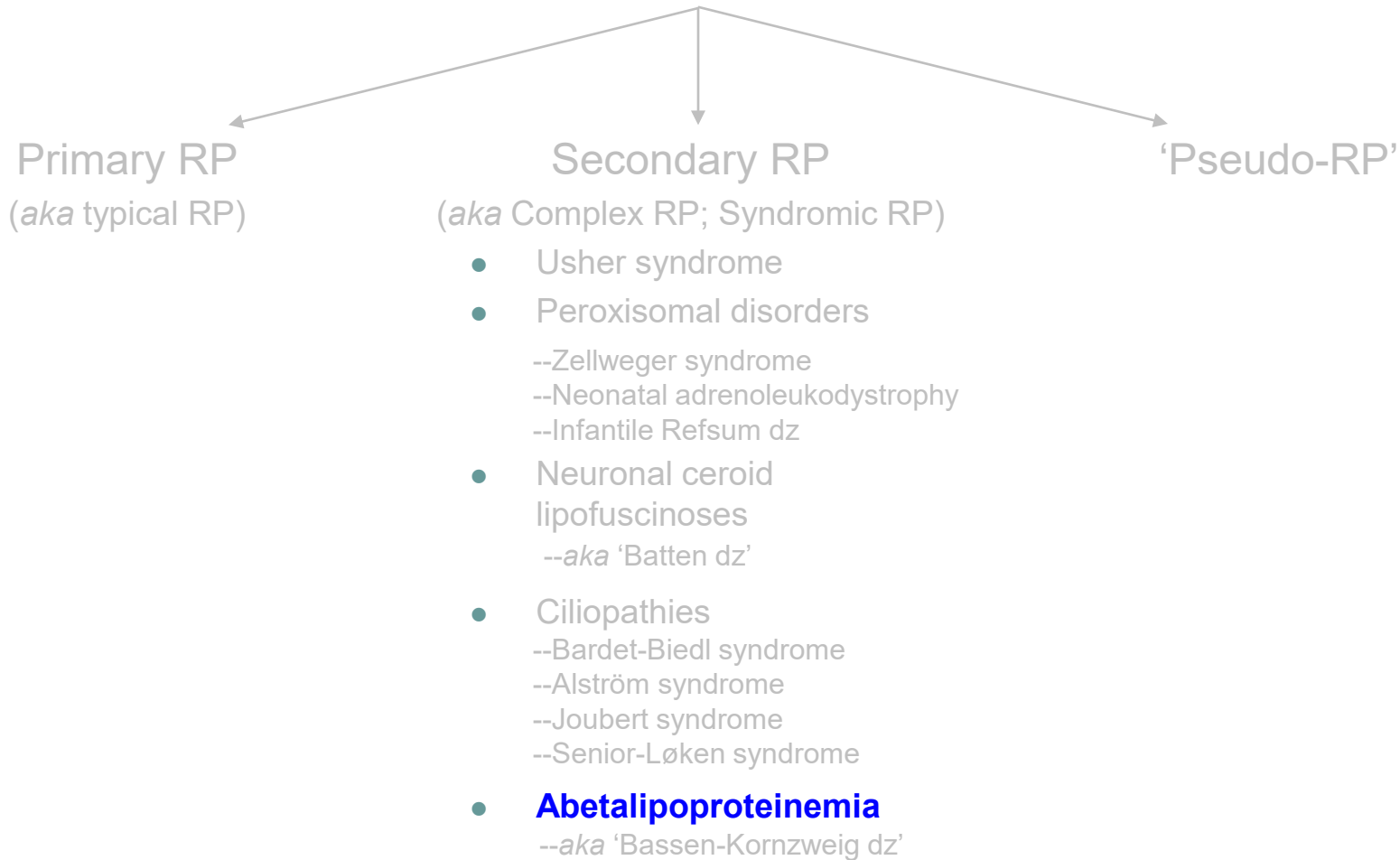
DDx for an RP-like Fundus



*In abetalipoproteinemia, β -lipoprotein is absent (that's what the prefix -a- indicates).
Is **hypobetalipoproteinemia** a thing?*



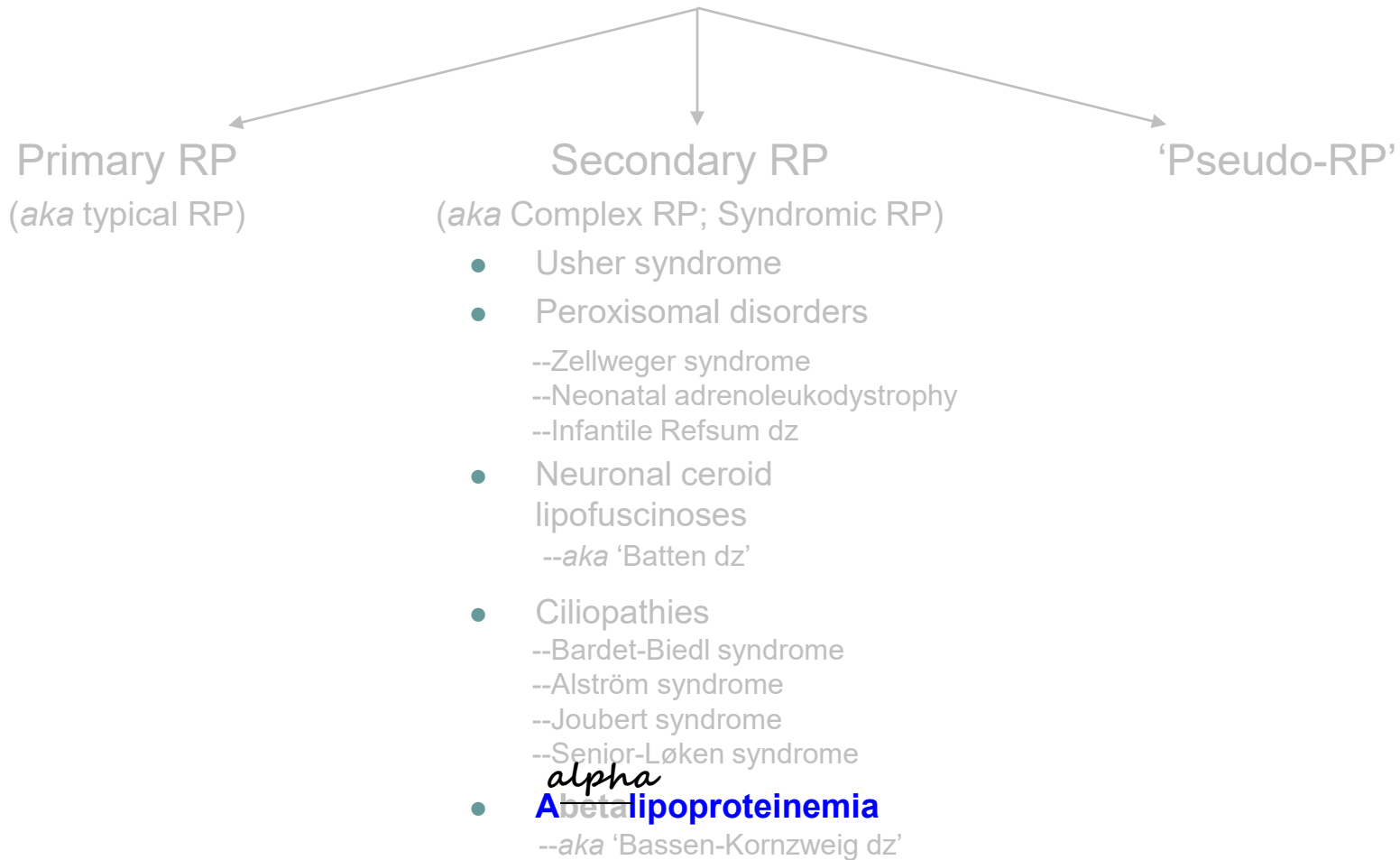
DDx for an RP-like Fundus



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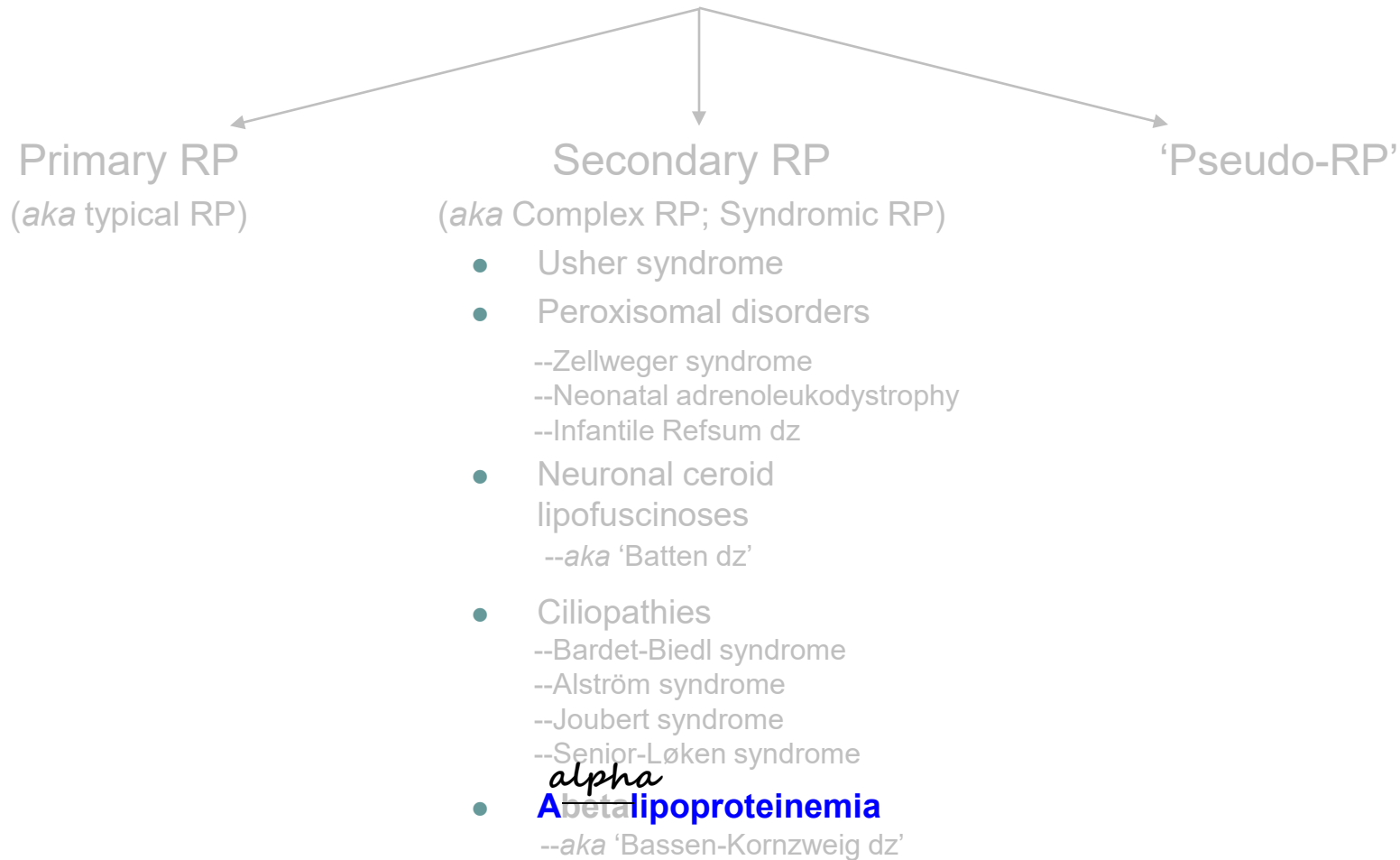
*Indeed it is, via a condition called 'familial hypobetalipoproteinemia,' and it can affect the retina (it's mentioned in the *BCSC* books, but not addressed in detail)*

DDx for an RP-like Fundus



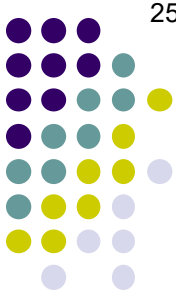
*Is a **alpha**-lipoproteinemia a thing?*

DDx for an RP-like Fundus

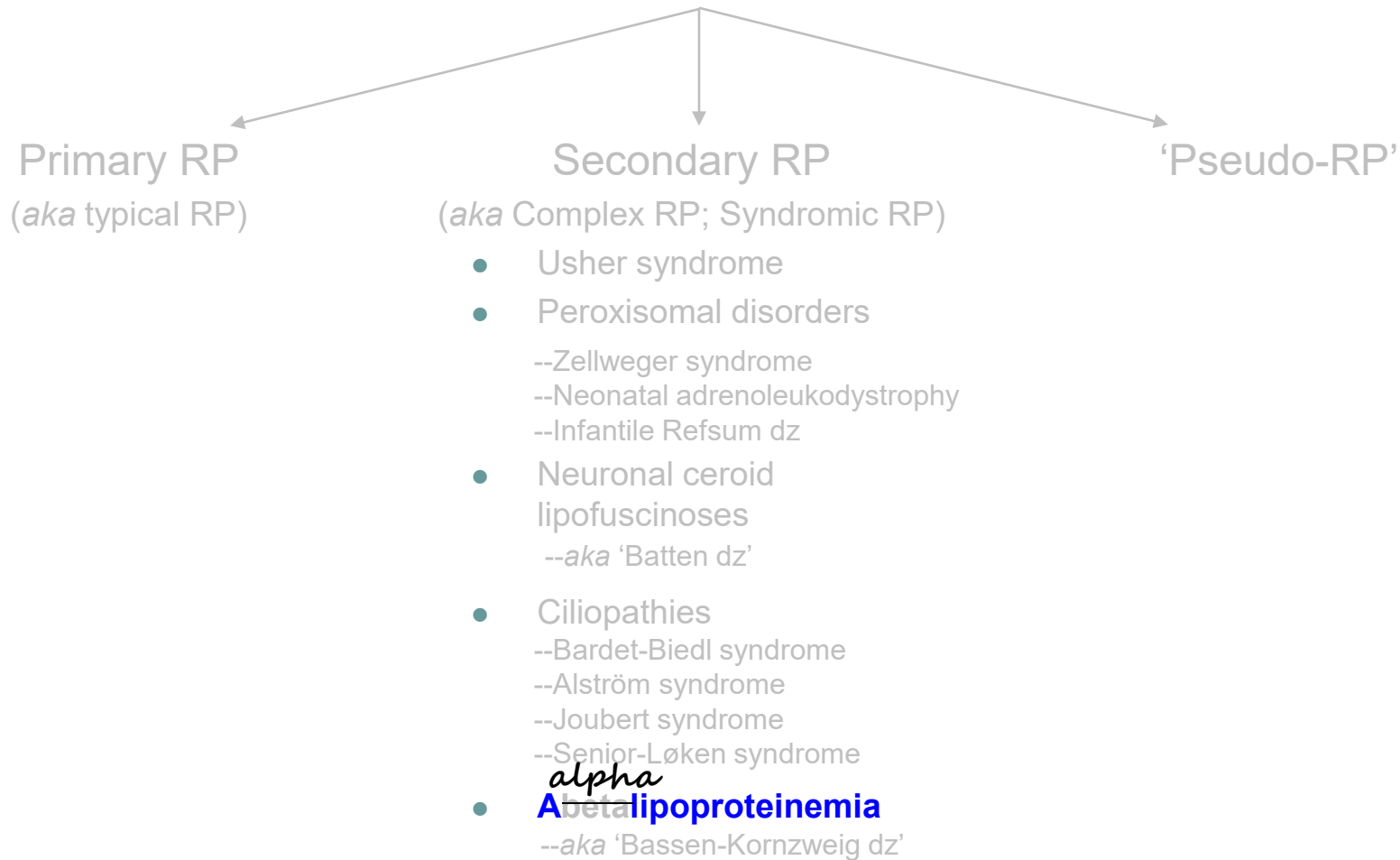


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Indeed it is



DDx for an RP-like Fundus



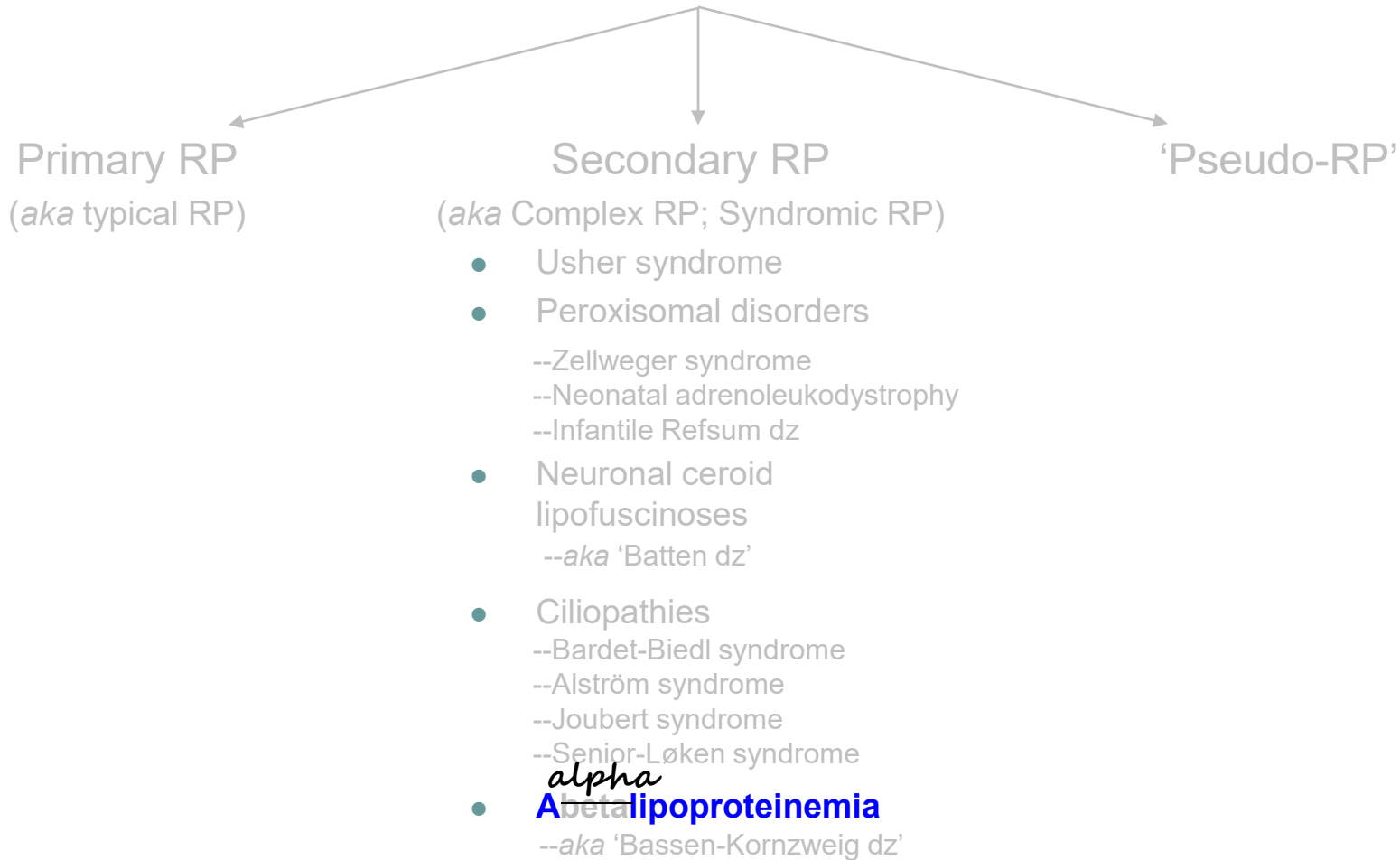
*Is a **alpha**-lipoproteinemia a thing?*

Indeed it is

Does the absence of α -lipoprotein affect the retina?



DDx for an RP-like Fundus

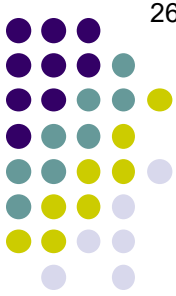


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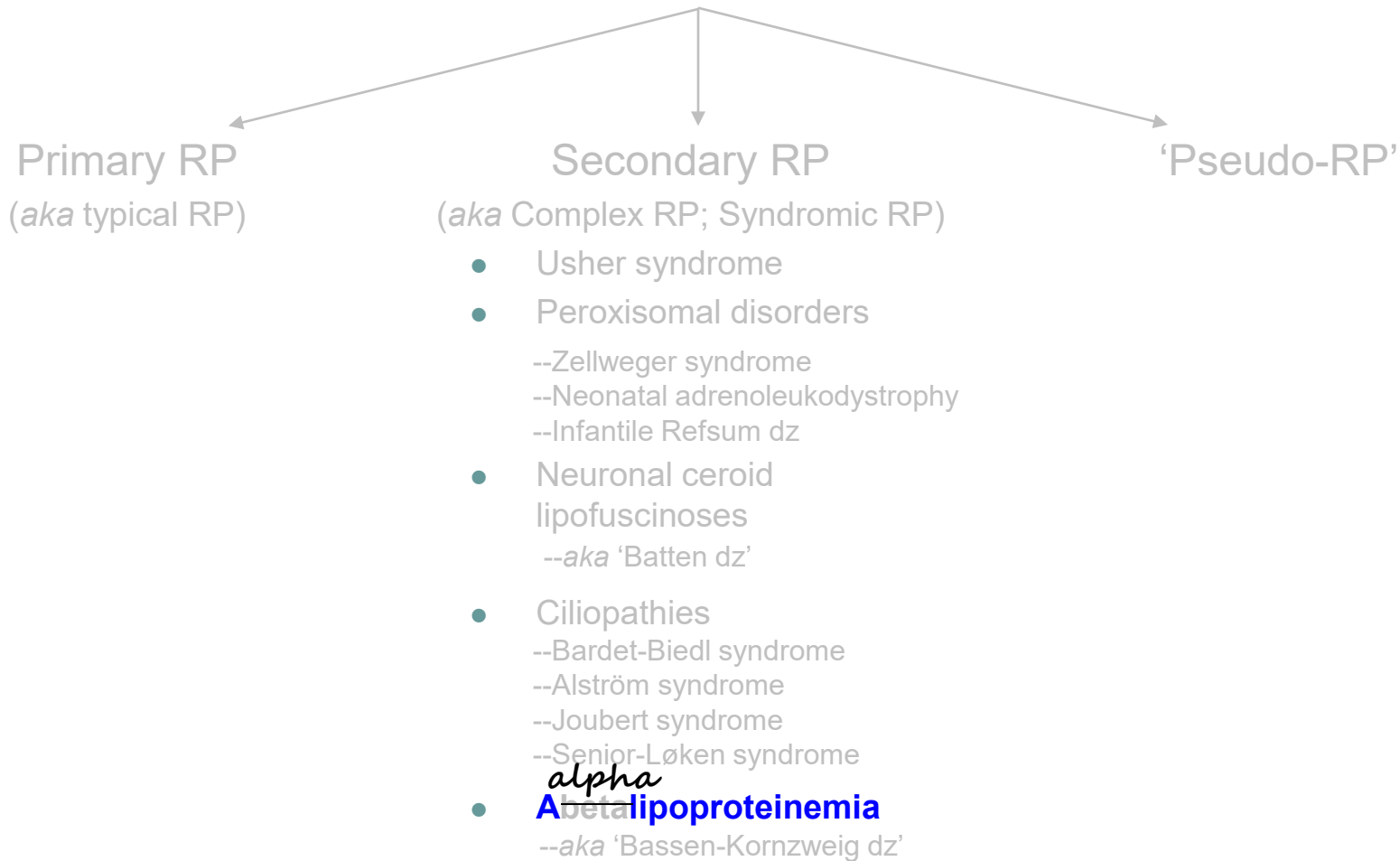
Indeed it is

Does the absence of α -lipoprotein affect the retina?

No, but it does affect the **eye structure**



DDx for an RP-like Fundus



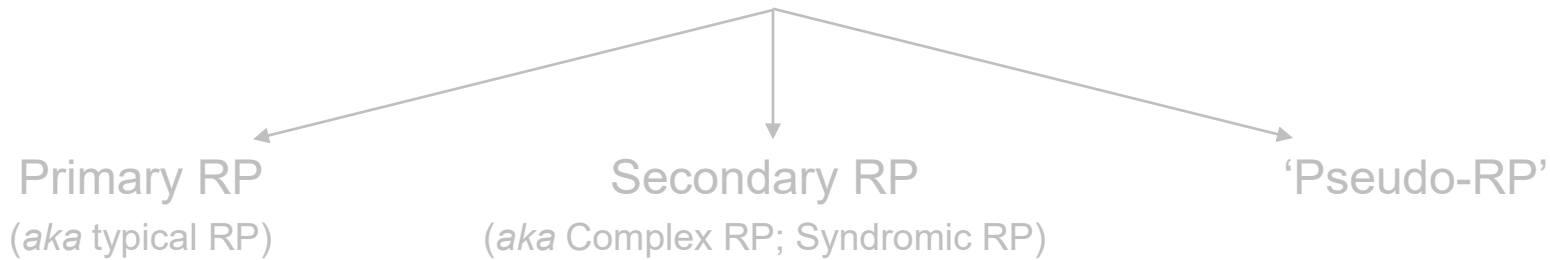
*Is a **alpha**-lipoproteinemia a thing?*

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Does the absence of α -lipoprotein affect the retina?

No, but it does affect the cornea

DDx for an RP-like Fundus



- Usher syndrome
- Peroxisomal disorders
 - Zellweger syndrome
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 - Infantile Refsum dz
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 - aka 'Batten dz'
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- **Abetalipoproteinemia**
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Is a-**alpha**-lipoprotein --?

Indeed it is

Low levels of α -lipoprotein are implicated in three corneal conditions. What are they?

--?

--?

--?

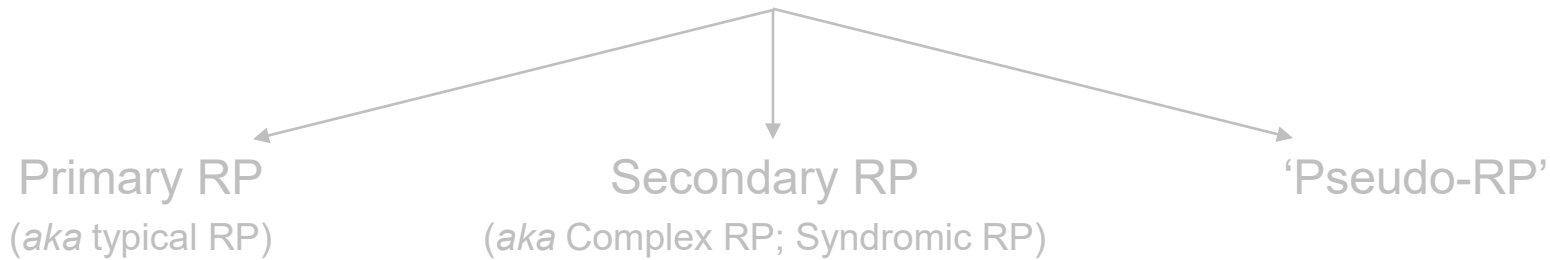
These are some serious zebras, so don't trip if you don't know them

Does the absence of α -lipoprotein affect the retina?

No, but it does affect the **cornea**



DDx for an RP-like Fundus



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Is a **alpha**-lipoprotein
Indeed it is

Low levels of α -lipoprotein are implicated in three corneal conditions. What are they?

- LCAT deficiency
- Fish eye disease
- Tangier disease

Does the absence of α -lipoprotein affect the retina?
No, but it does affect the **cornea**



DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP
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'Pseudo-RP'

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So, the hypolipoproteinemias can be divided into those involving **α -lipoproteins**, which lead to pathology of the cornea...

Low levels of α -lipoprotein are implicated in three corneal conditions. What are they?

- LCAT deficiency**
- Fish eye disease**
- Tangier disease**

Does the absence of α -lipoprotein affect the retina?

No, but it does affect the **cornea**



DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP
(aka Complex RP; Syndromic RP)

'Pseudo-RP'

- Usher syndrome
- Peroxisomal disorders
 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz
- Neuronal ceroid lipofuscinoses
 - aka 'Batten dz'
- Ciliopathies
 - Bardet-Biedl syndrome
 - Alström syndrome
 - Joubert syndrome
 - Senior-Løken syndrome
- **Abetalipoproteinemia**
 - aka 'Bassen-Kor...' (partially obscured)

So, the hypolipoproteinemias can be divided into those involving **α -lipoproteins**, which lead to pathology of the cornea...

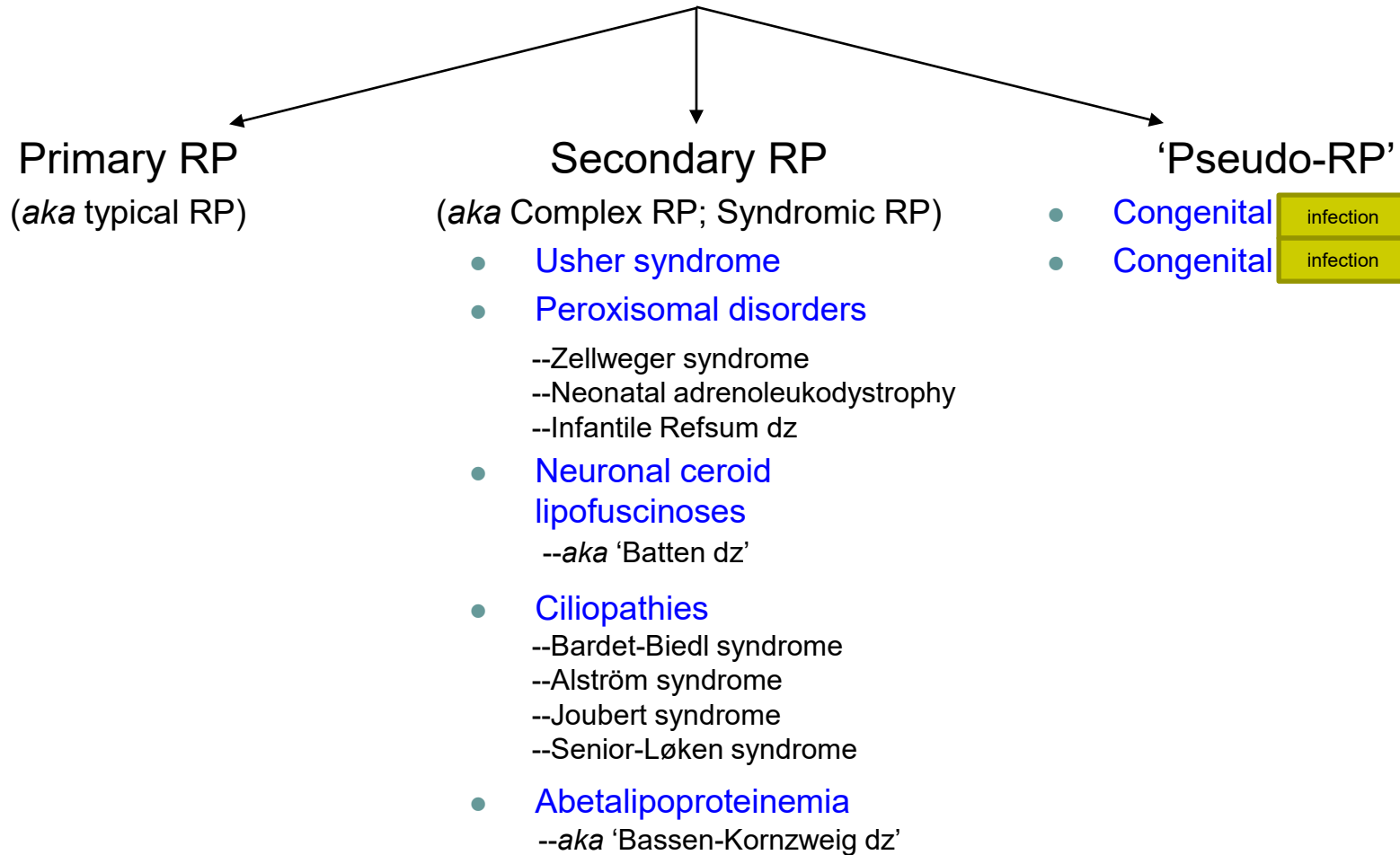
...and **β -lipoproteins**, which lead to pathology of the retina

Low levels of α -lipoprotein are implicated in three corneal conditions. What are they?

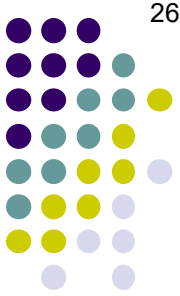
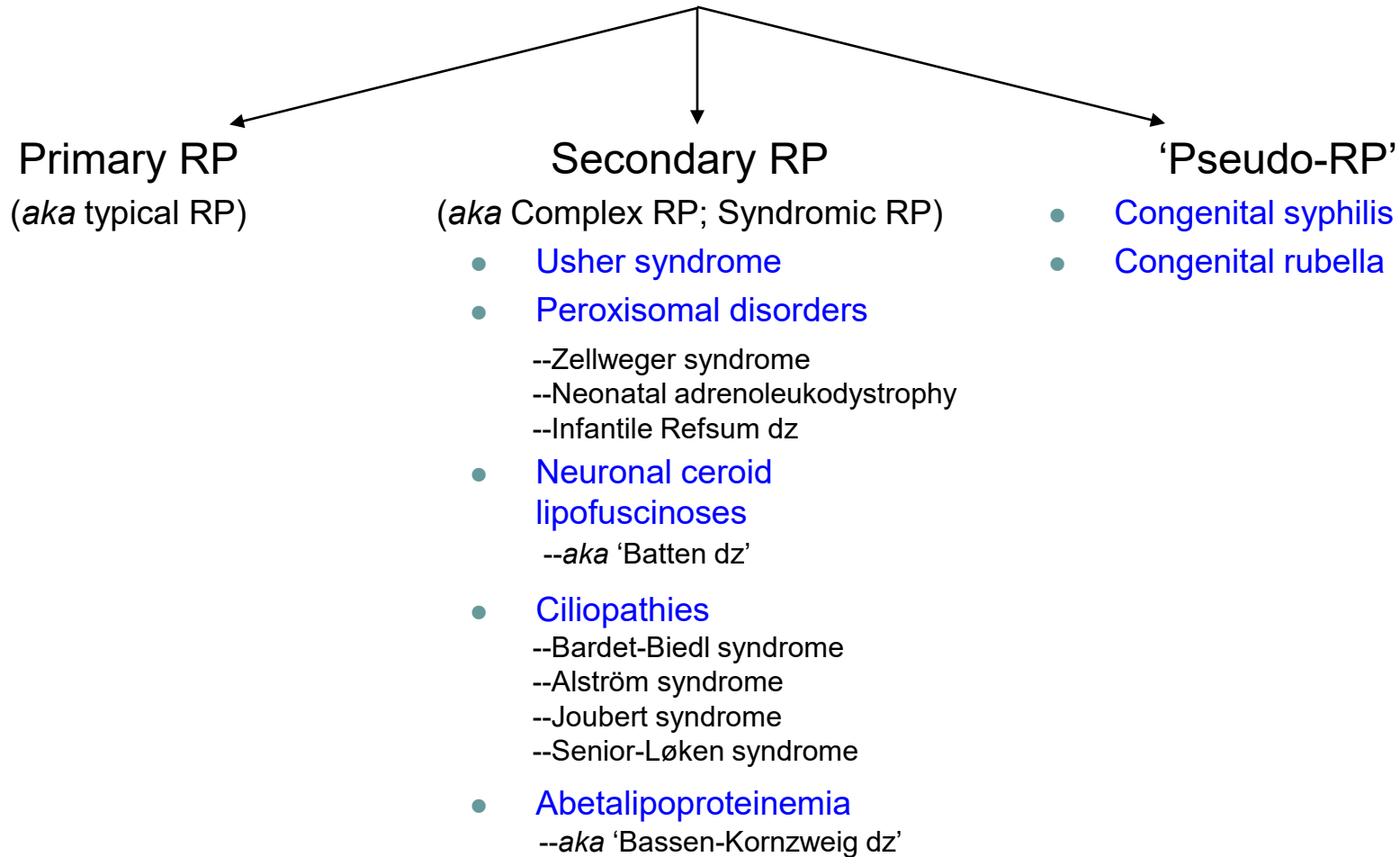
- LCAT deficiency**
- Fish eye disease**
- Tangier disease**

- Abetalipoproteinemia (Bassen-Korzweig)**
- Familial hypobetalipoproteinemia**

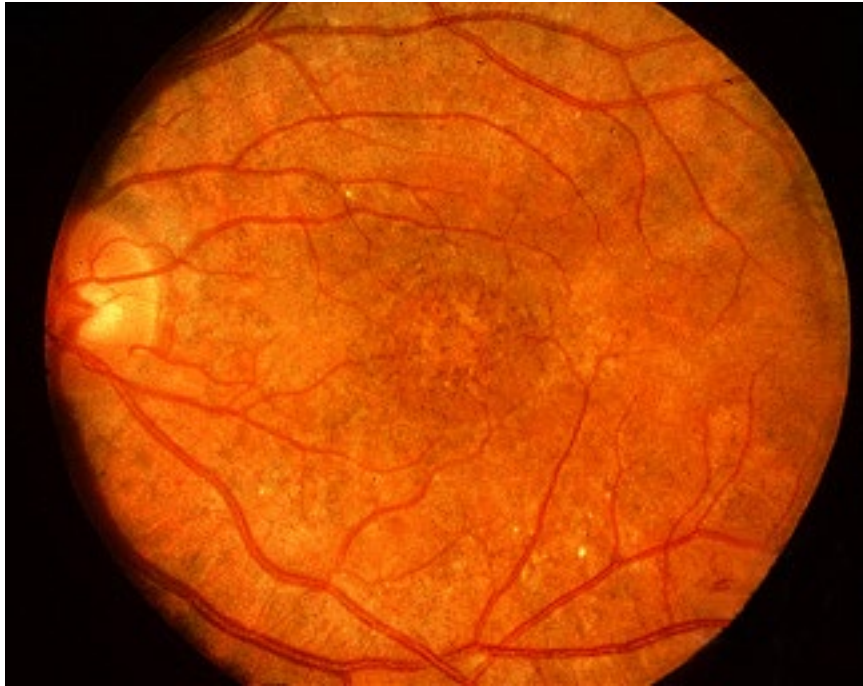
DDx for an RP-like Fundus



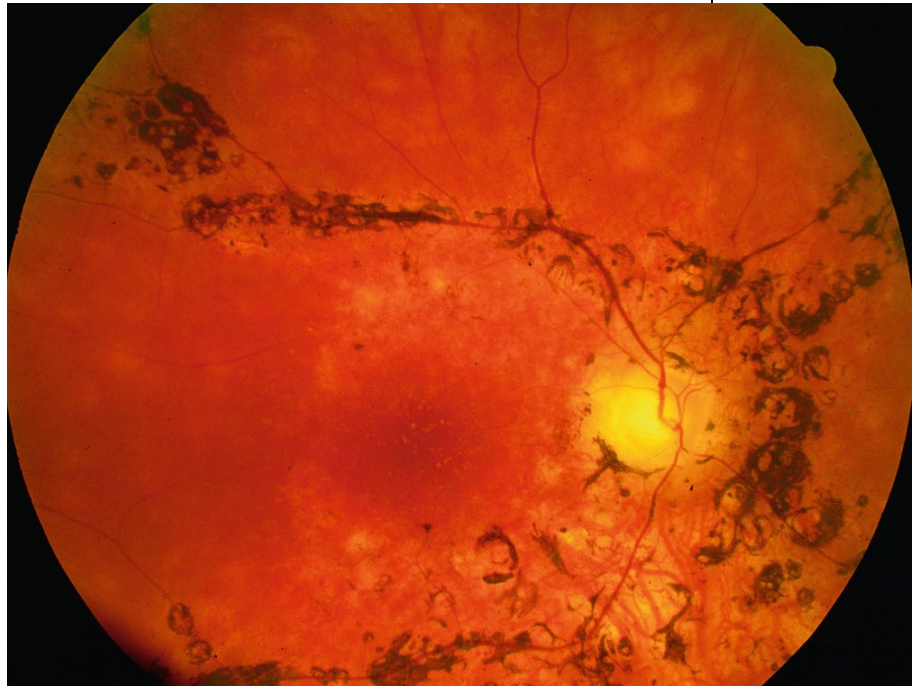
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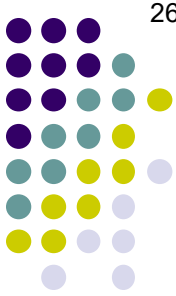
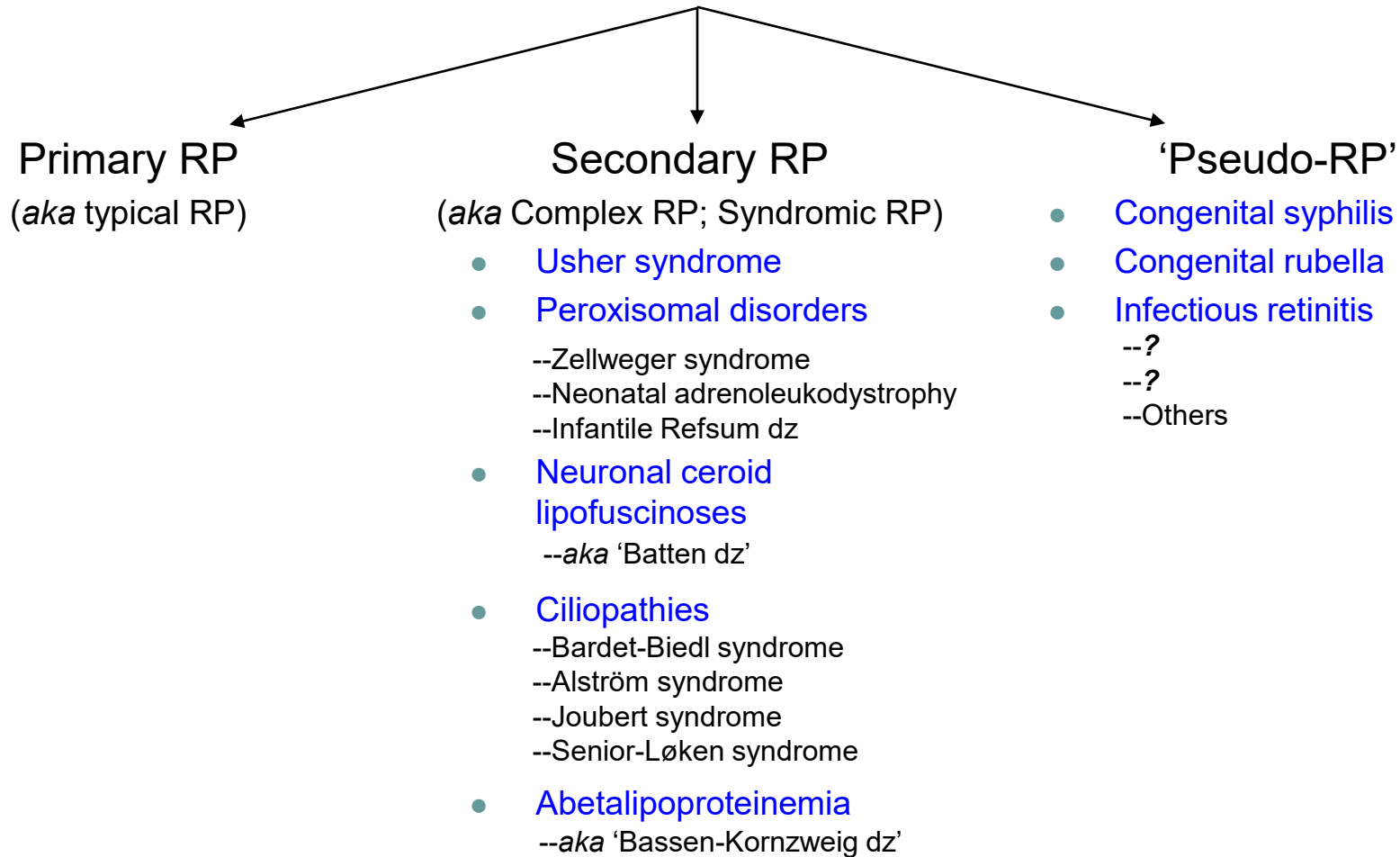


Congenital rubella

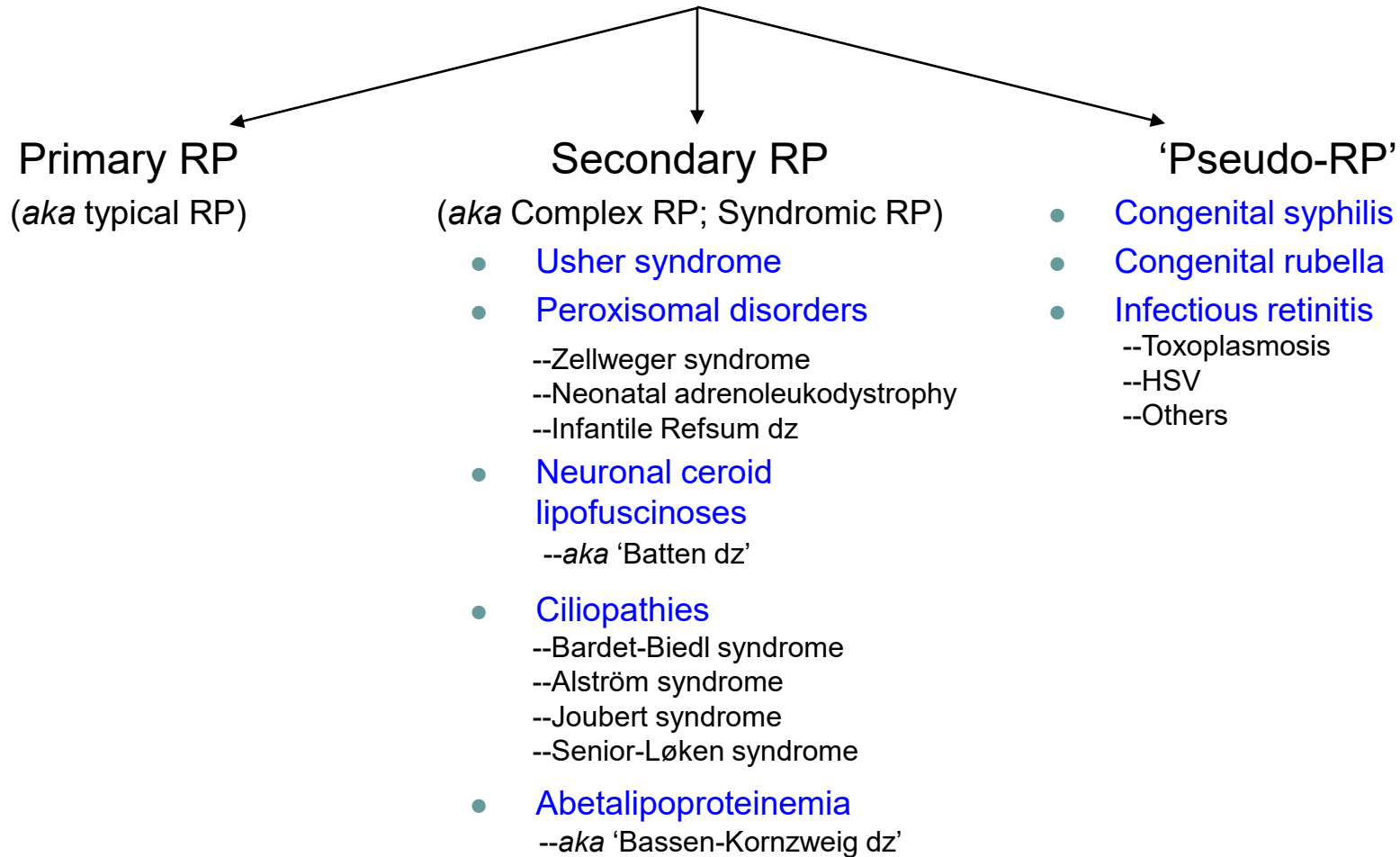


Congenital syphilis

DDx for an RP-like Fundus



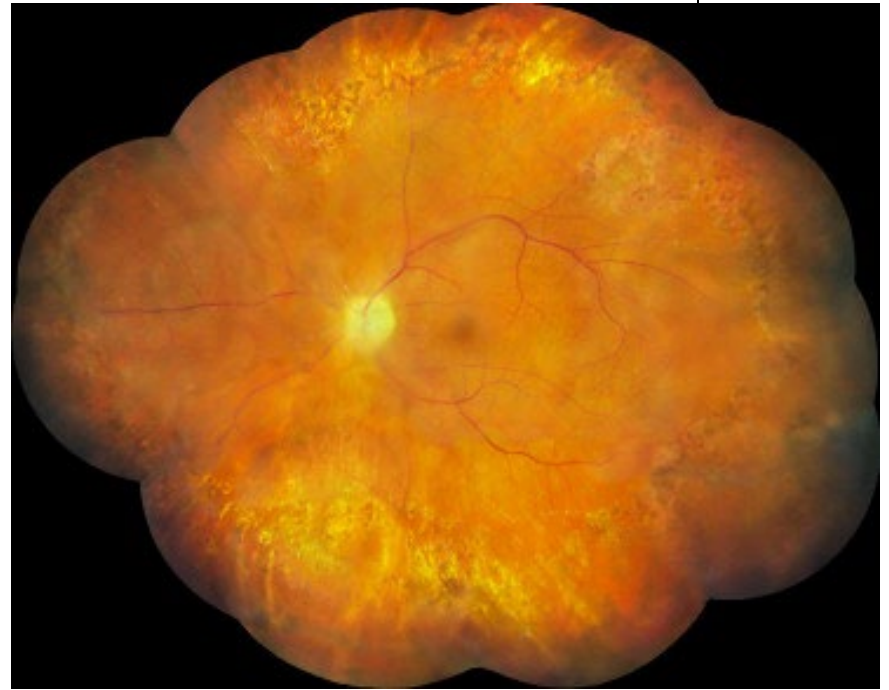
DDx for an RP-like Fundus



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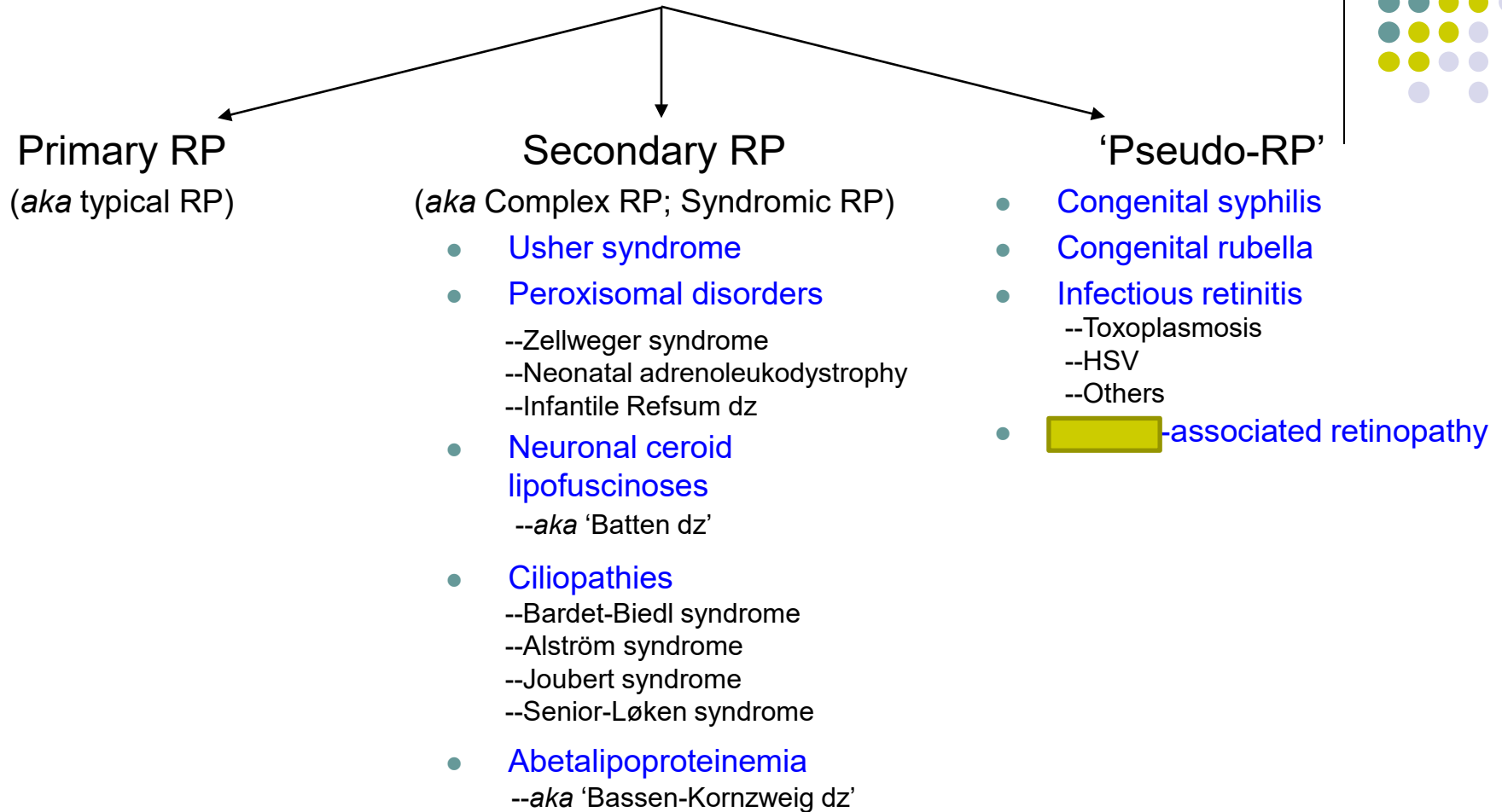


Toxoplasmosis

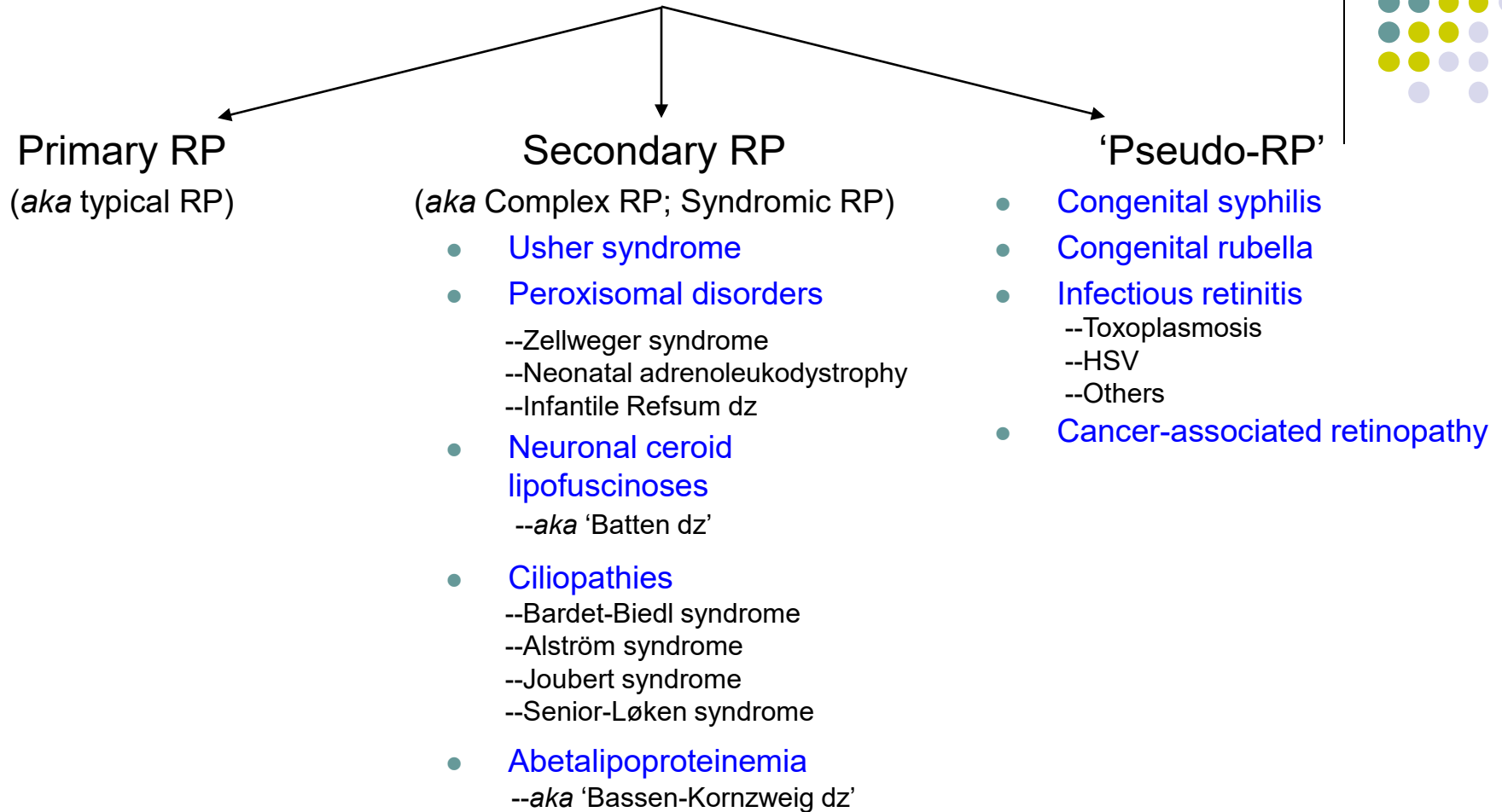


HSV

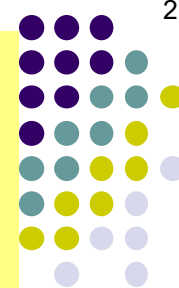
DDx for an RP-like Fundus



DDx for an RP-like Fundus



What is cancer-associated retinopathy (CAR)?



Cancer-associated retinopathy

--aka 'Bassen-Kornzweig dz'

What is cancer-associated retinopathy (CAR)?

A paraneoplastic process in which, by unhappy coincidence, retinal cells possess surface proteins that cross-react with antigens found on cancer cells. If/when the immune system becomes sensitized to the cancer-cell antigens, it will subsequently target the same proteins in the retina, with devastating results.



Cancer-associated retinopathy

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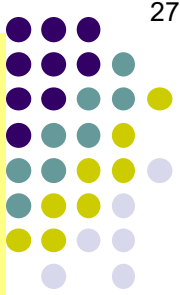
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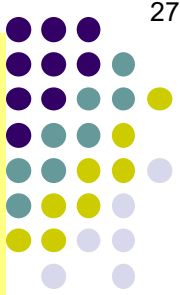
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The pt will c/o progressive bilateral loss of VA and color vision, as well as nyctalopia

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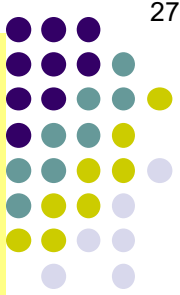
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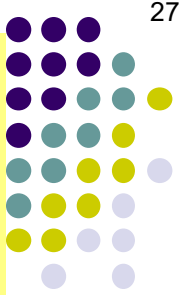
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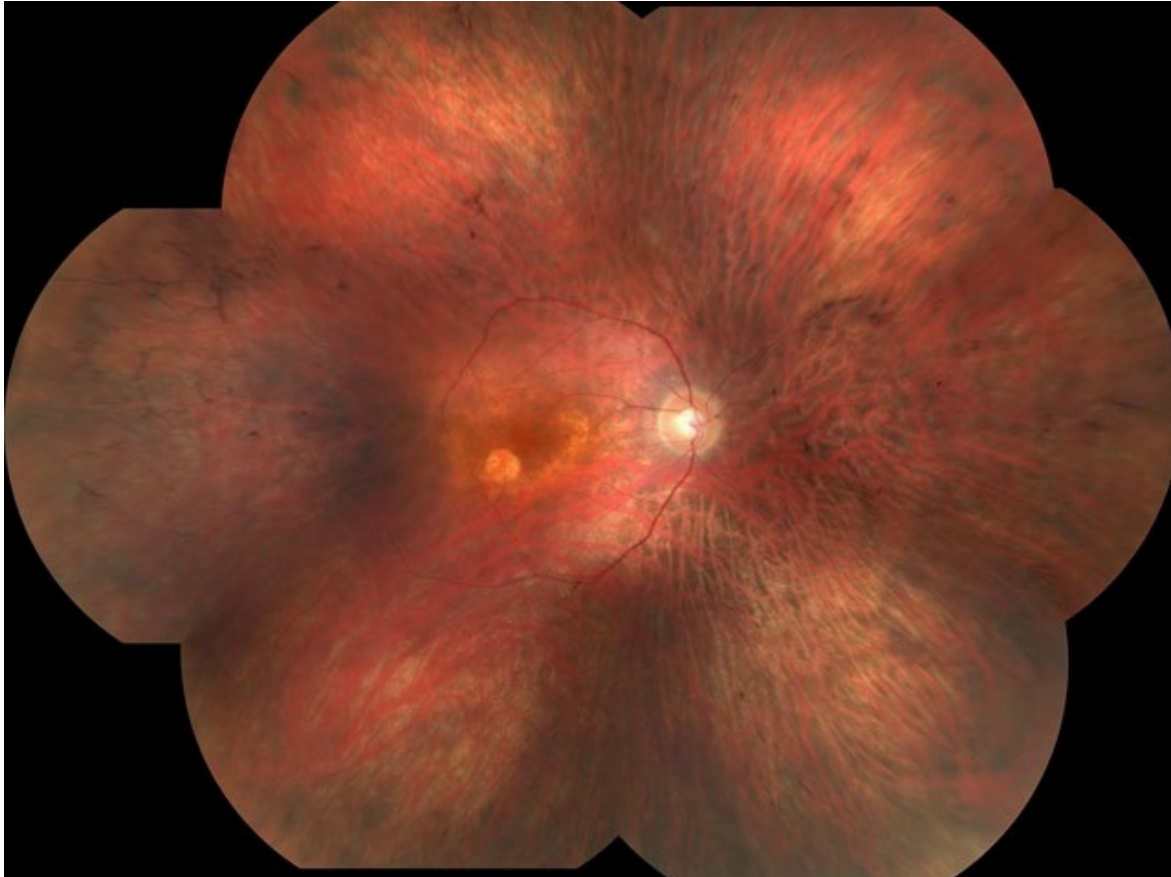
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Next Q

How does CAR present? What is the appearance of the retina on exam? What does testing reveal?

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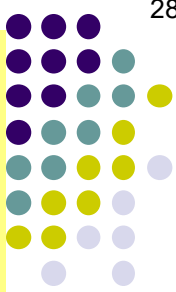
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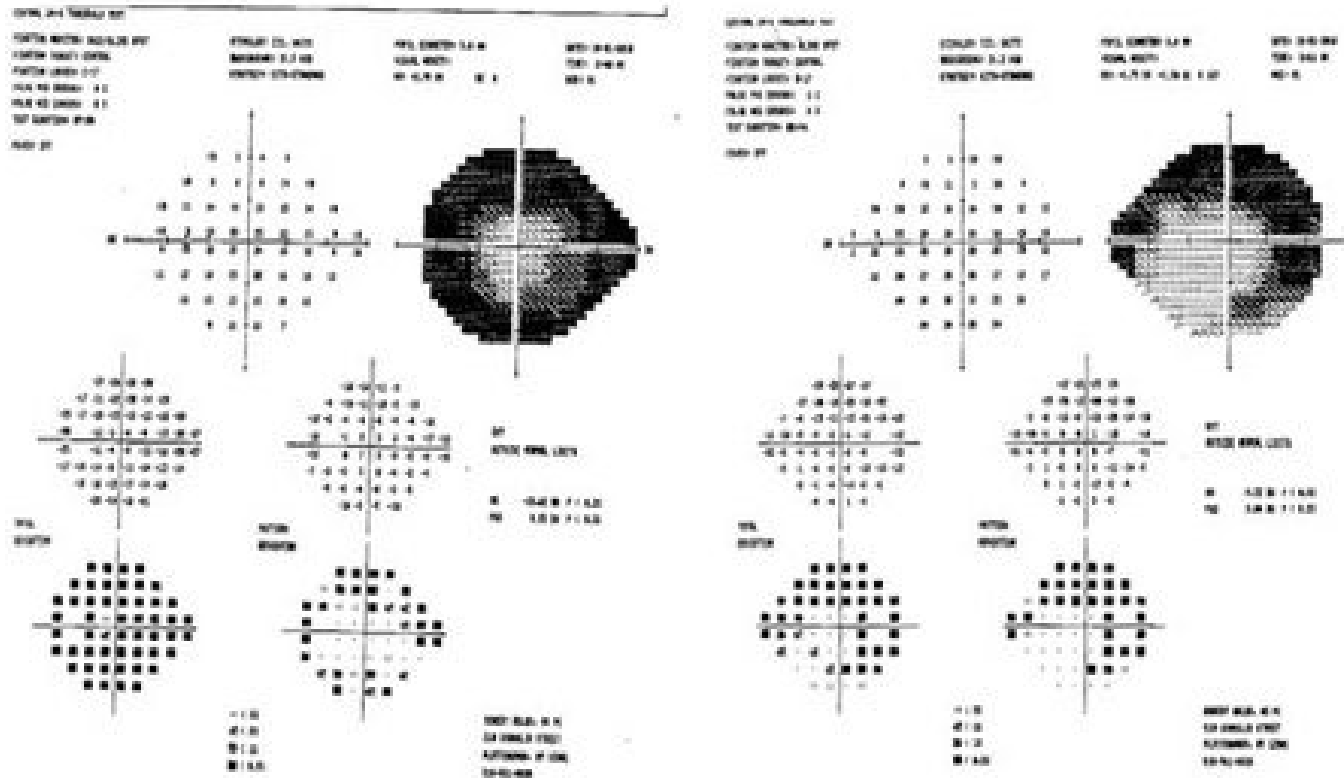
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CAR-associated VF loss

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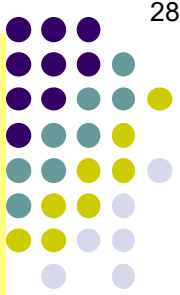
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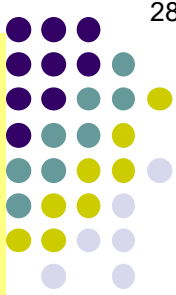
Which cancer is most likely to produce CAR?

subtype

lung cancer is far and away the biggest culprit

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Small-cell lung cancer is far and away the biggest culprit

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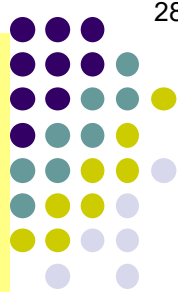
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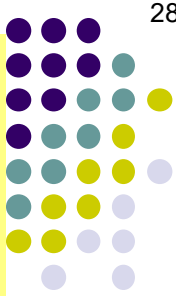
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Is CAR treatable?

--aka 'Bassen-Kornzweig dz'

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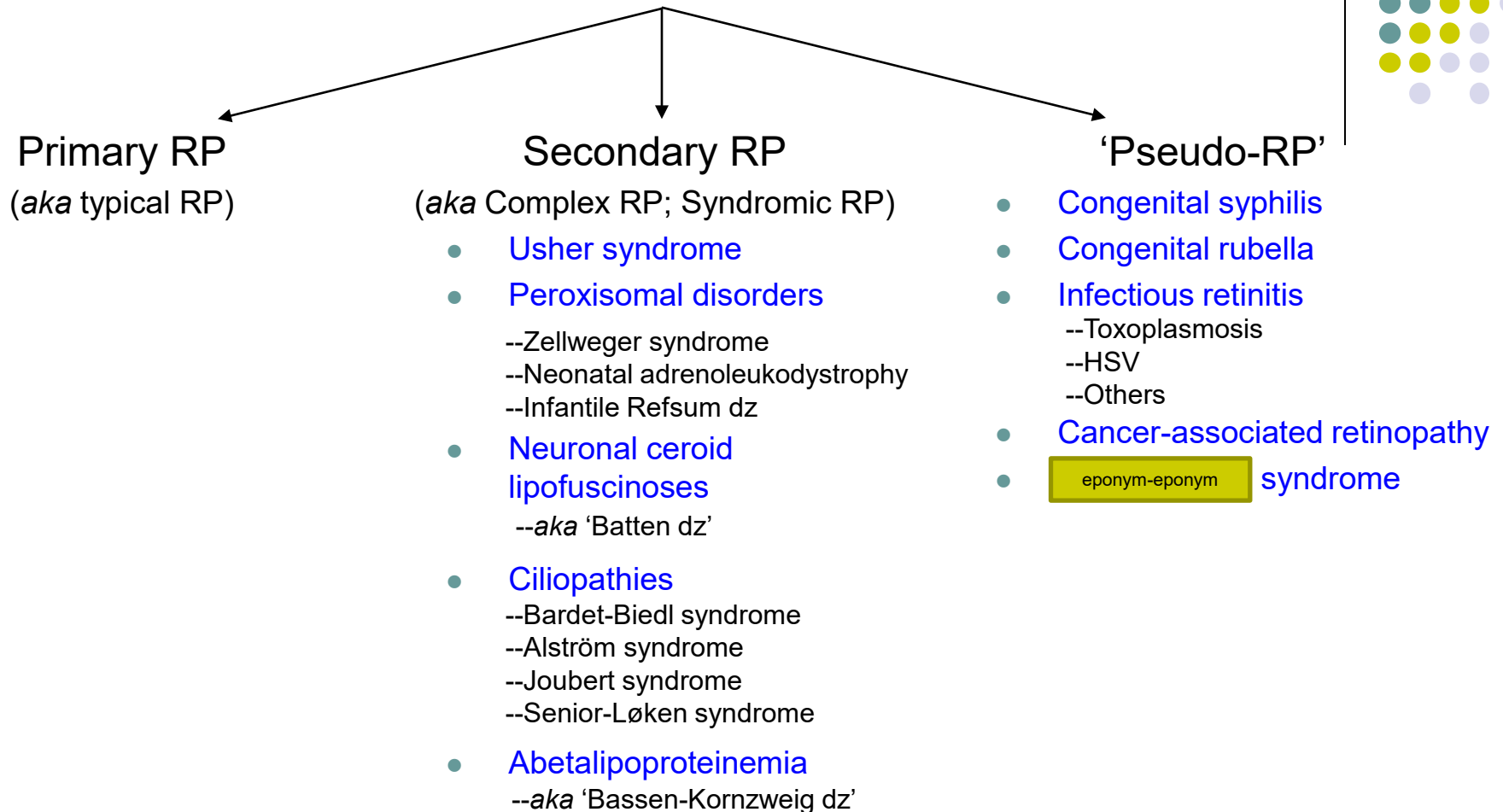
Is CAR treatable?

Steroids, plasmapheresis, and/or IVIG have been thrown at it, but the visual prognosis is dismal

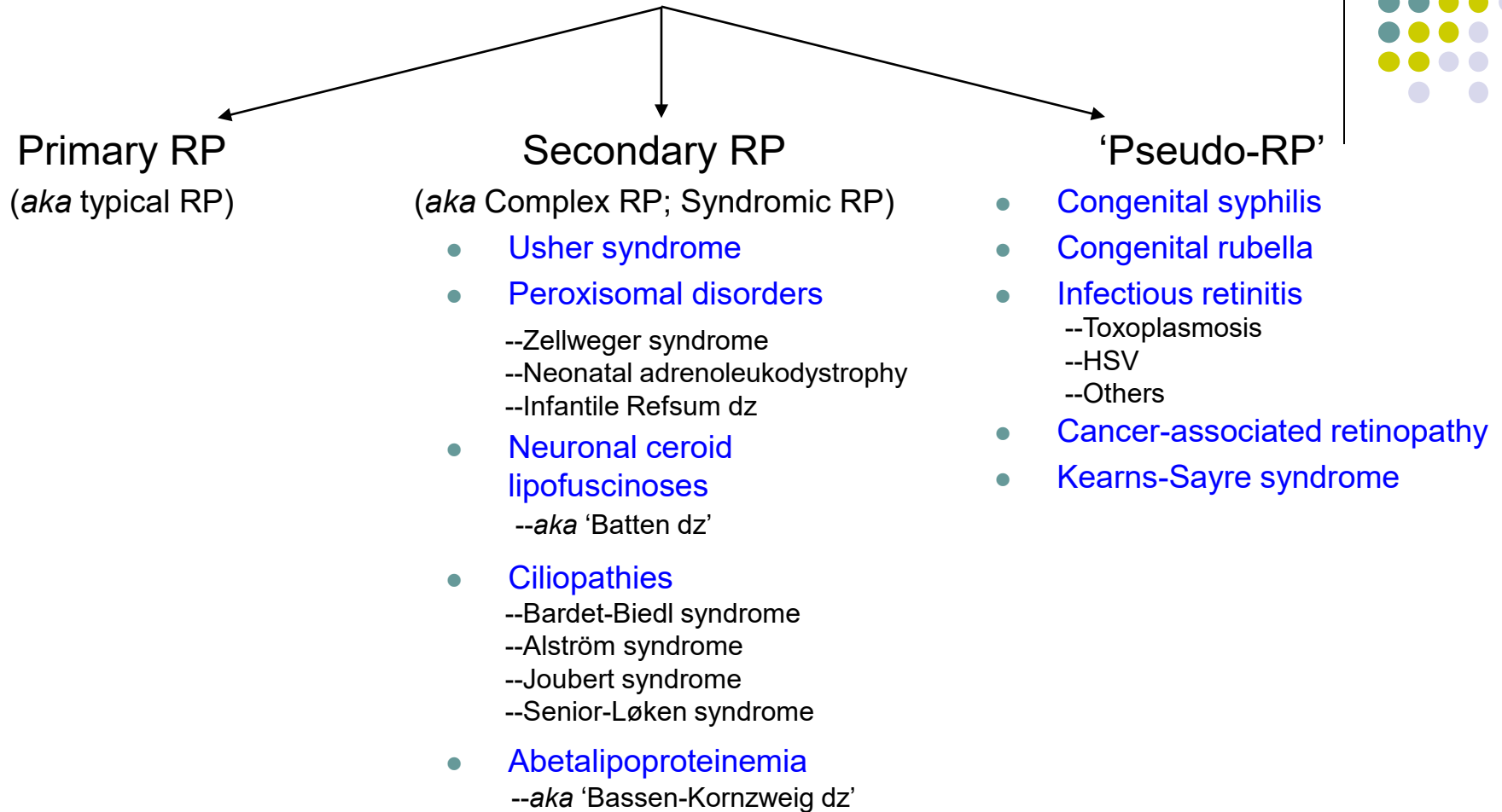
--aka 'Bassen-Kornzweig dz'



DDx for an RP-like Fundus



DDx for an RP-like Fundus



DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP

'Pseudo-RP'

What is the classic triad of Kearns-Sayre syndrome?

--?
--?
--?

Congenital syphilis

Congenital rubella

Infectious retinitis

--Toxoplasmosis

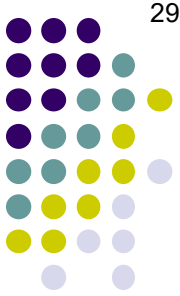
--HSV

--Others

Cancer-associated retinopathy

Kearns-Sayre syndrome

--aka 'Bassen-Kornzweig dz'



DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP

What is the classic triad of Kearns-Sayre syndrome?
 --Pigmentary retinopathy
 --CPEO
 --Cardiac conduction abnormalities

--aka 'Bassen-Kornzweig dz'

'Pseudo-RP'

Congenital syphilis

Congenital rubella

Infectious retinitis

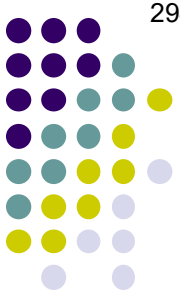
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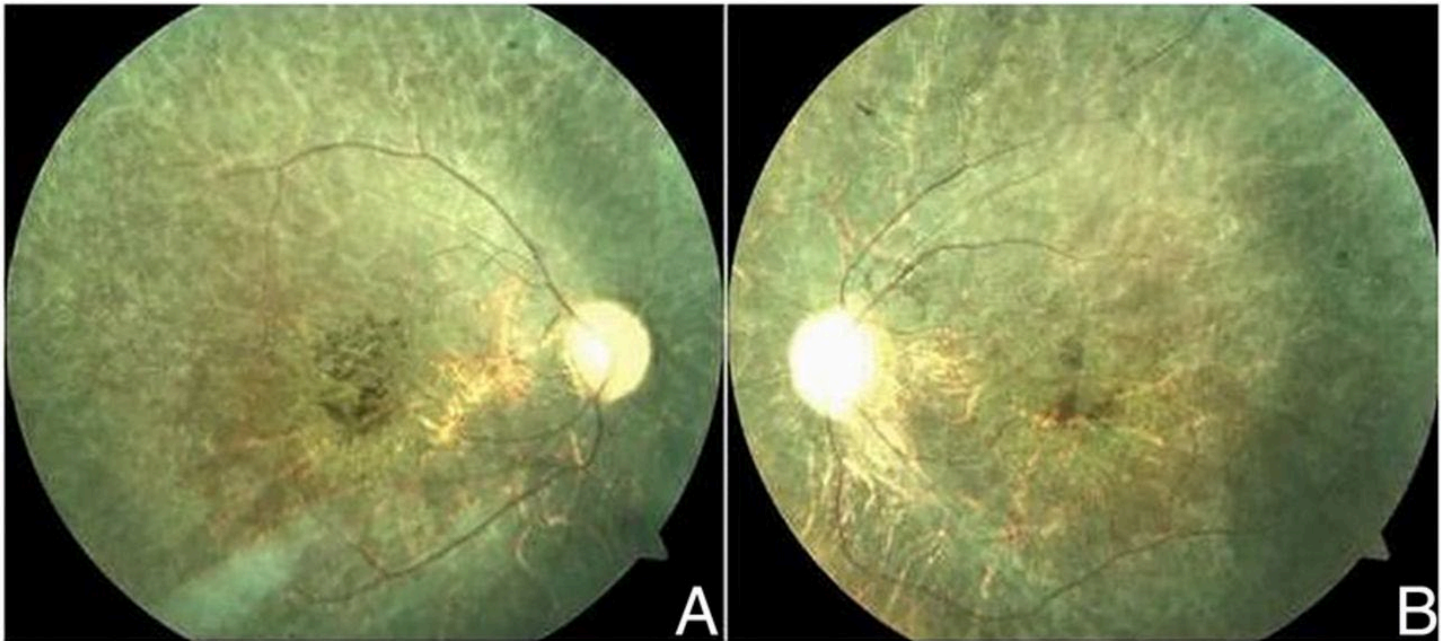
--Others

Cancer-associated retinopathy

Kearns-Sayre syndrome



DDx for an RP-like Fundus



Kearns-Sayre syndrome: Pigmentary retinopathy



DDx for an RP-like Fundus

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What is the classic triad of Kearns-Sayre syndrome?

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What does CPEO stand for?

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What does CPEO stand for?

Chronic progressive external ophthalmoplegia

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Cancer-associated retinopathy

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Chronic progressive **external ophthalmoplegia**

What does it mean to say an ophthalmoplegia is 'external'?

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Infectious retinitis

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Cancer-associated retinopathy

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What does CPEO stand for?

Chronic progressive **external ophthalmoplegia**

What does it mean to say an ophthalmoplegia is 'external'?

It means the iris and CB are not affected/involved

--aka 'Bassen-Kornzweig dz'

Congenital syphilis

Congenital rubella

Infectious retinitis

--Toxoplasmosis

--HSV

--Others

Cancer-associated retinopathy

Kearns-Sayre syndrome

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What does CPEO stand for?

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Which EOMs are typically affected first?

--aka 'Bassen-Kornzweig dz'

Congenital syphilis

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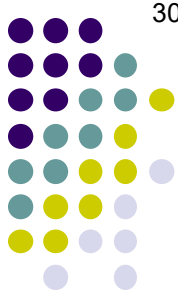
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Which EOMs are typically affected first?

The levators; ie, ptosis is the first manifestation

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--HSV

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Cancer-associated retinopathy

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Chronic progressive external ophthalmoplegia

Which EOMs are typically affected first?

The levators; ie, ptosis is the first manifestation.

However, the disease is relentlessly progressive, and eventually all of the EOMs are paralyzed.

--aka 'Bassen-Kornzweig dz'

Congenital syphilis

Congenital rubella

Infectious retinitis

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--HSV

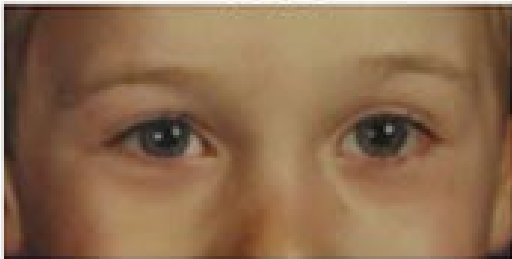
--Others

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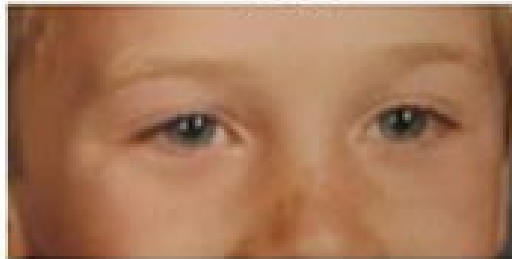
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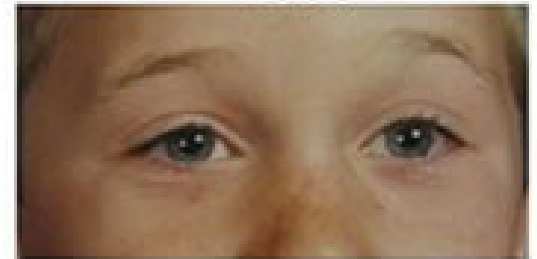
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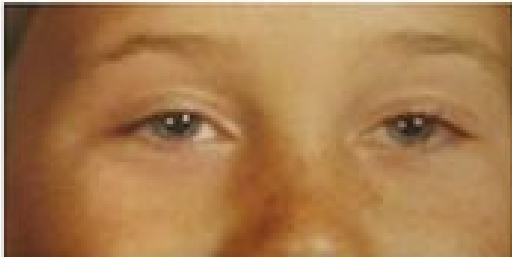
1999



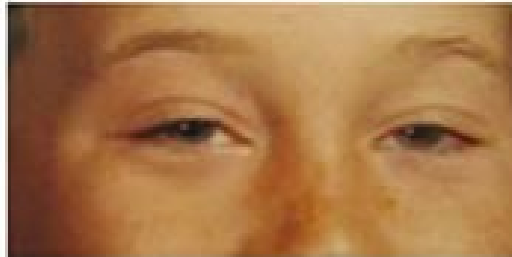
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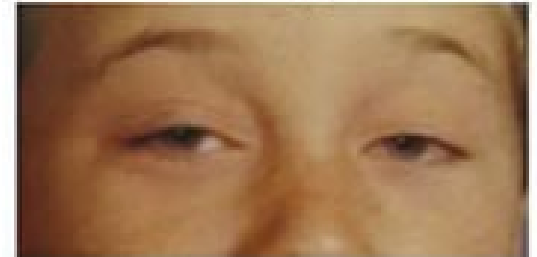
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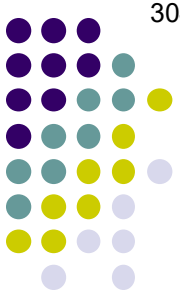
2003



2004



CPEO



DDx for an RP-like Fundus

Primary RP
(aka typical RP)

Secondary RP

'Pseudo-RP'

What is the classic triad of Kearns-Sayre syndrome?

--Pigmentary retinopathy

--CPEO

--**Cardiac conduction abnormalities**

Are the cardiac-conduction problems serious?

Congenital syphilis

Congenital rubella

Infectious retinitis

--Toxoplasmosis

--HSV

--Others

Cancer-associated retinopathy

Kearns-Sayre syndrome

--aka 'Bassen-Kornzweig dz'



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What is the classic triad of Kearns-Sayre syndrome?

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--**Cardiac conduction abnormalities**

Are the cardiac-conduction problems serious?

Yes, they can be life-threatening

Congenital syphilis

Congenital rubella

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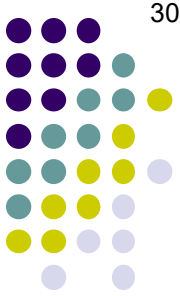
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In very general terms, what sort of disease is K-SS?

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Infectious retinitis

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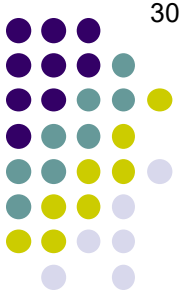
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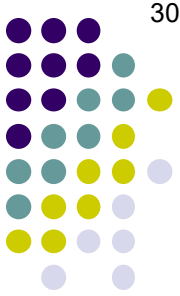
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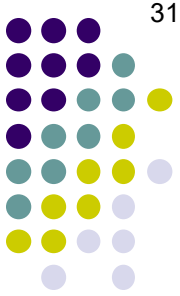
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Kearns-Sayre syndrome



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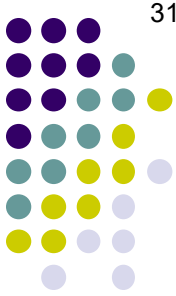
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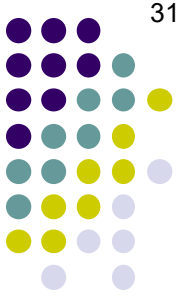
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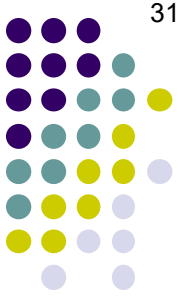
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The ophthalmoplegia (usually the ptosis)

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Why is the order important?

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Usually around 10 years

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The ophthalmoplegia (usually the ptosis)

Why is the order important?

Because in making the proper diagnosis, the astute eye dentist can refer the pt to a cardiologist **before** s/he has a fatal dysrhythmia

Congenital syphilis

Congenital rubella

Infectious retinitis

--Toxoplasmosis

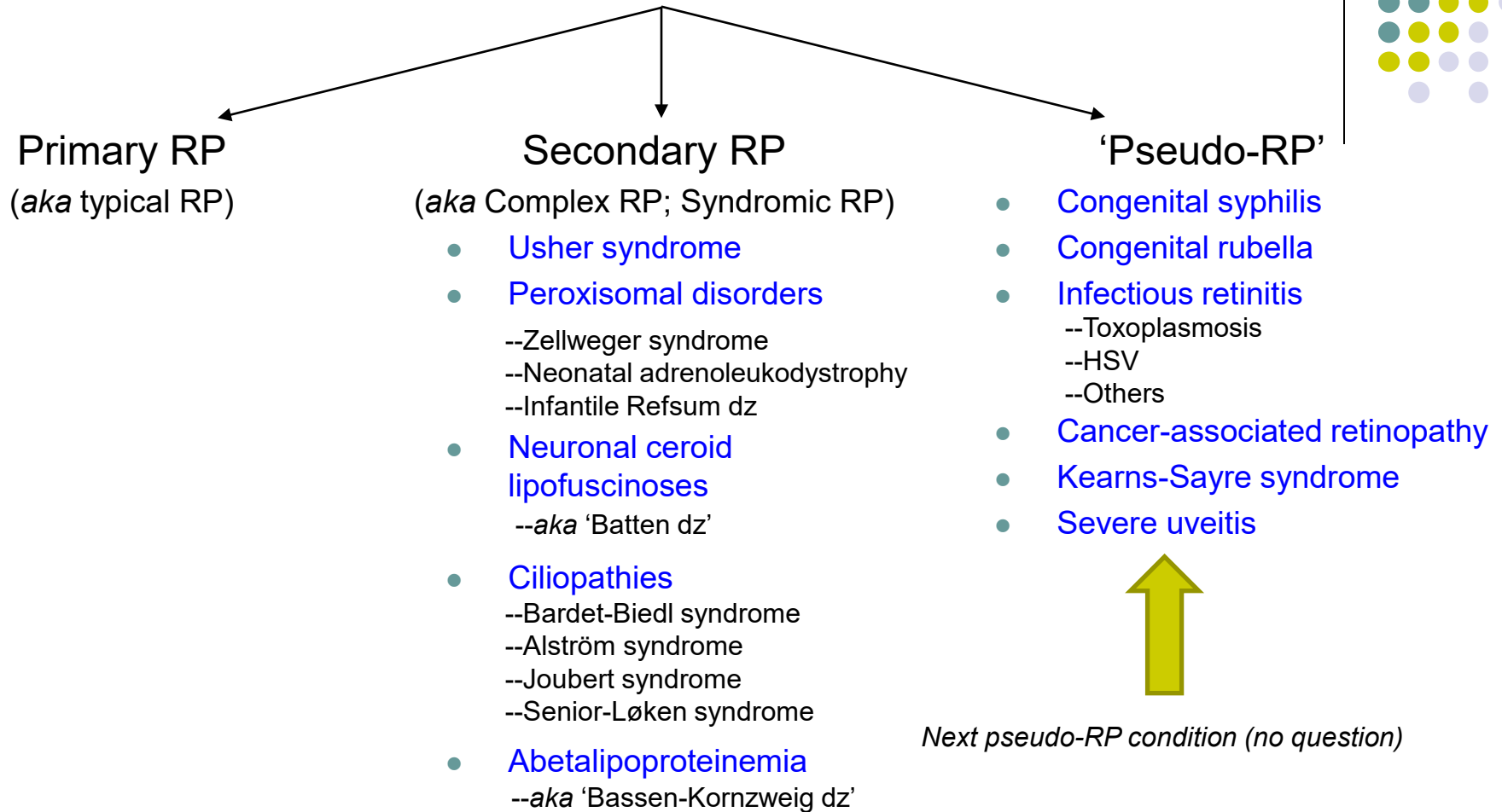
--HSV

--Others

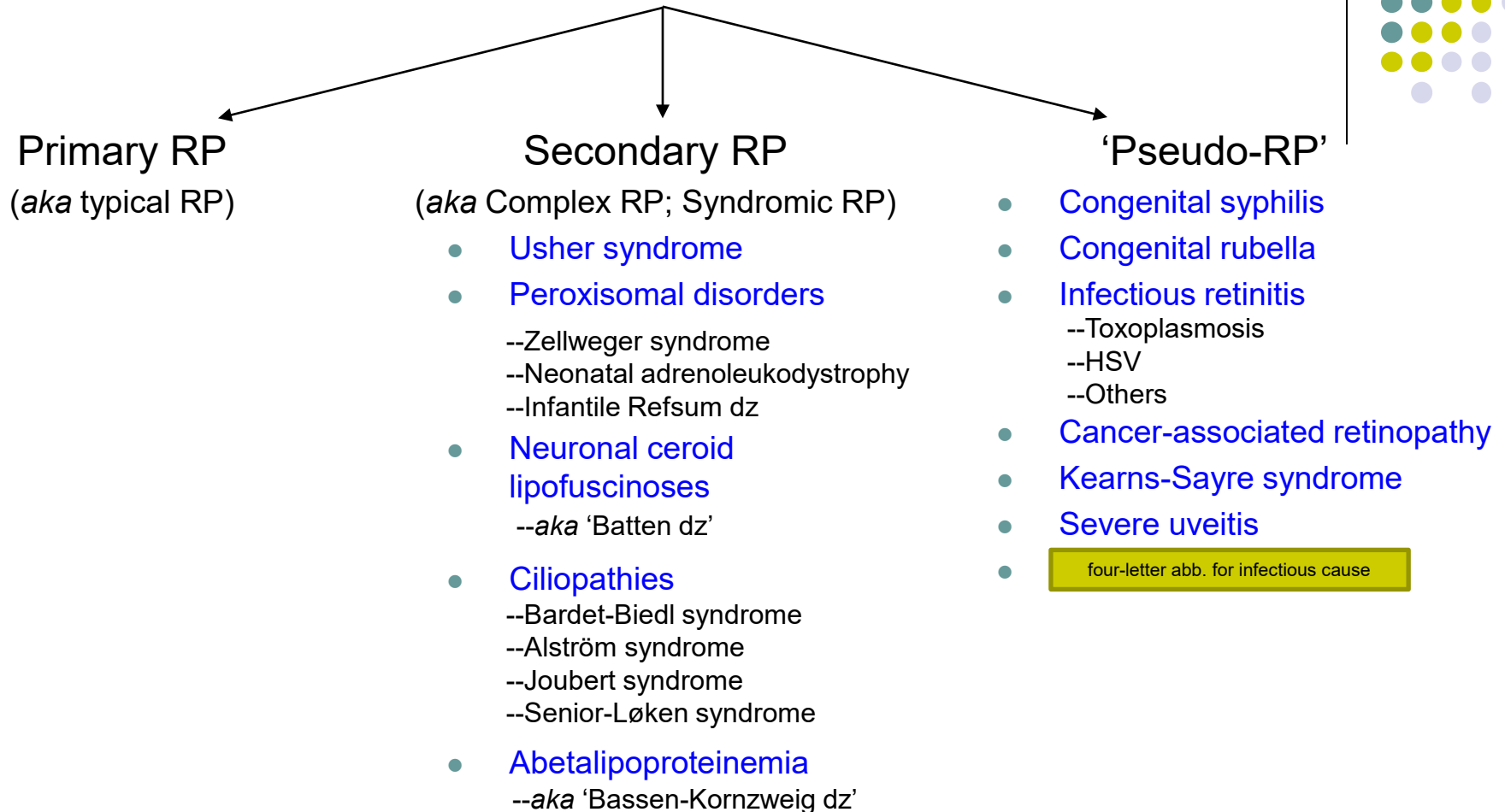
Cancer-associated retinopathy

Kearns-Sayre syndrome

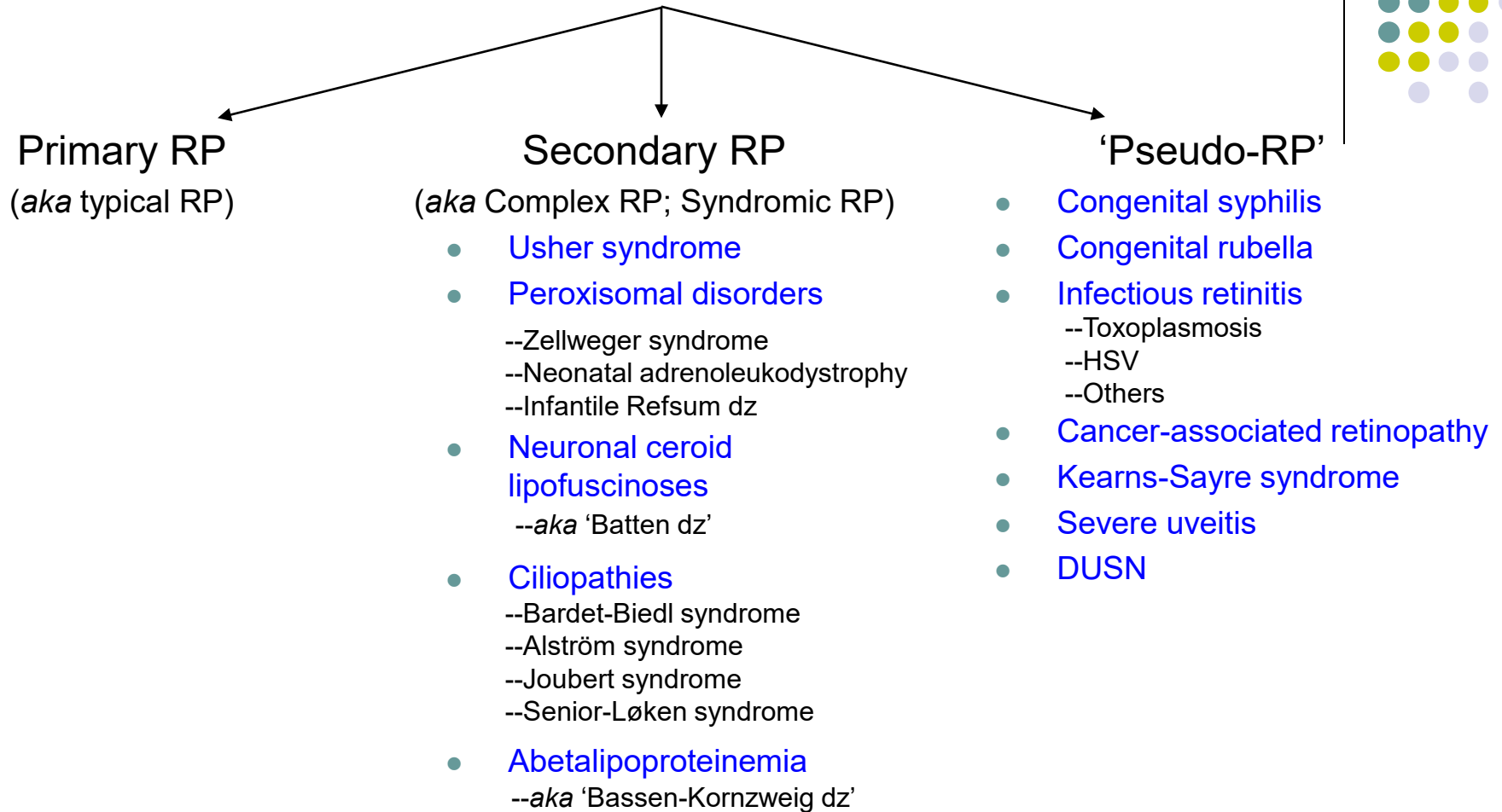
DDx for an RP-like Fundus



DDx for an RP-like Fundus



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DDx for an RP-like Fundus

Primary RP
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Secondary RP

(aka Complex RP; Syndromic RP)

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 - Zellweger syndrome
 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz
- Neuronal ceroid lipofuscinoses
 - aka 'Batten dz'
- Ciliopathies
 - Bardet-Biedl syndrome

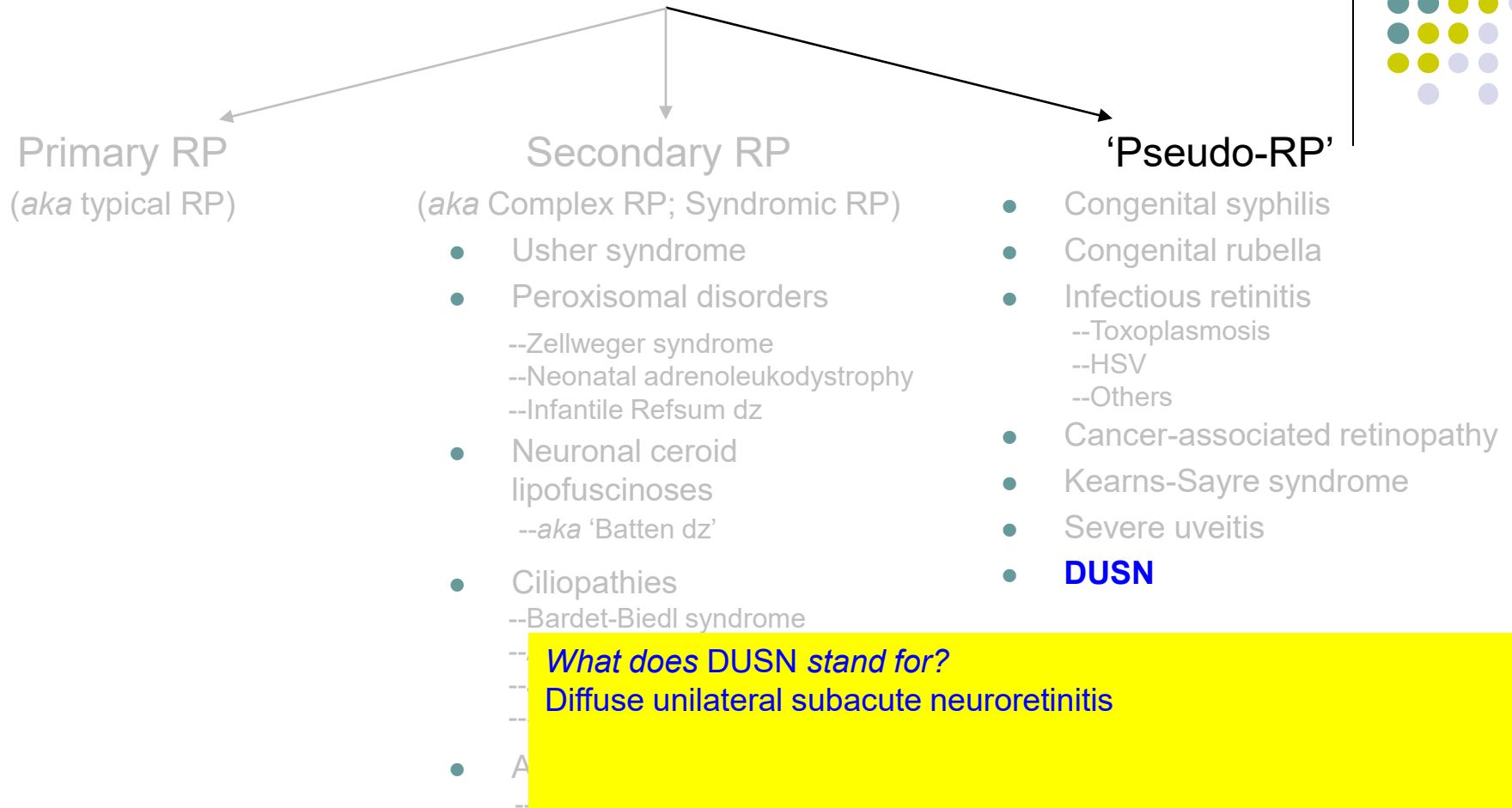
'Pseudo-RP'

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- Infectious retinitis
 - Toxoplasmosis
 - HSV
 - Others
- Cancer-associated retinopathy
- Kearns-Sayre syndrome
- Severe uveitis
- **DUSN**

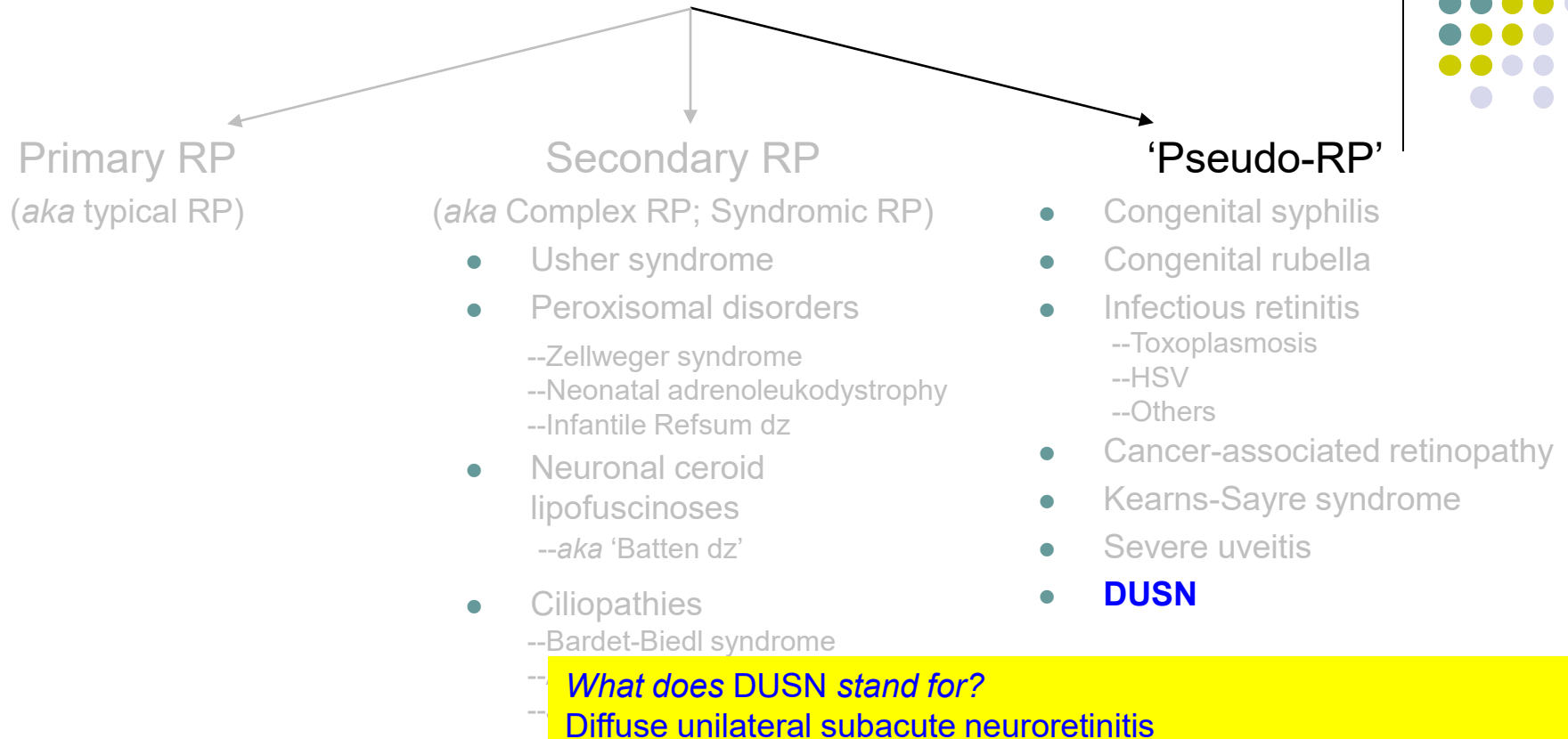
What does DUSN stand for?



DDx for an RP-like Fundus



DDx for an RP-like Fundus



What is the cause?

DDx for an RP-like Fundus

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Secondary RP

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 - HSV
 - Others
- Cancer-associated retinopathy
- Kearns-Sayre syndrome
- Severe uveitis
- **DUSN**

What does DUSN stand for?

Diffuse unilateral subacute neuroretinitis

What is the cause?

Infestation by a type of bug



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(aka typical RP)

Secondary RP

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- Usher syndrome
- Peroxisomal disorders
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'Pseudo-RP'

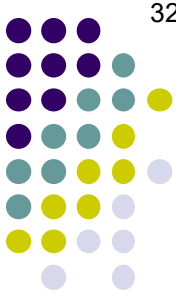
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- **DUSN**

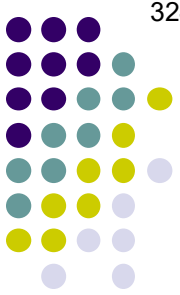
What does DUSN stand for?

Diffuse unilateral subacute neuroretinitis

What is the cause?

Infestation by a worm





DDx for an RP-like Fundus

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 - Others
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- Kearns-Sayre syndrome
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- **DUSN**

What does DUSN stand for?

Diffuse unilateral subacute neuroretinitis

What is the cause?

Infestation by a worm (most commonly, specific worm)



DDx for an RP-like Fundus

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(aka typical RP)

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(aka Complex RP; Syndromic RP)

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 - Zellweger syndrome
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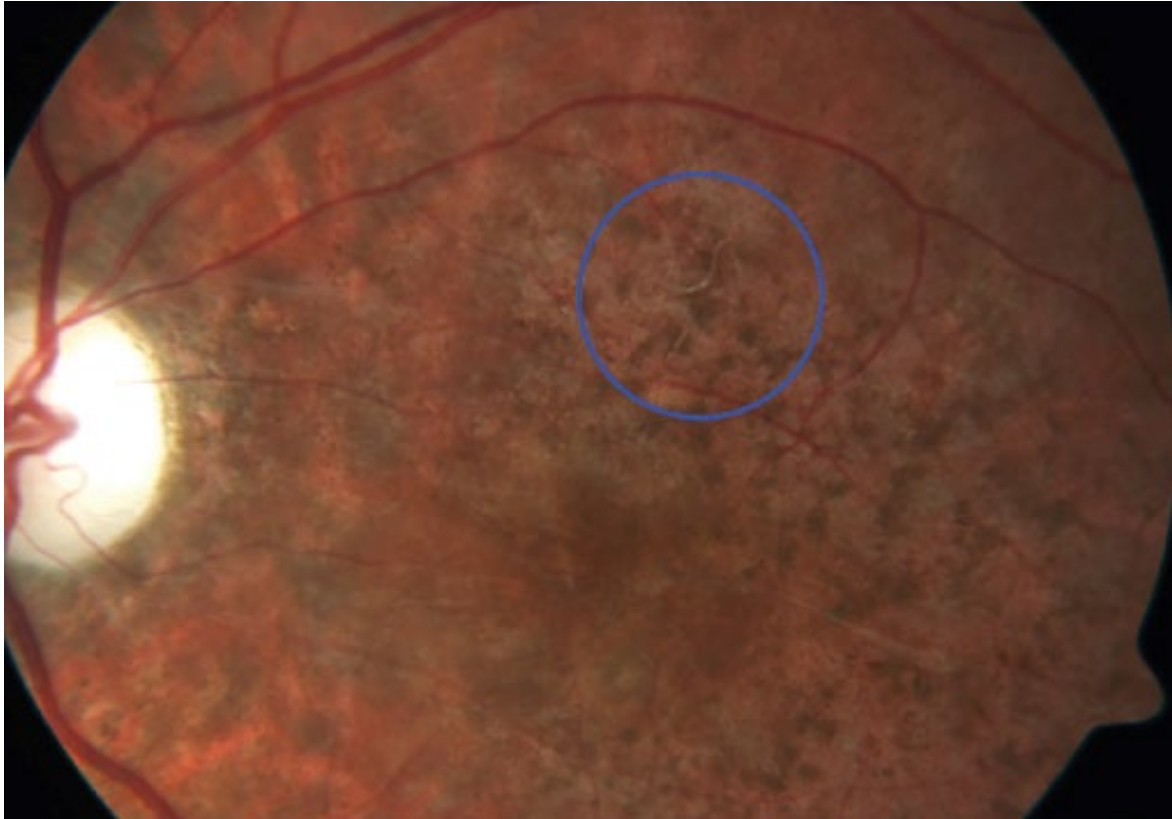
What does DUSN stand for?

Diffuse unilateral subacute neuroretinitis

What is the cause?

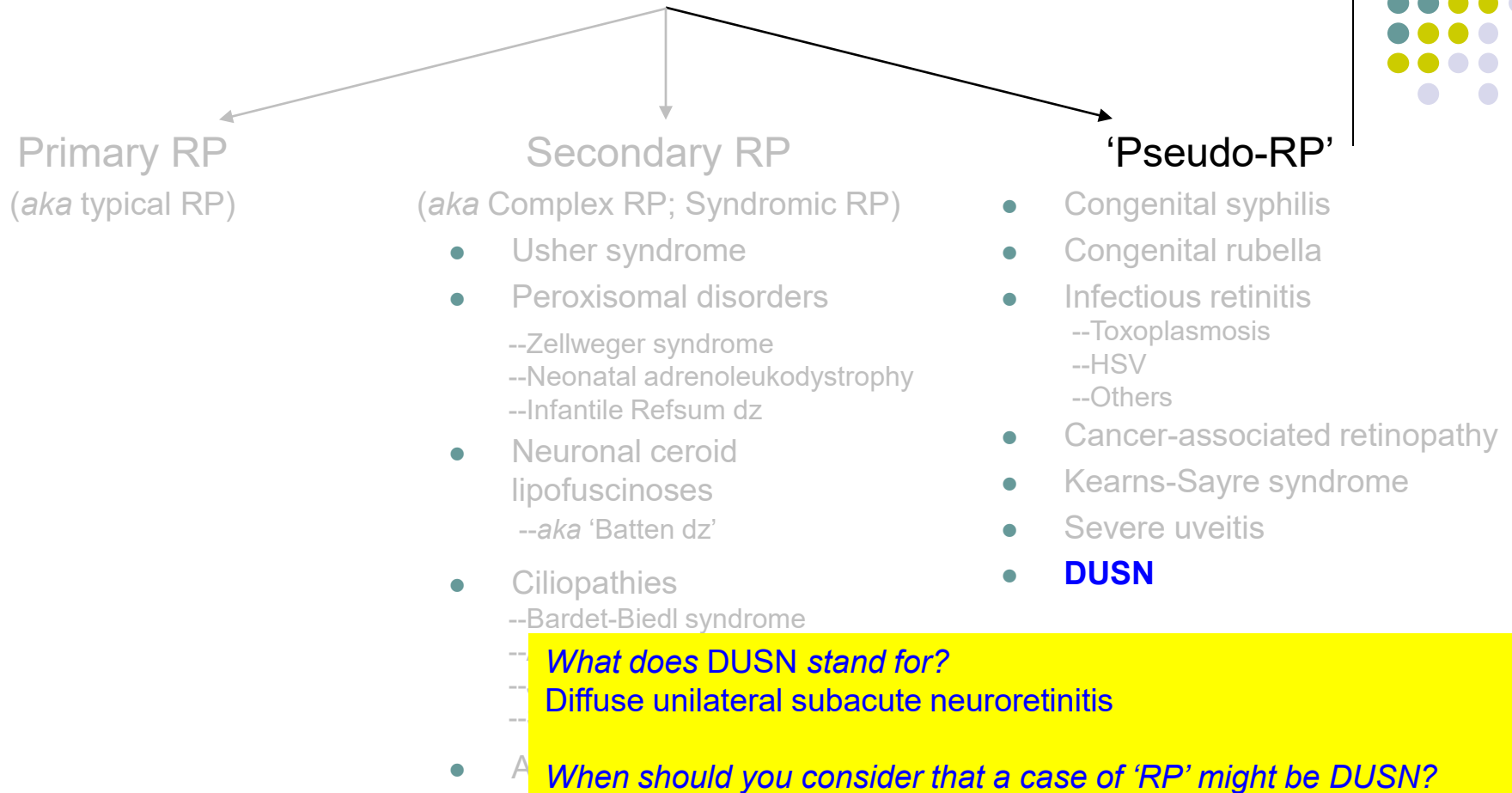
Infestation by a worm (most commonly, *Baylisacaris*)

DDx for an RP-like Fundus

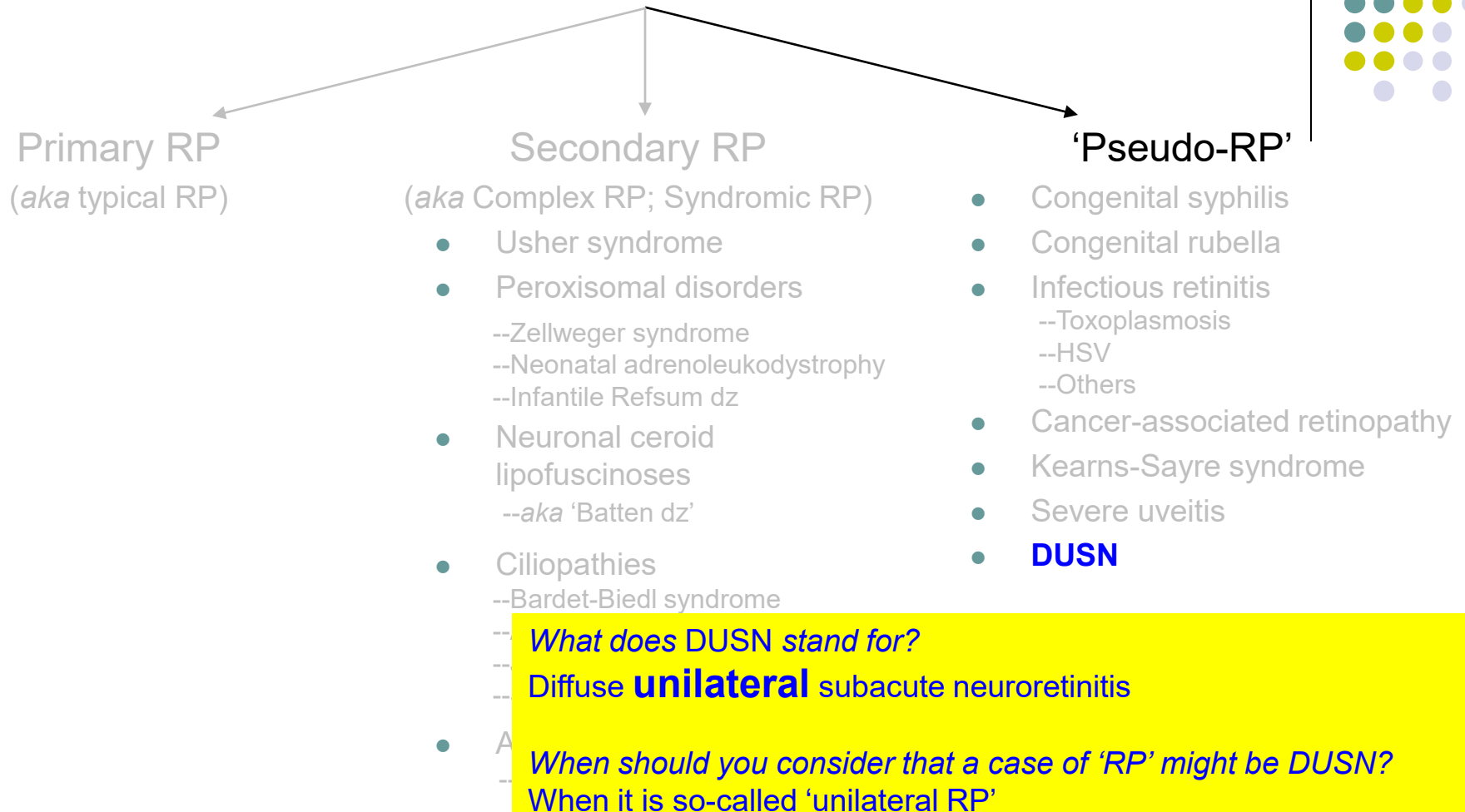


DUSN (circle indicates the worm's location)

DDx for an RP-like Fundus



DDx for an RP-like Fundus



DDx for an RP-like Fundus

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(aka typical RP)

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 - Others

For more on DUSN see slide-set R15

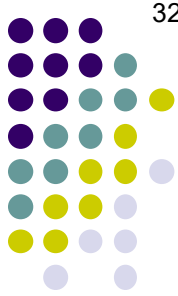
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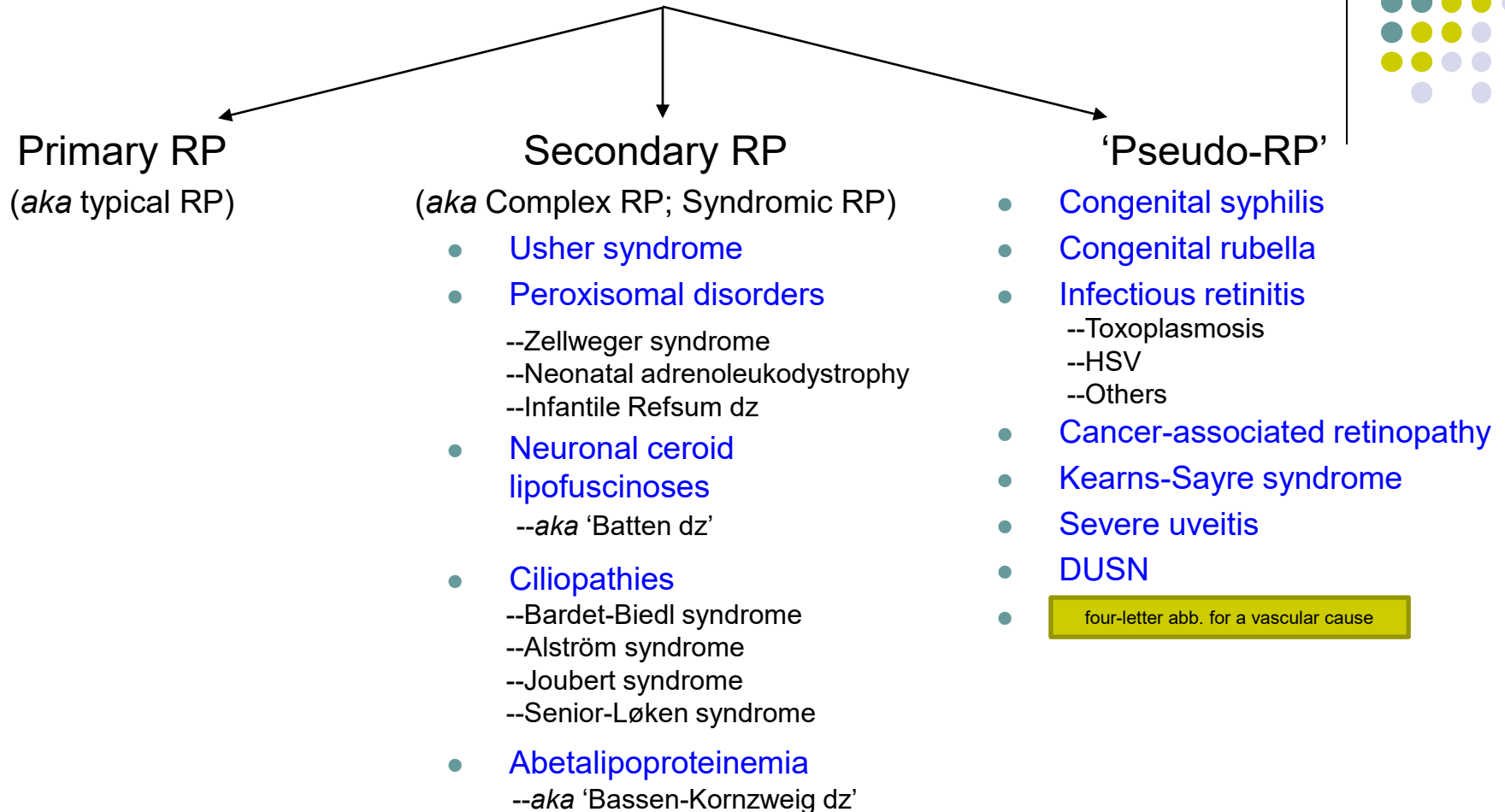
What does DUSN stand for?

Diffuse **unilateral** subacute neuroretinitis

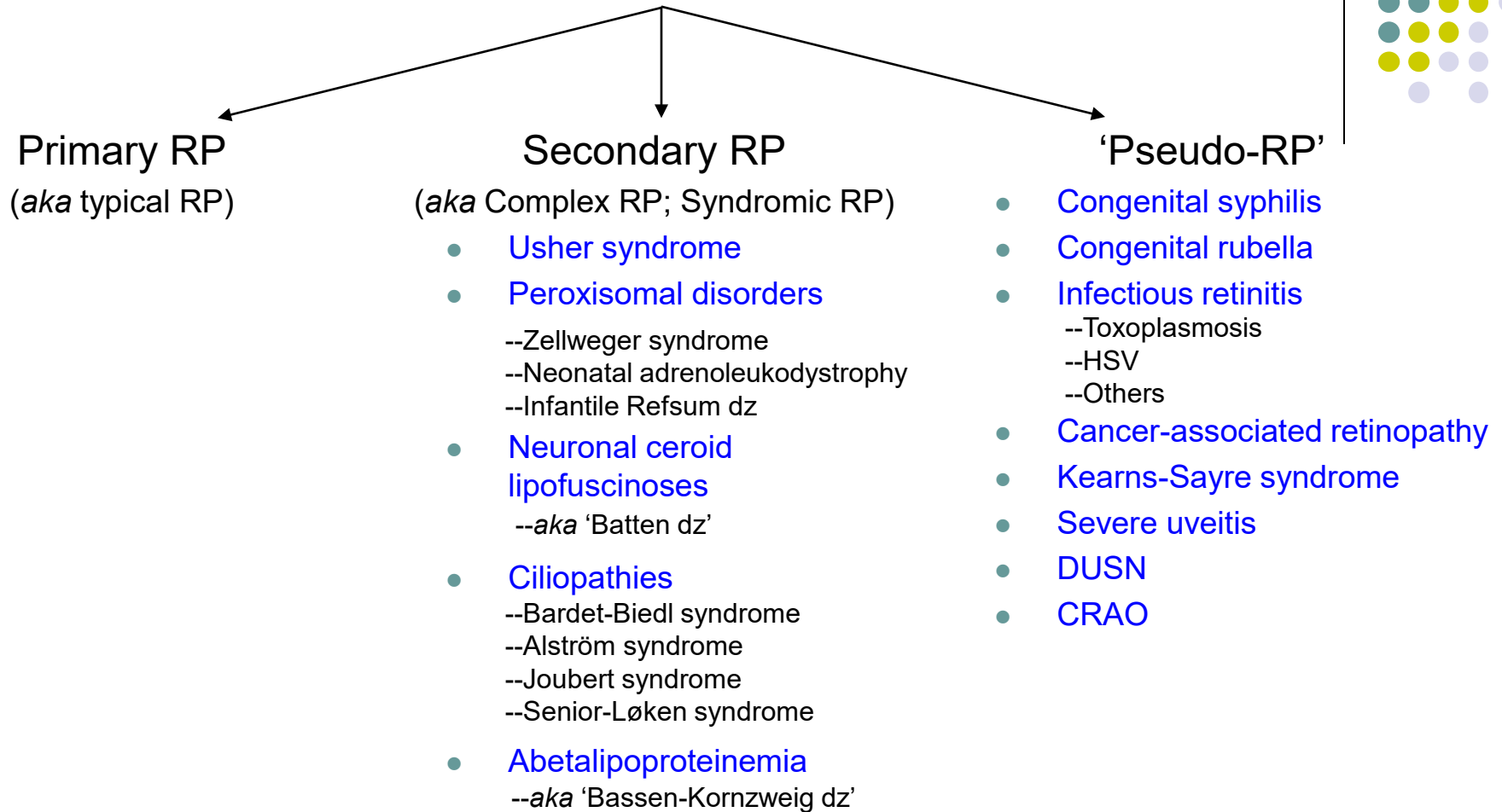
When should you consider that a case of 'RP' might be DUSN?
When it is so-called 'unilateral RP'



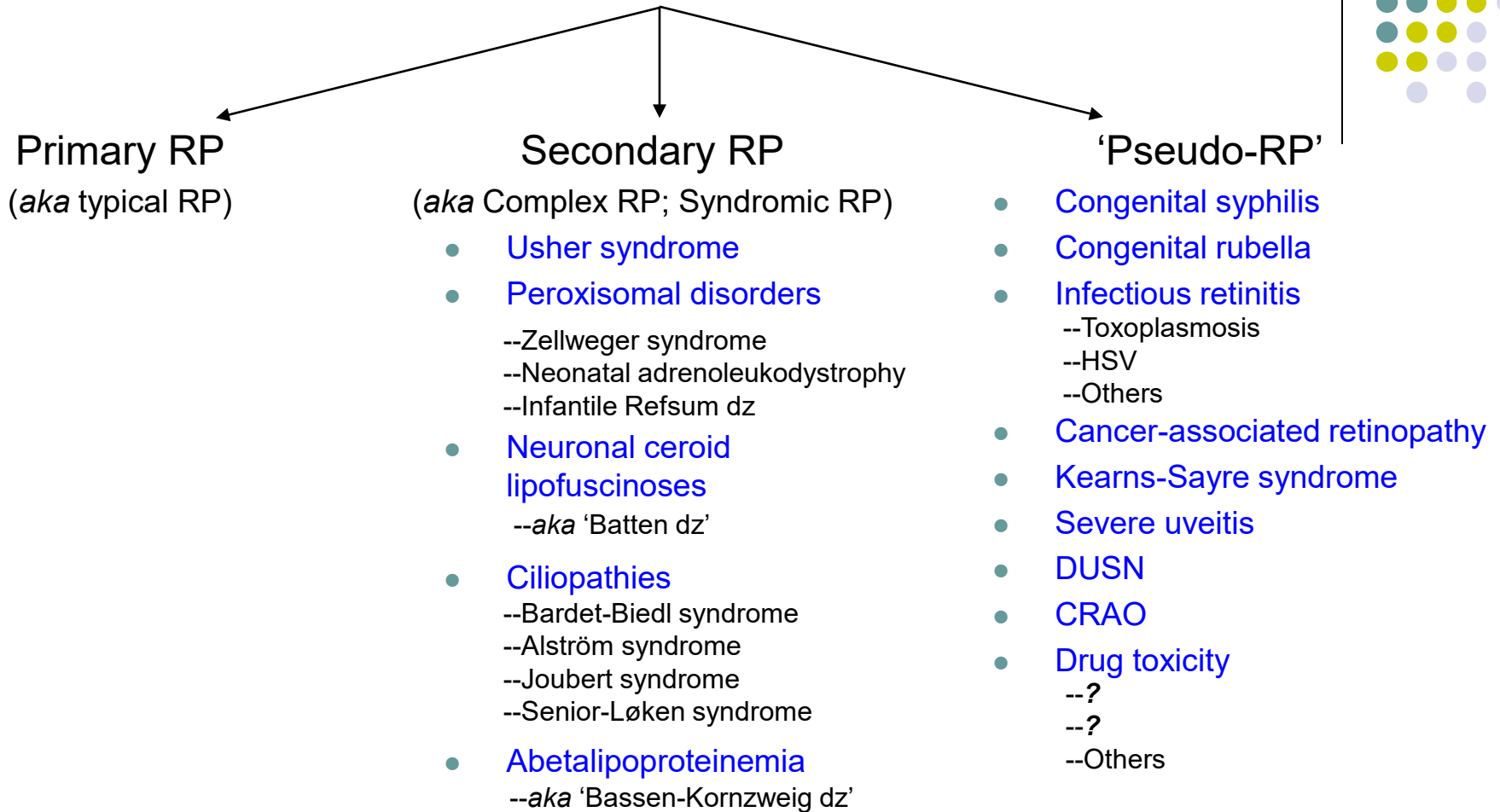
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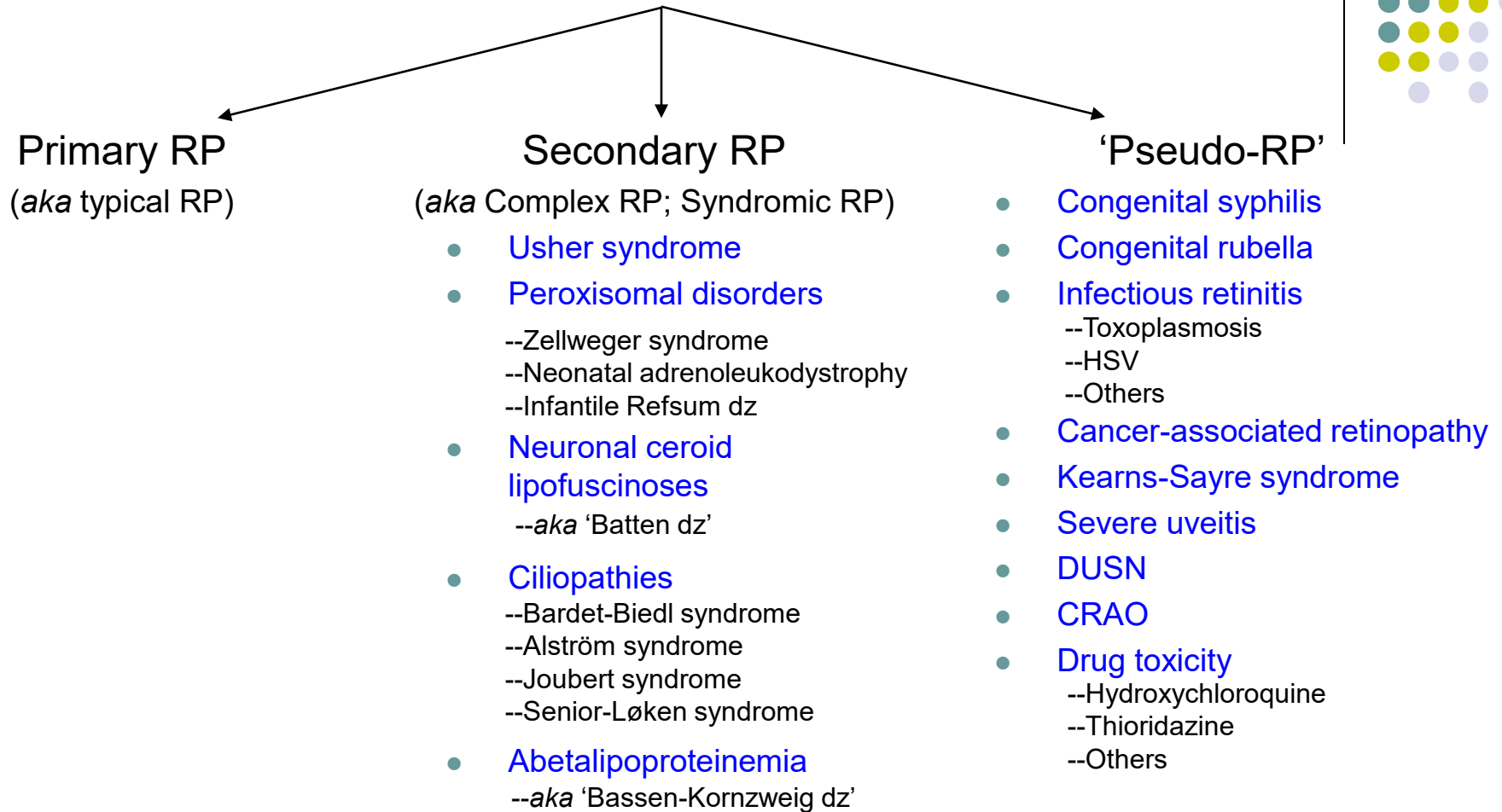
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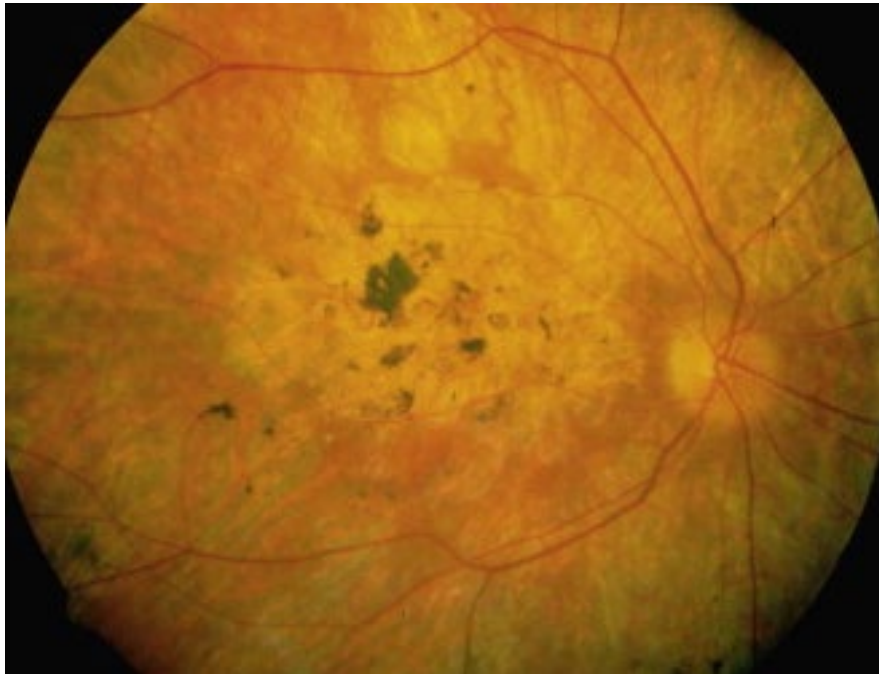
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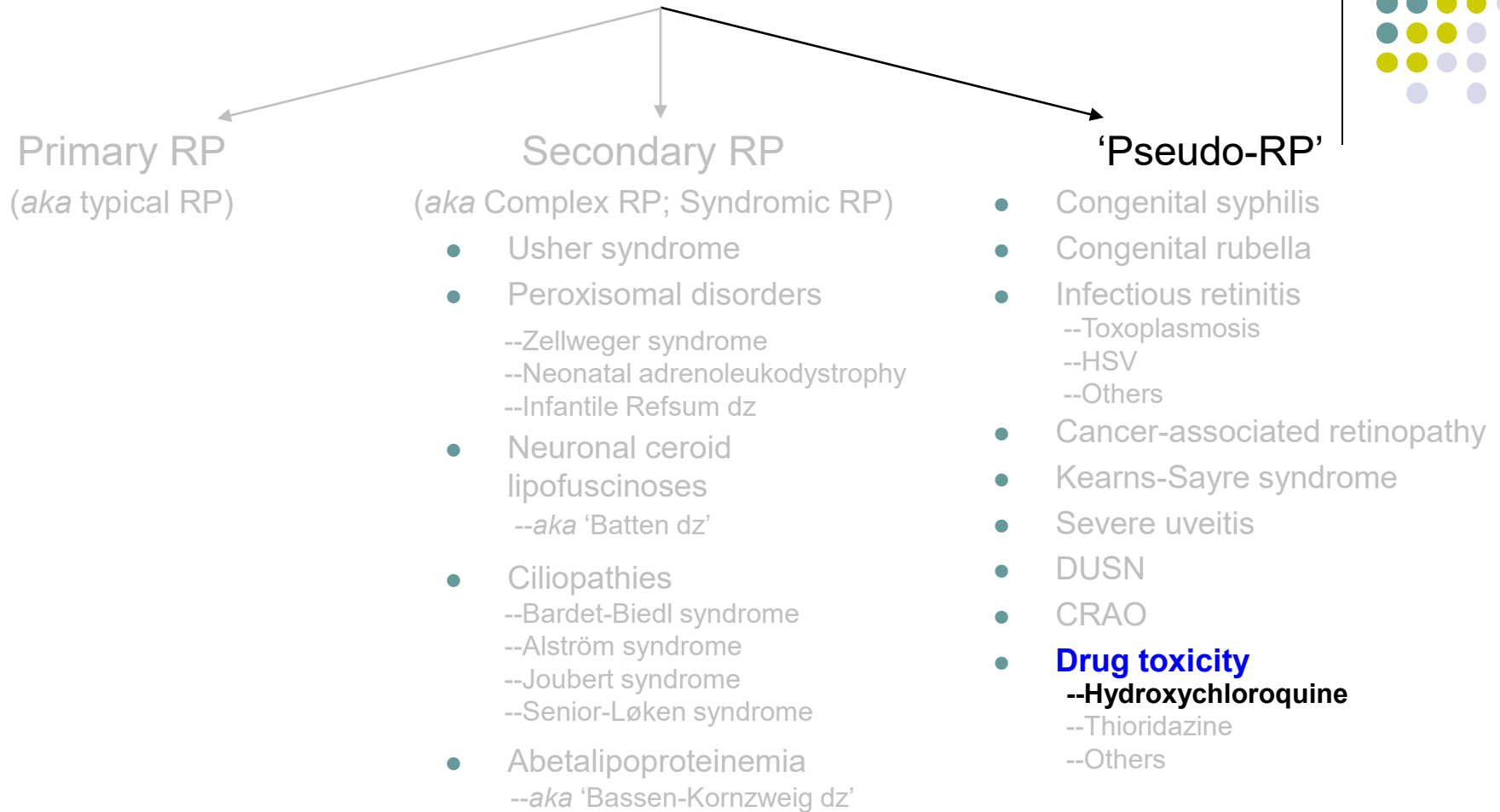


Thioridazine: Pigmentary retinopathy



Hydroxychloroquine retinopathy

DDx for an RP-like Fundus



Hydroxychloroquine (Plaquenil) toxicity is addressed in detail in R25

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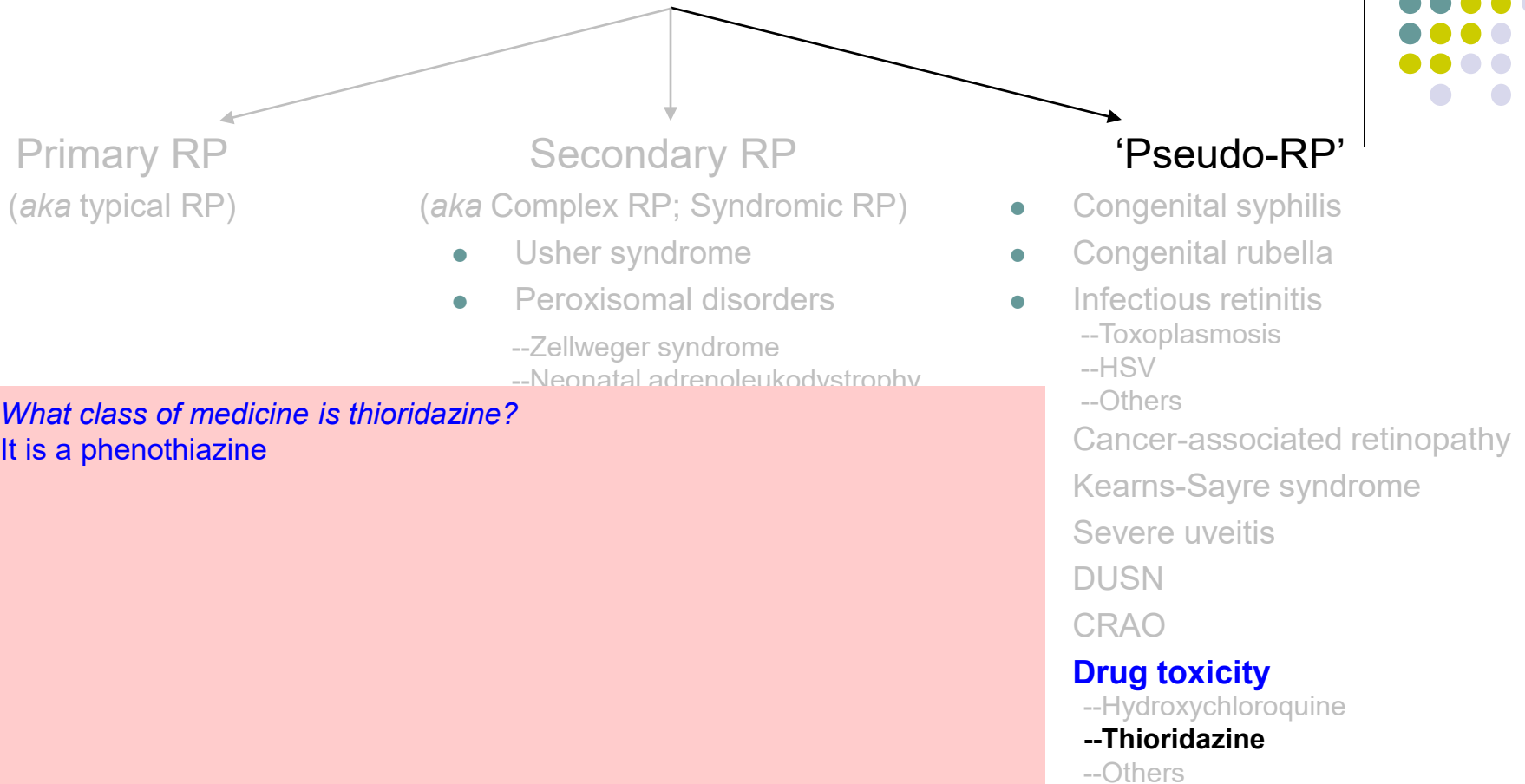
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 - Others
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- Kearns-Sayre syndrome
- Severe uveitis
- DUSN
- CRAO
- Drug toxicity**
 - Hydroxychloroquine
 - Thioridazine**
 - Others

What class of medicine is thioridazine?



DDx for an RP-like Fundus



What class of medicine is thioridazine?

It is a phenothiazine

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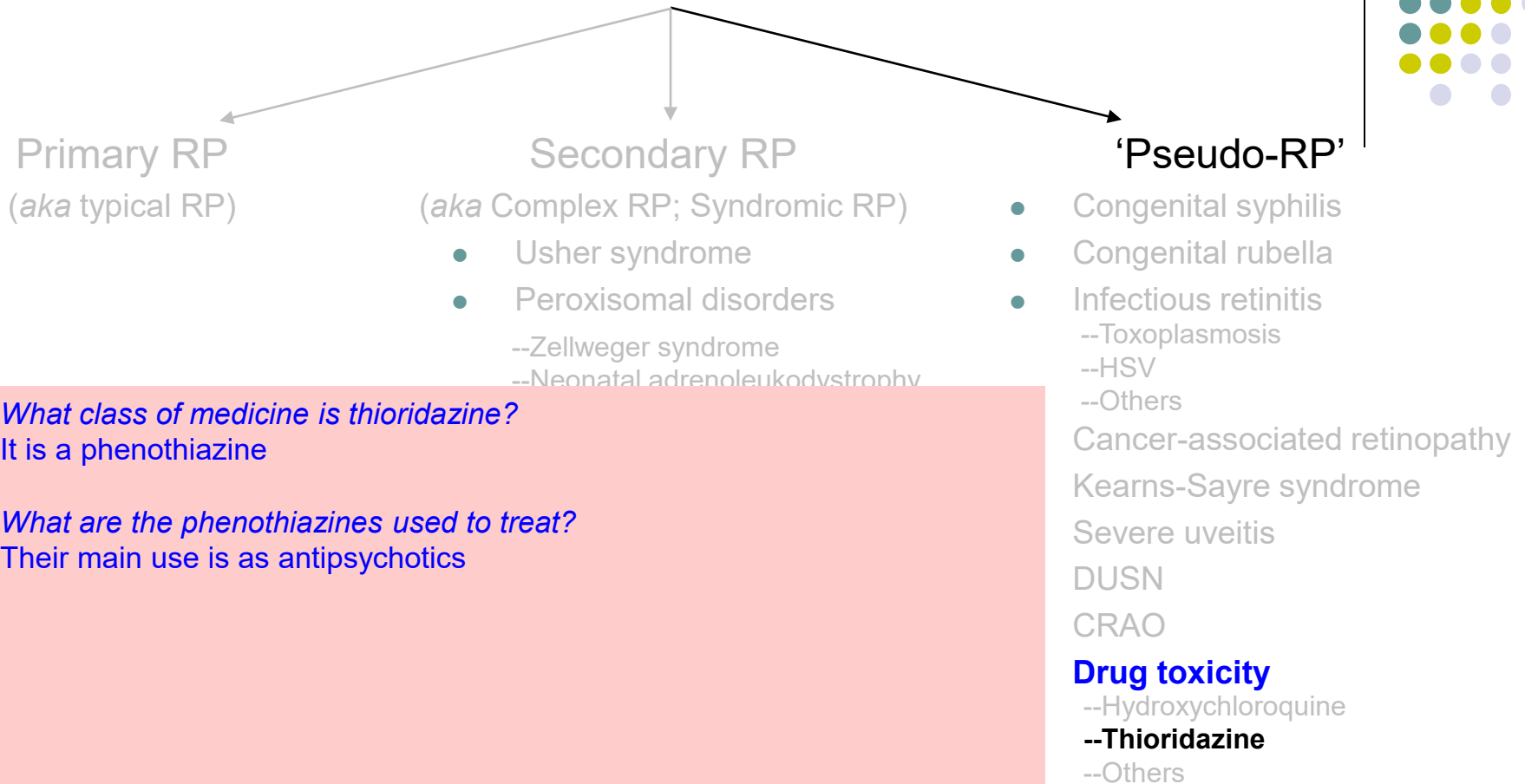
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It is a phenothiazine

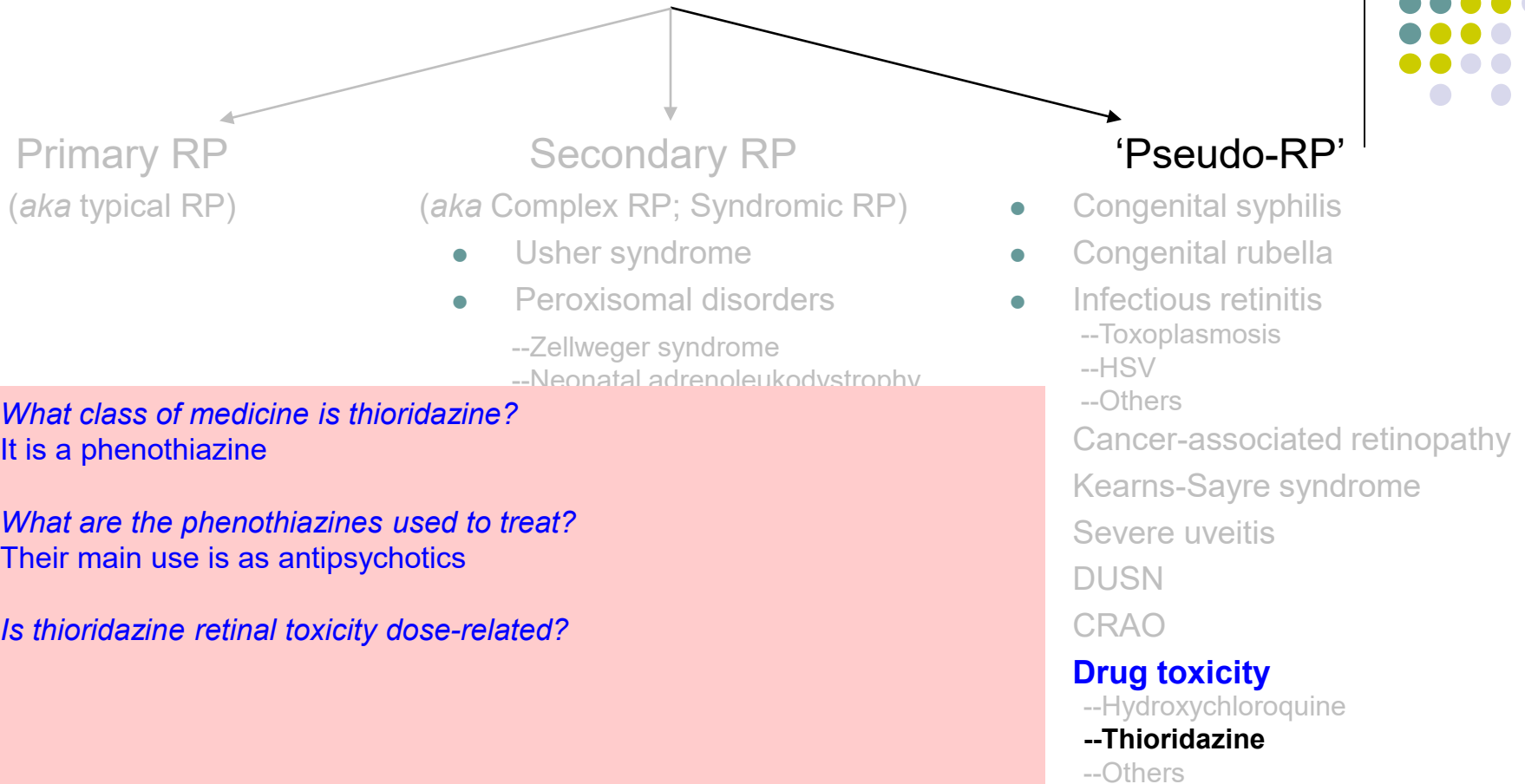
What are the phenothiazines used to treat?



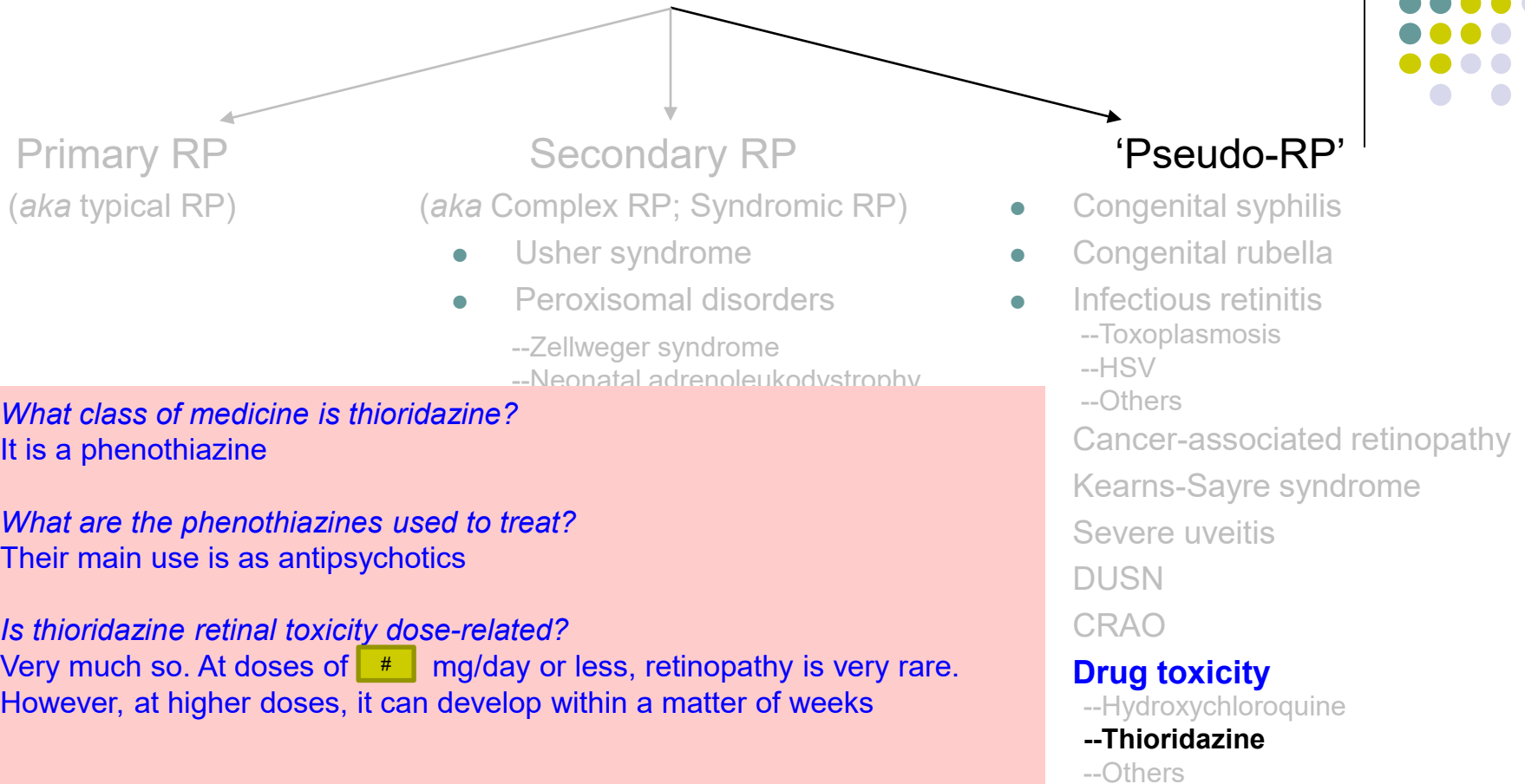
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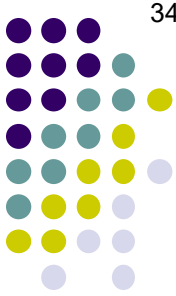
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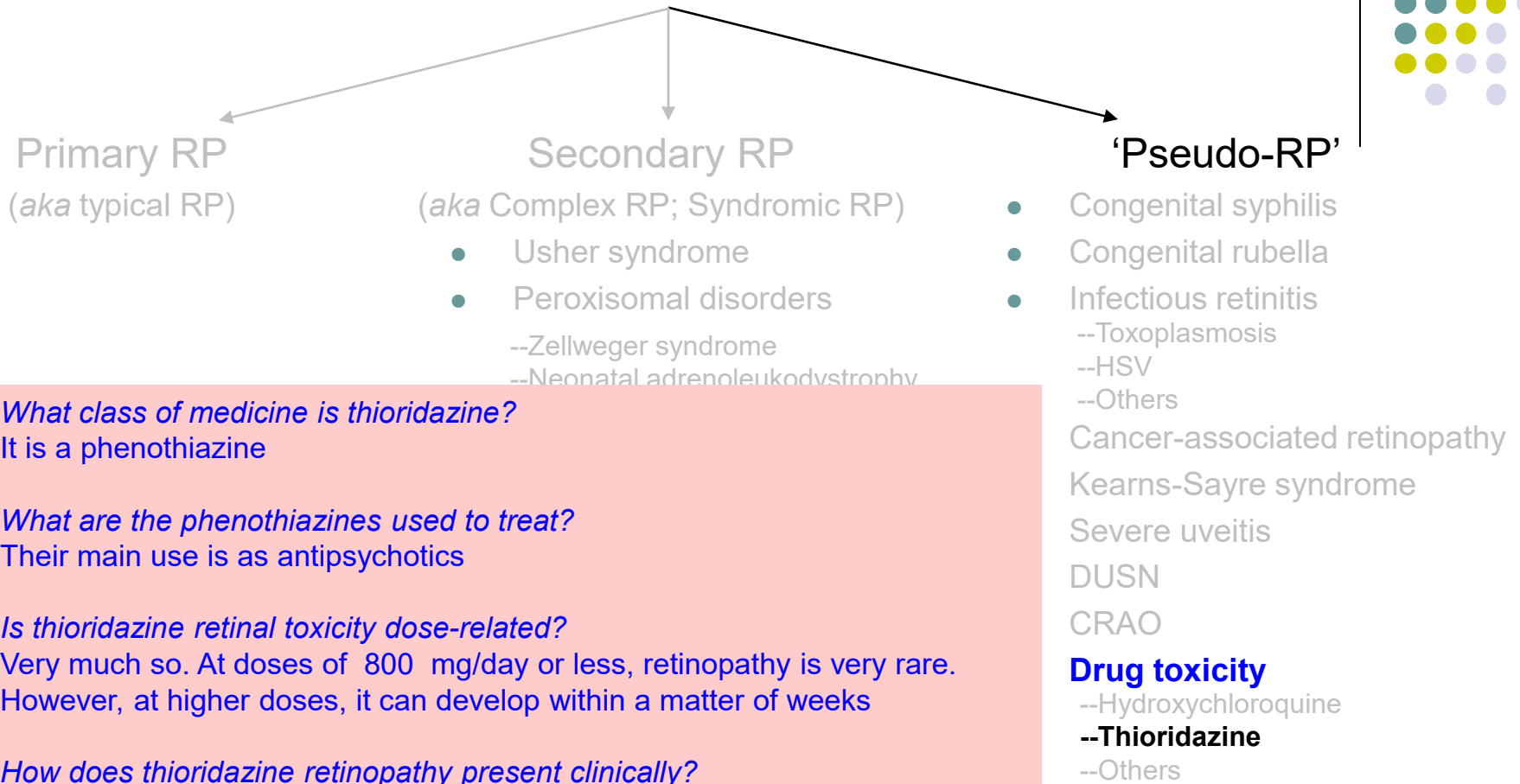
Their main use is as antipsychotics

Is thioridazine retinal toxicity dose-related?

Very much so. At doses of 800 mg/day or less, retinopathy is very rare. However, at higher doses, it can develop within a matter of weeks



DDx for an RP-like Fundus



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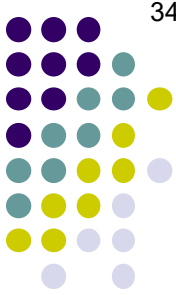
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How does thioridazine retinopathy present clinically?

The pt with c/o blurry vision; DFE will reveal pigment stippling in the macula





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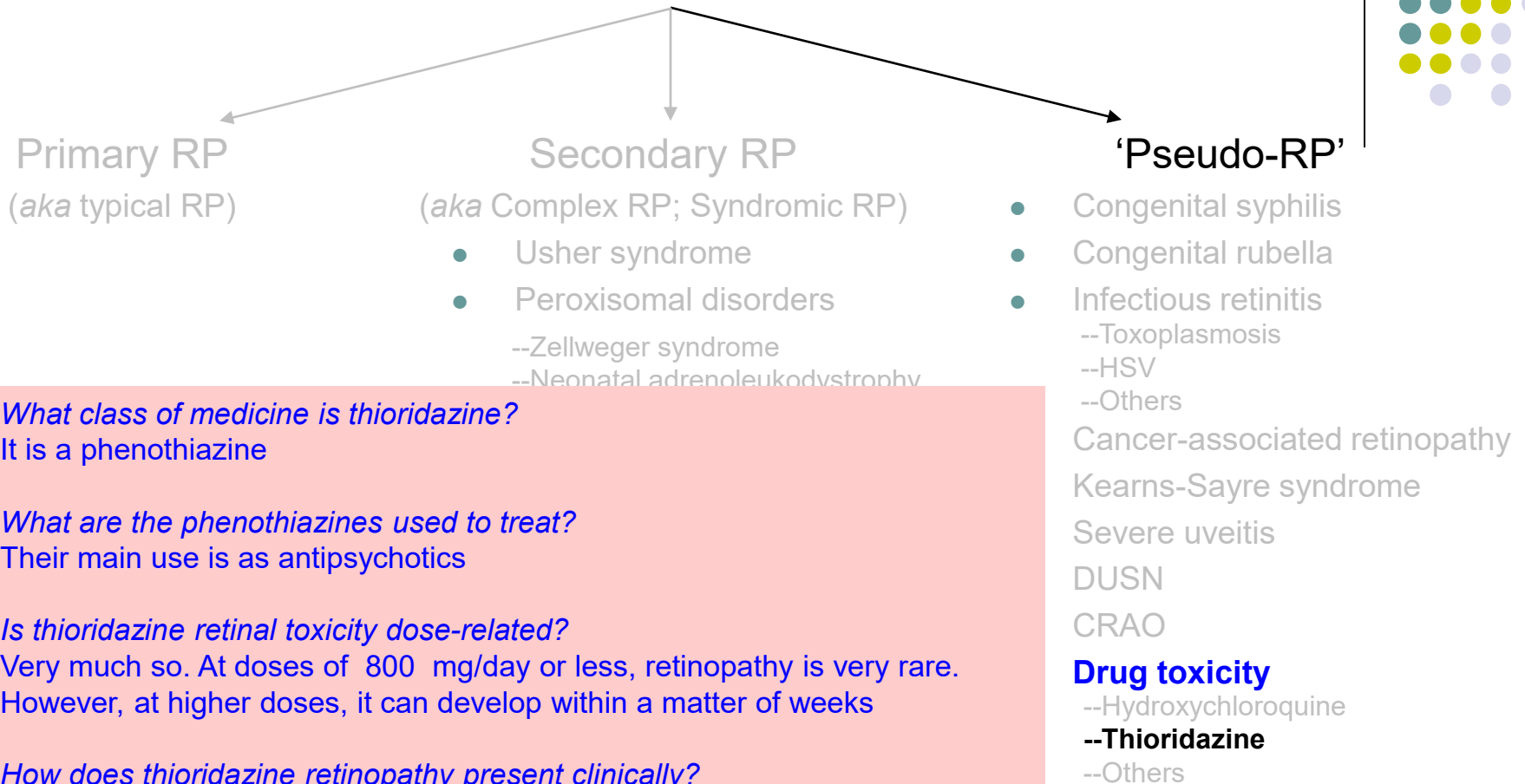
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How does thioridazine retinopathy present clinically?

The pt with c/o blurry vision; DFE will reveal pigment stippling in the macula

Does thioridazine use require periodic ophthalmic evaluations like hydroxychloroquine does?

DDx for an RP-like Fundus



What class of medicine is thioridazine?

It is a phenothiazine

What are the phenothiazines used to treat?

Their main use is as antipsychotics

Is thioridazine retinal toxicity dose-related?

Very much so. At doses of 800 mg/day or less, retinopathy is very rare. However, at higher doses, it can develop within a matter of weeks

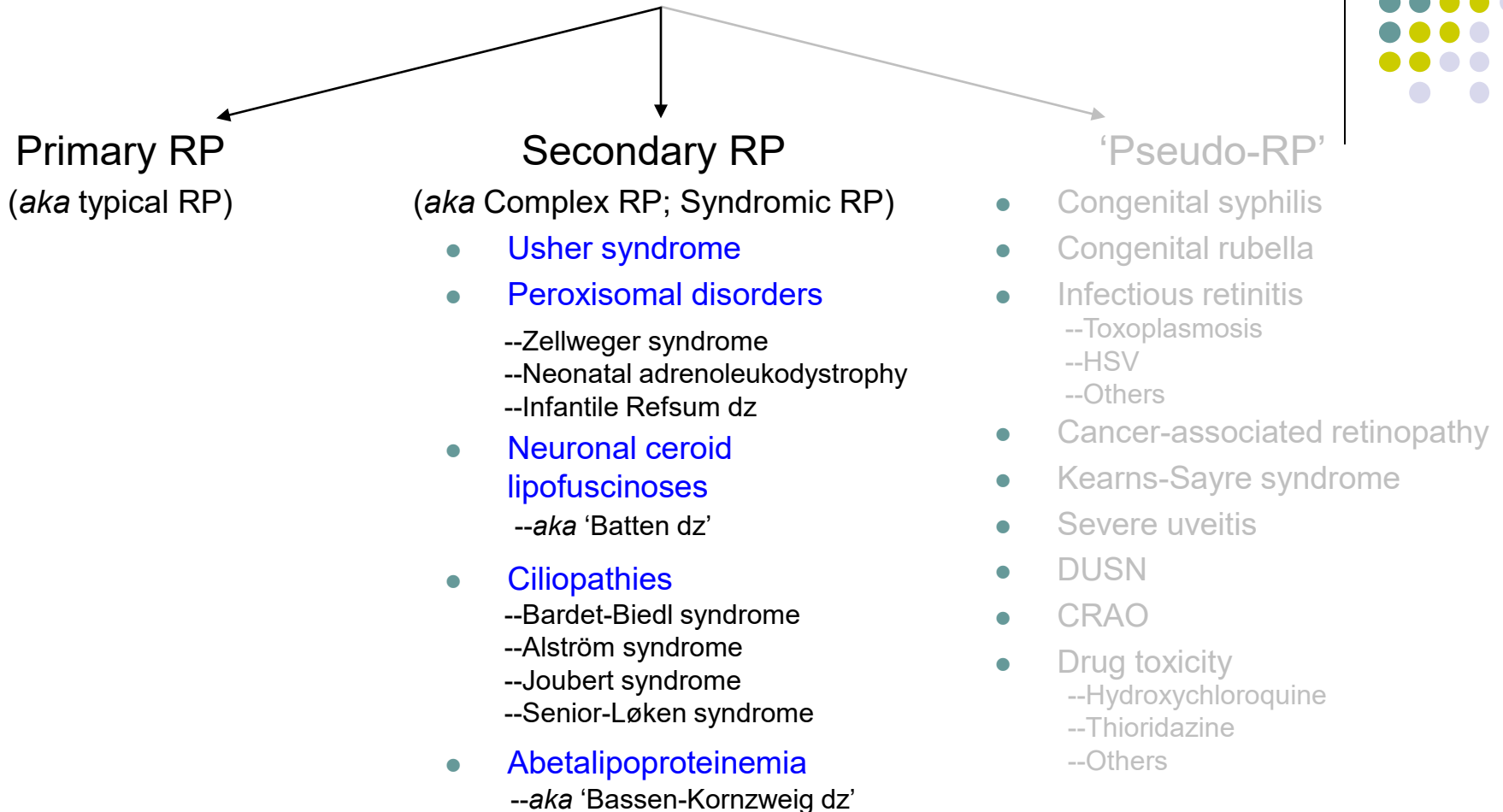
How does thioridazine retinopathy present clinically?

The pt with c/o blurry vision; DFE will reveal pigment stippling in the macula

Does thioridazine use require periodic ophthalmic evaluations like hydroxychloroquine does?

Not so long as the dose is at or below 800 mg/day

DDx for an RP-like Fundus



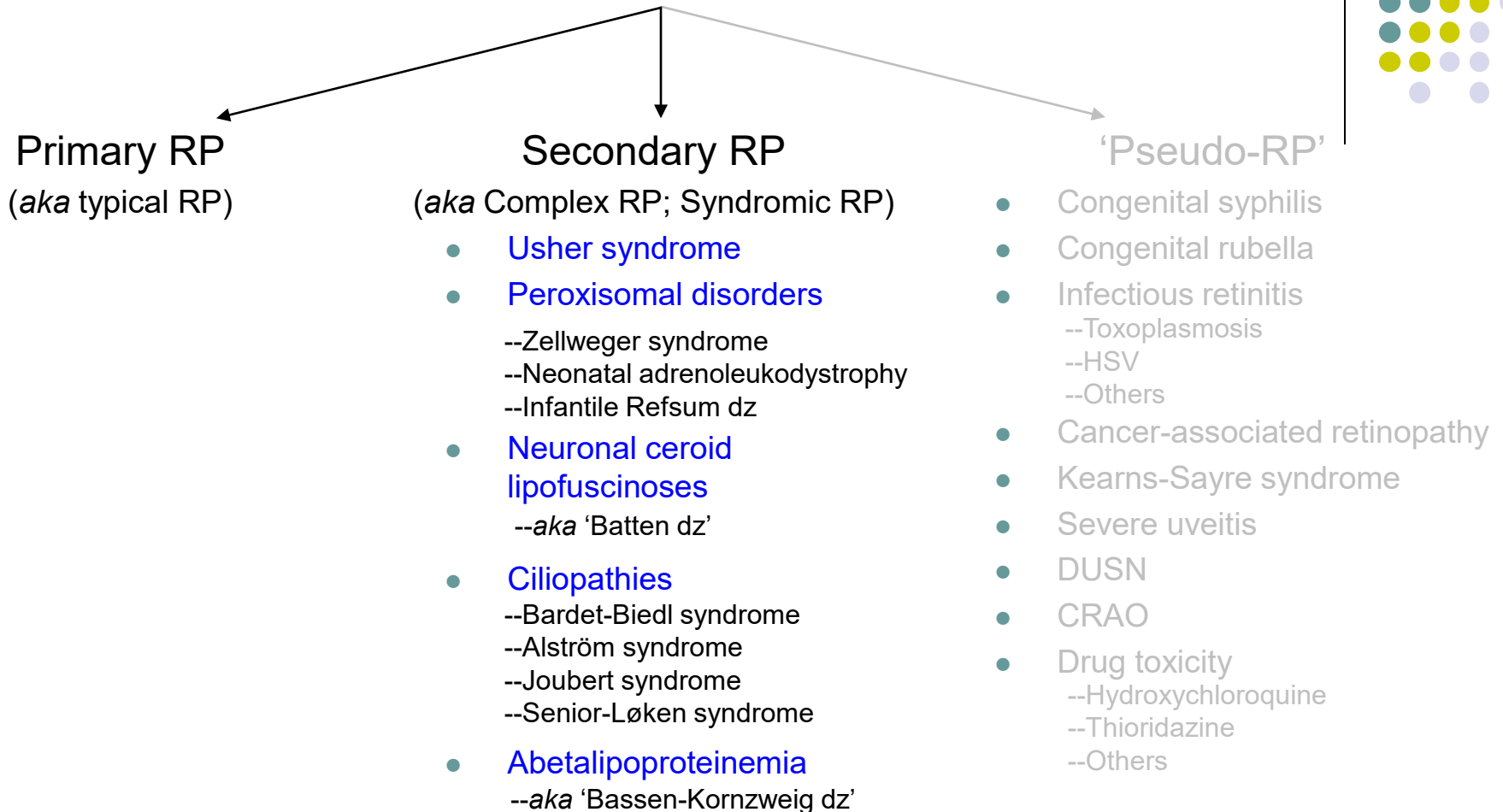
What tests should be run to determine whether a pt has RP?

--?

--?

--?

DDx for an RP-like Fundus



What tests should be run to determine whether a pt has RP?

--An ERG (if it's not markedly abnormal, it's not RP)

--**Kinetic** (ie, Goldmann, *not* Humphrey) VF testing. Again—if it's not abnormal, it's not RP.

--Dark adaptometry (ditto)

DDx for an RP-like Fundus

Primary RP

(aka typical RP)

Secondary RP

(aka Complex RP; Syndromic RP)

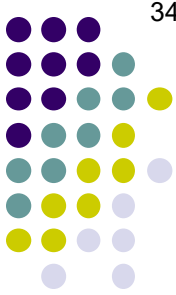
- Usher syndrome
- Peroxisomal disorders

How do you rule-in pseudo-RP?

- Ciliopathies
 - Bardet-Biedl syndrome
 - Alström syndrome
 - Joubert syndrome
 - Senior-Løken syndrome
- Abetalipoproteinemia
 - aka 'Bassen-Kornzweig dz'

'Pseudo-RP'

- Congenital syphilis
- Congenital rubella
- Infectious retinitis
 - Toxoplasmosis
 - HSV
 - Others
- Cancer-associated retinopathy
- Kearns-Sayre syndrome
- Severe uveitis
- DUSN
- CRAO
- Drug toxicity
 - Hydroxychloroquine
 - Thioridazine
 - Others



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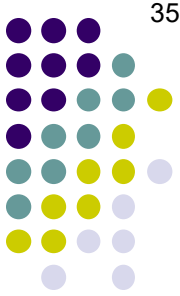
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Some causes can be identified by the presence (or absence) of certain signs/symptoms...

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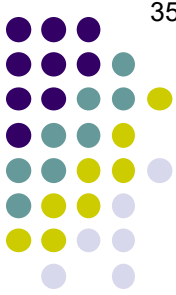
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Some via pertinent lab results...

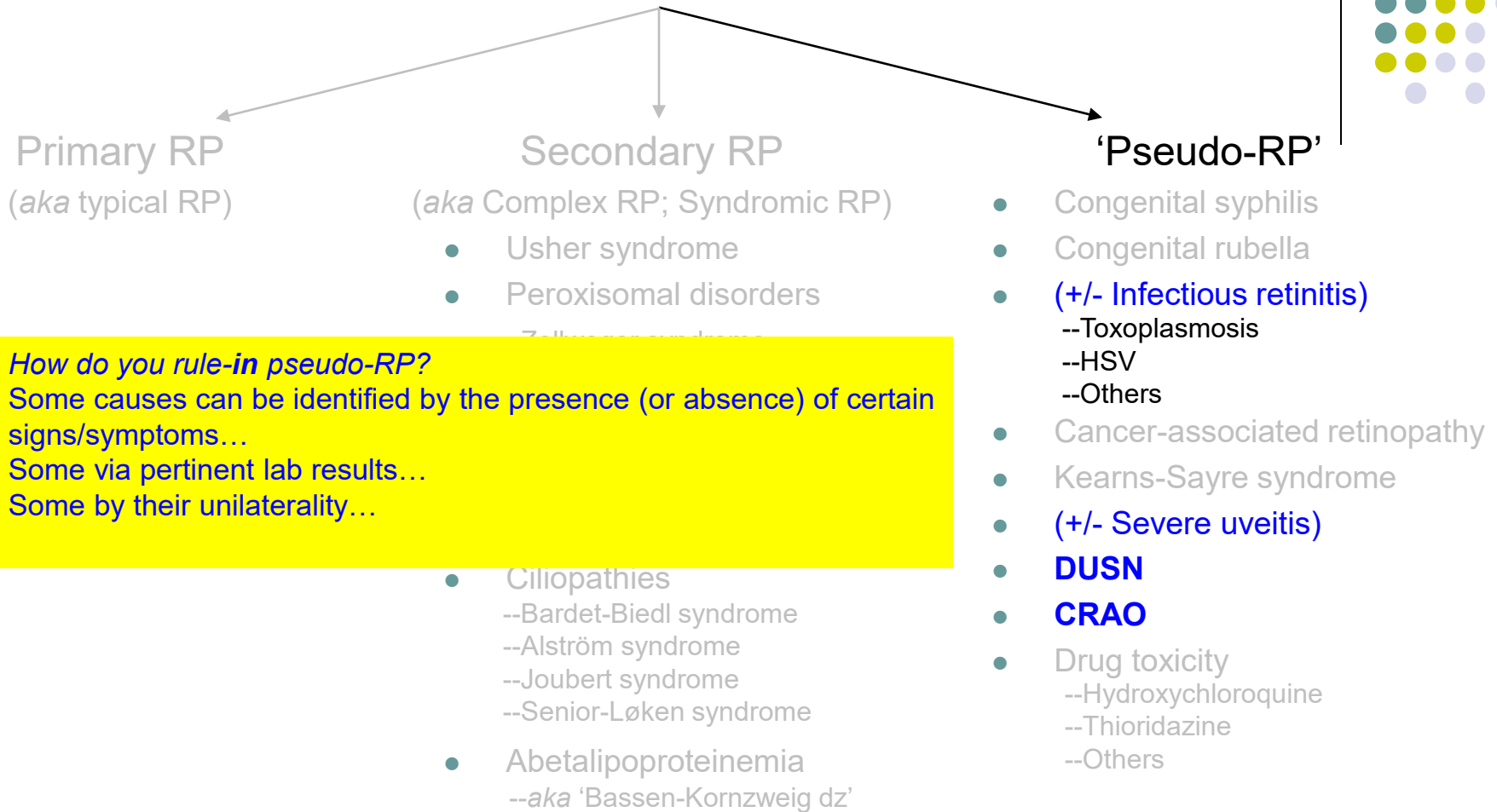
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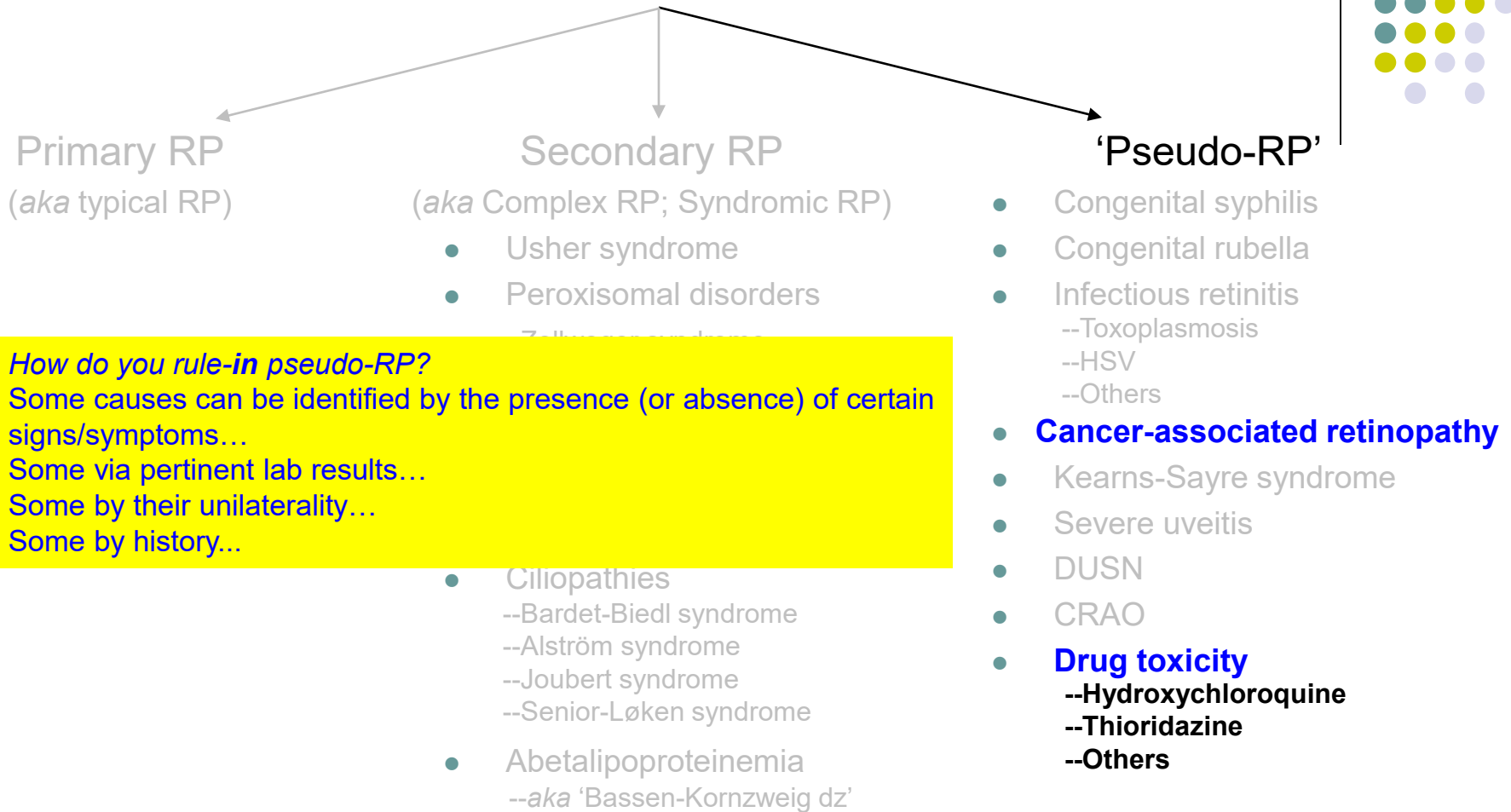
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DDx for an RP-like Fundus



DDx for an RP-like Fundus



DDx for an RP-like Fundus

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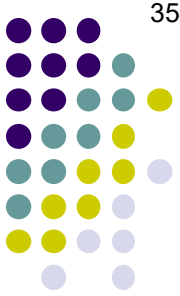
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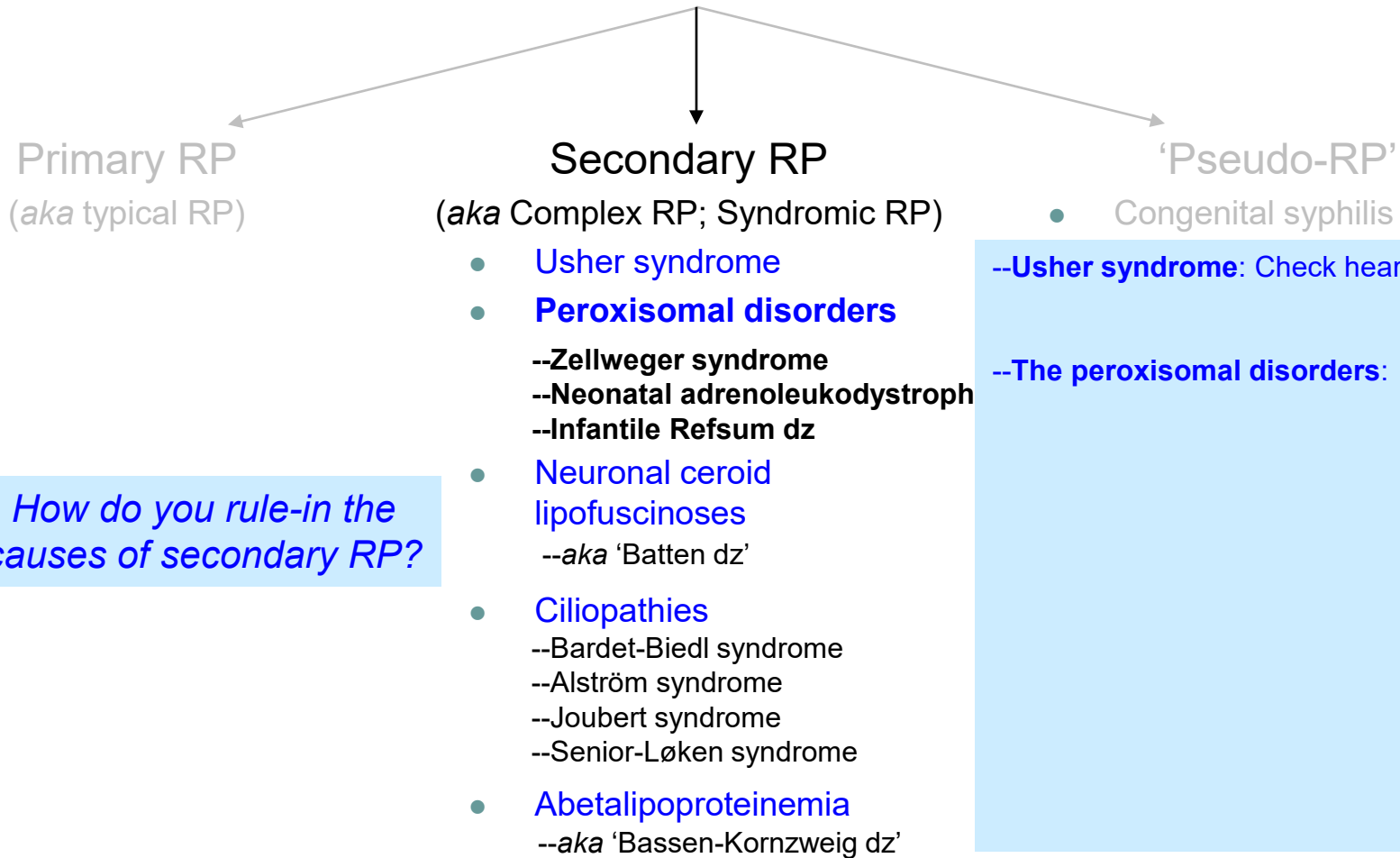
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--Usher syndrome: Check hearing

How do you rule-in the causes of secondary RP?



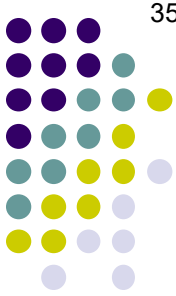
DDx for an RP-like Fundus



How do you rule-in the causes of secondary RP?

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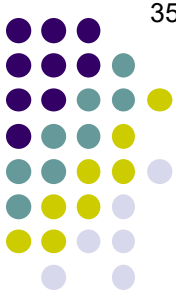
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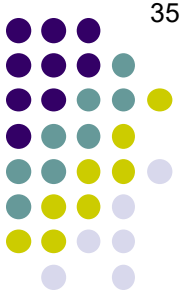
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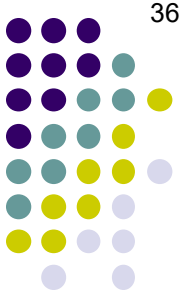
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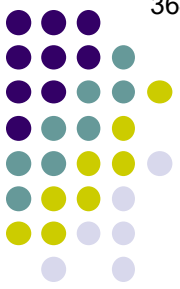
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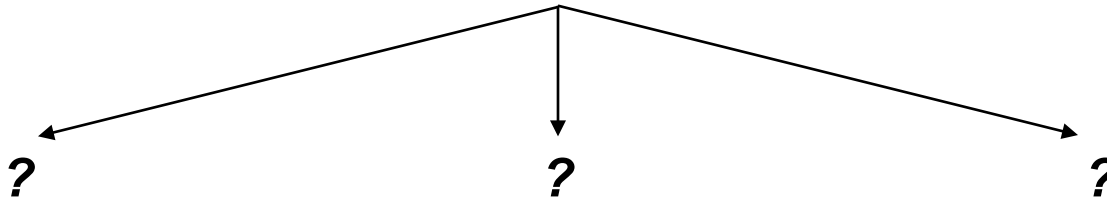
--Abetalipoproteinemia: As discussed



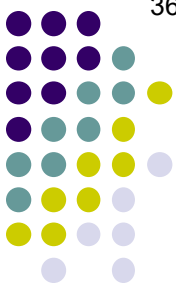


tl;dr starts on the next slide

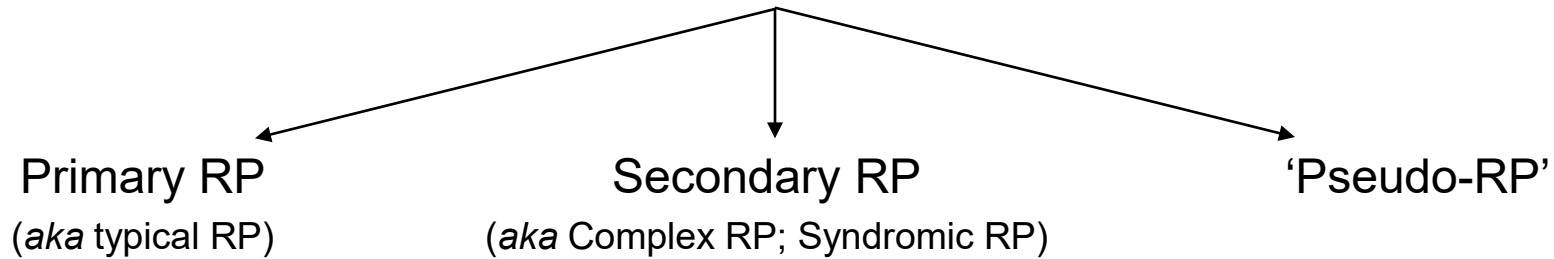
DDx for an RP-like Fundus



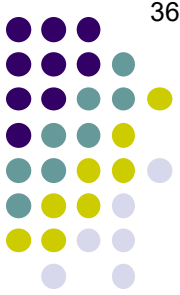
(When you hear *RP-like fundus*...



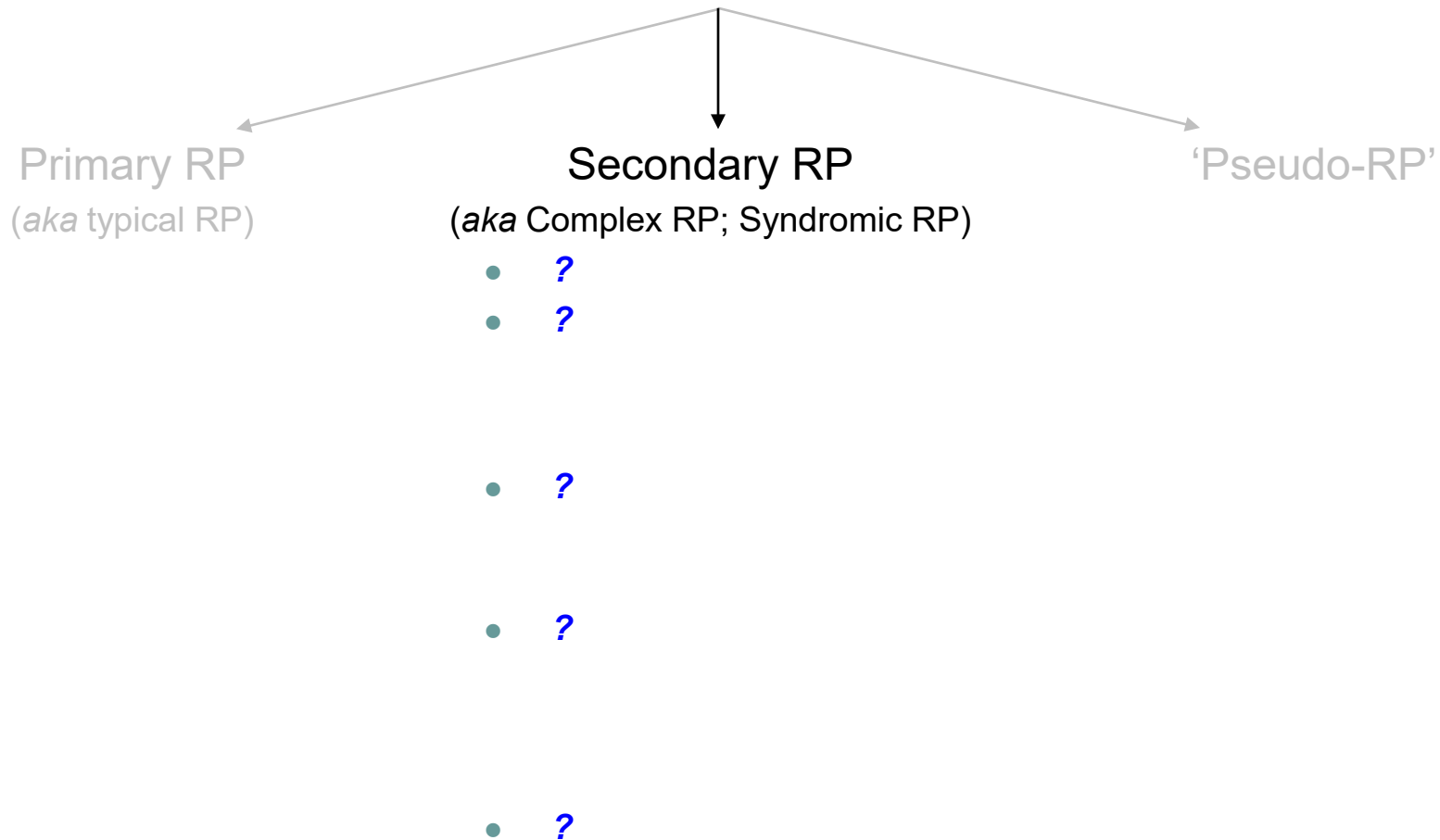
DDx for an RP-like Fundus



(When you hear *RP-like fundus*...these three categories should instantly spring to mind—make sure they do!)

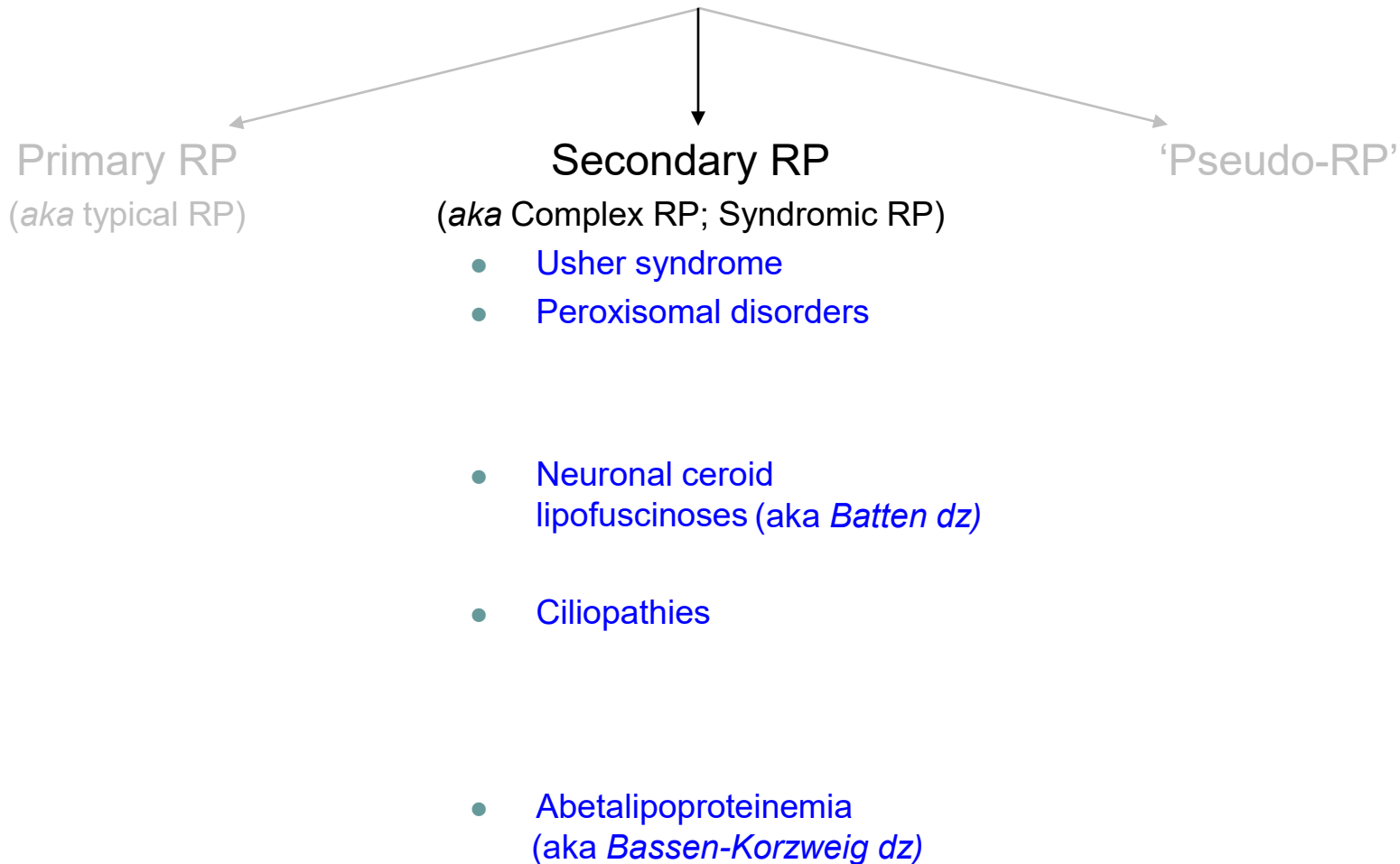


DDx for an RP-like Fundus



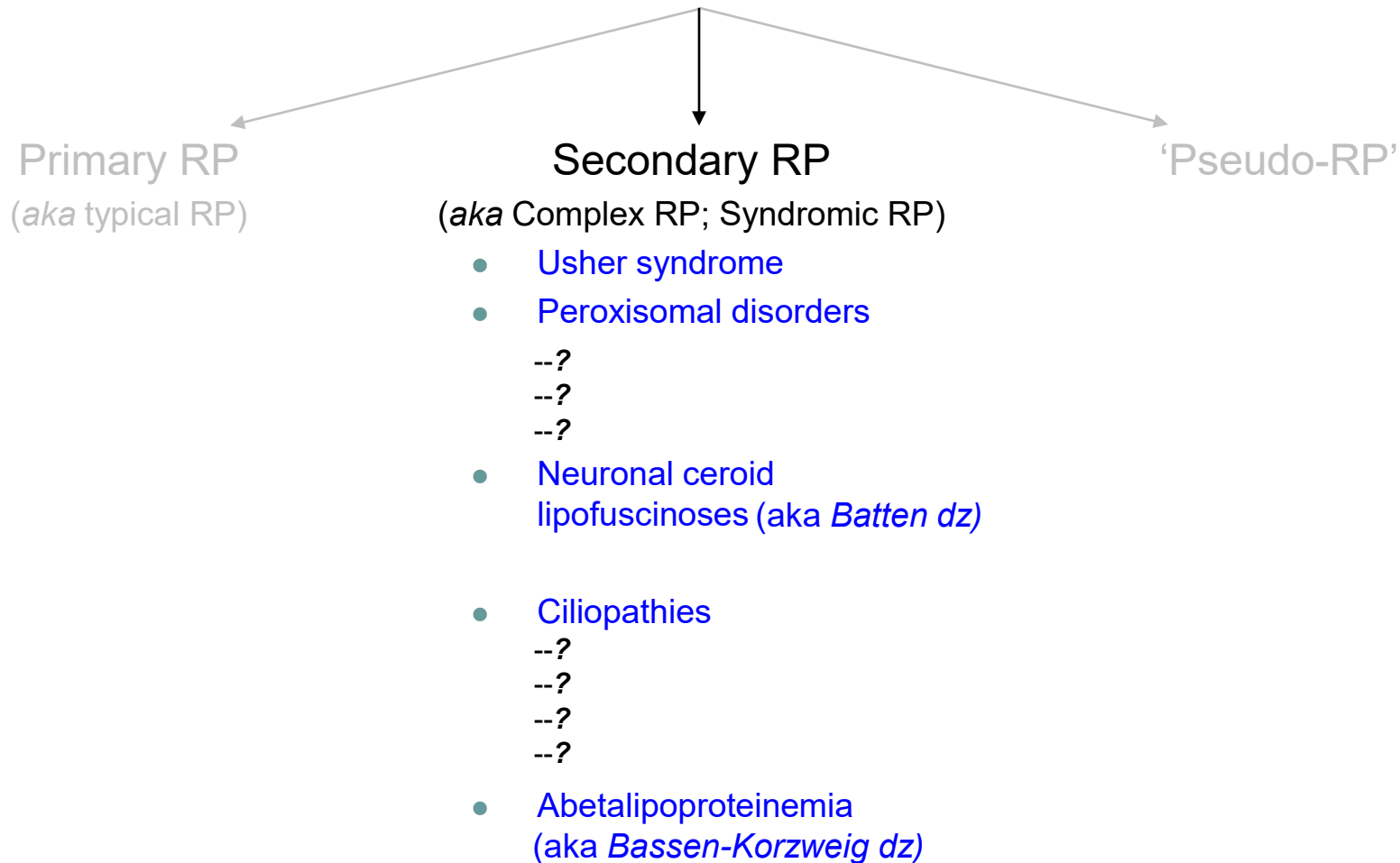
Next, make sure you can name the *five categories of secondary/syndromic RP*.

DDx for an RP-like Fundus



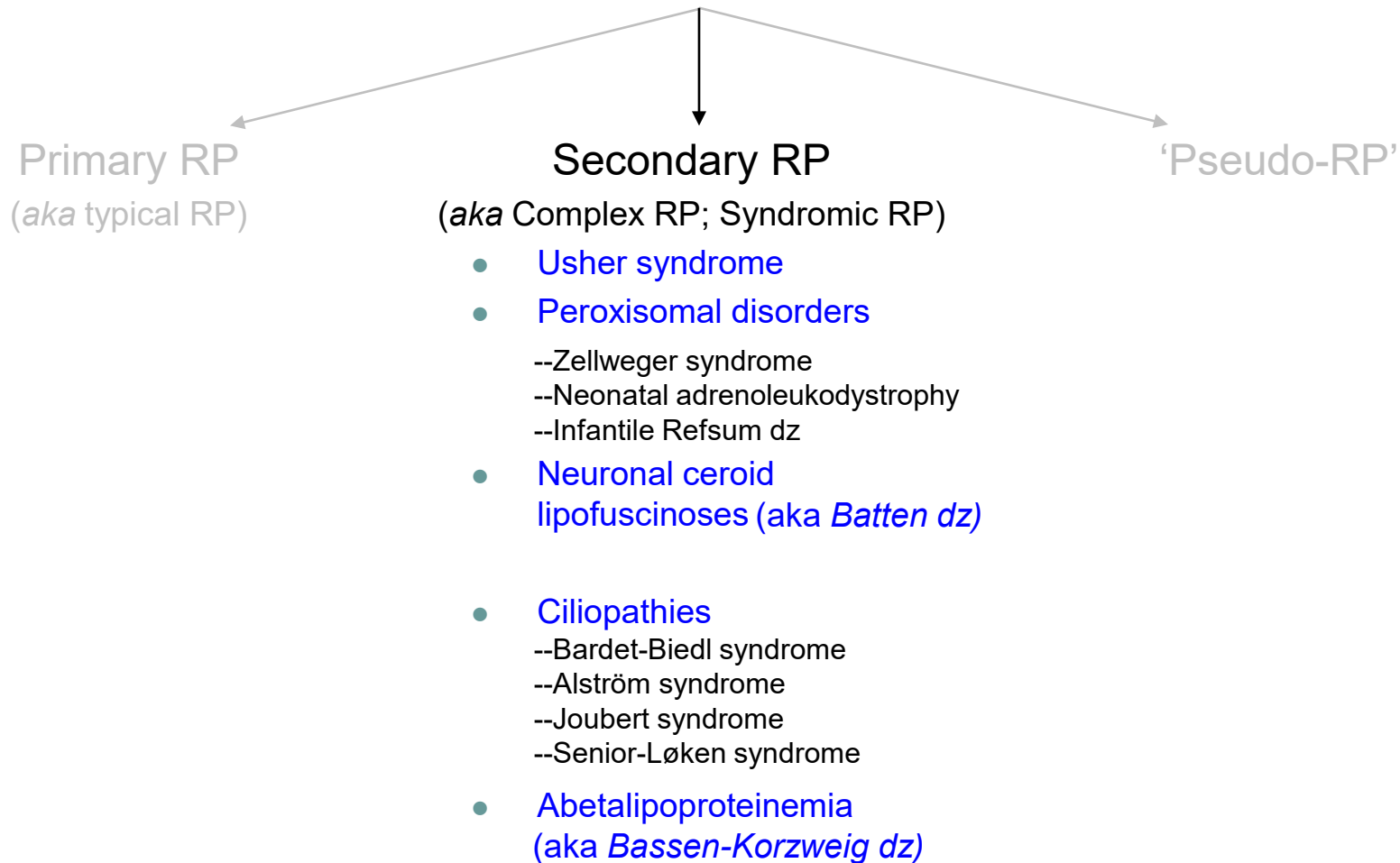
Next, make sure you can name the *five categories of secondary/syndromic RP*. Toggle back and forth between this slide and the previous one until you can name all five with ease!

DDx for an RP-like Fundus



Then, make sure you can name the three *peroxisomal disorders* and the four *ciliopathies*.

DDx for an RP-like Fundus



Then, make sure you can name the three *peroxisomal disorders* and the four *ciliopathies*. Again, toggle back and forth between this slide and the previous one until you've mastered them all.








DDx for an RP-like Fundus

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(aka typical RP)

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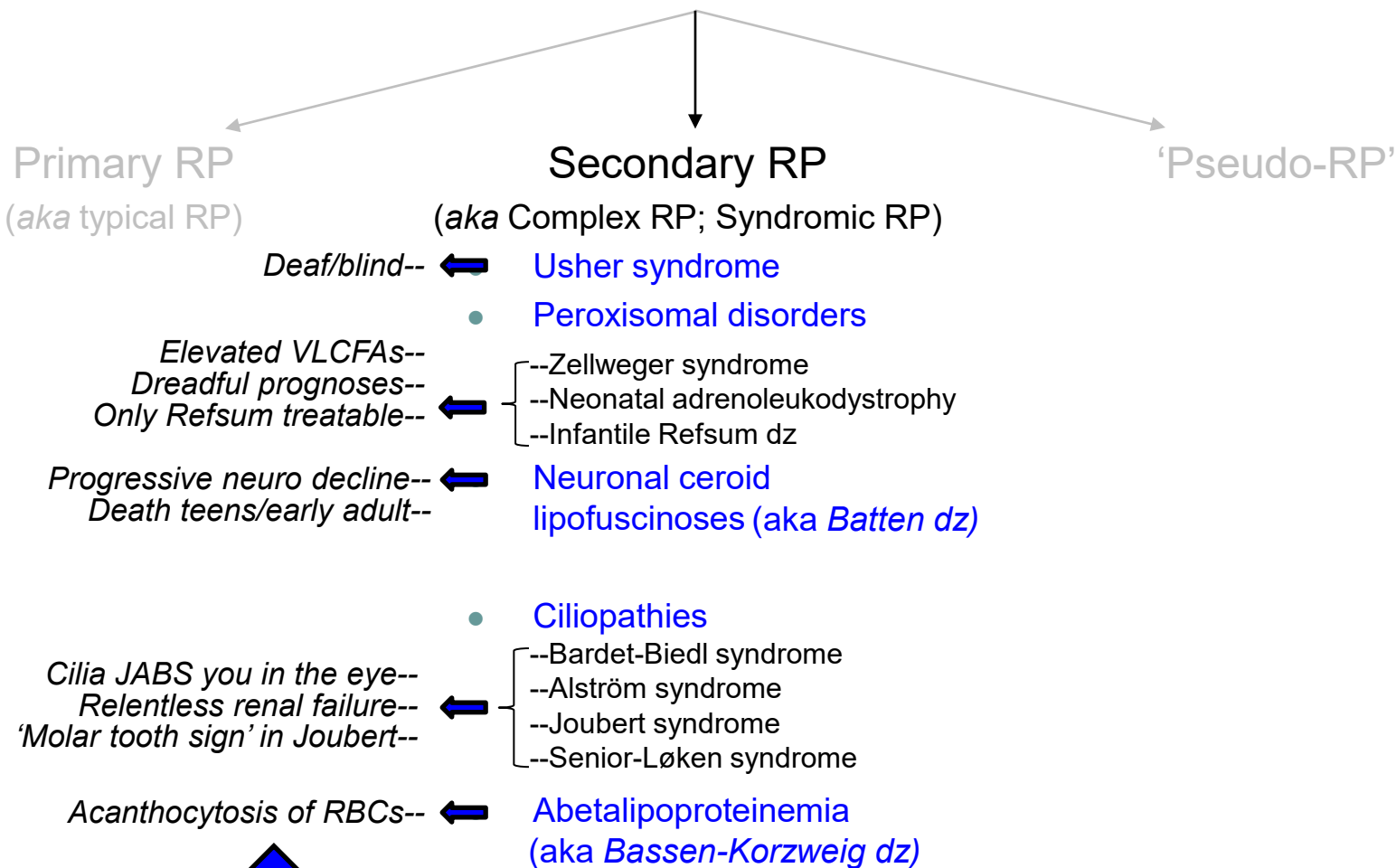
- ?--  Usher syndrome
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- ?--
- ?--  {
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 - Neonatal adrenoleukodystrophy
 - Infantile Refsum dz
- ?--
- ?--  Neuronal ceroid
- ?-- lipofuscinoses (aka *Batten dz*)
- Ciliopathies
- ?--
- ?--  {
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- ?--
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(aka *Bassen-Korzweig dz*)



These are my best guesses (emphasis on *guesses*) regarding factoids that should be kept in mind for each.

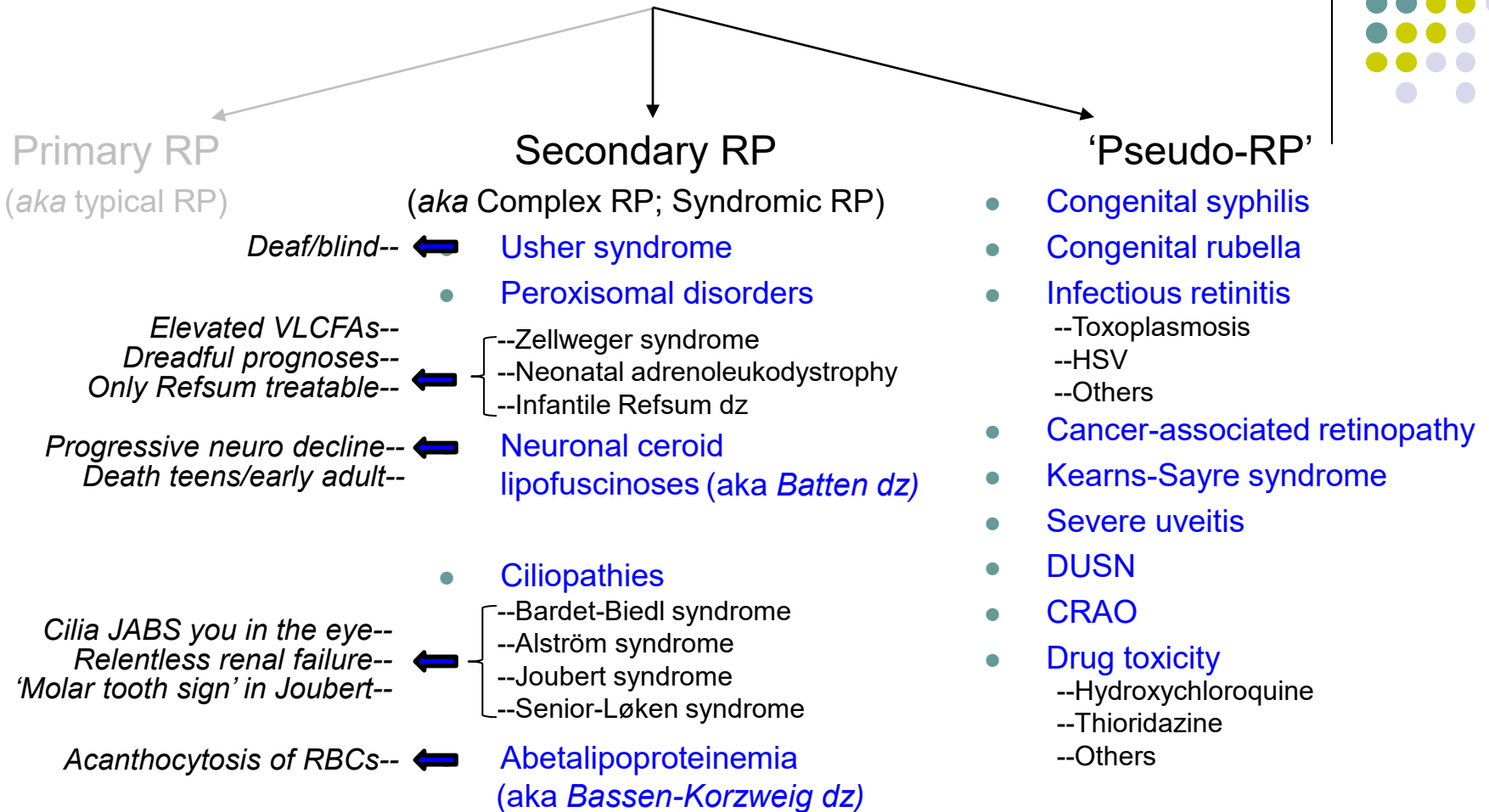


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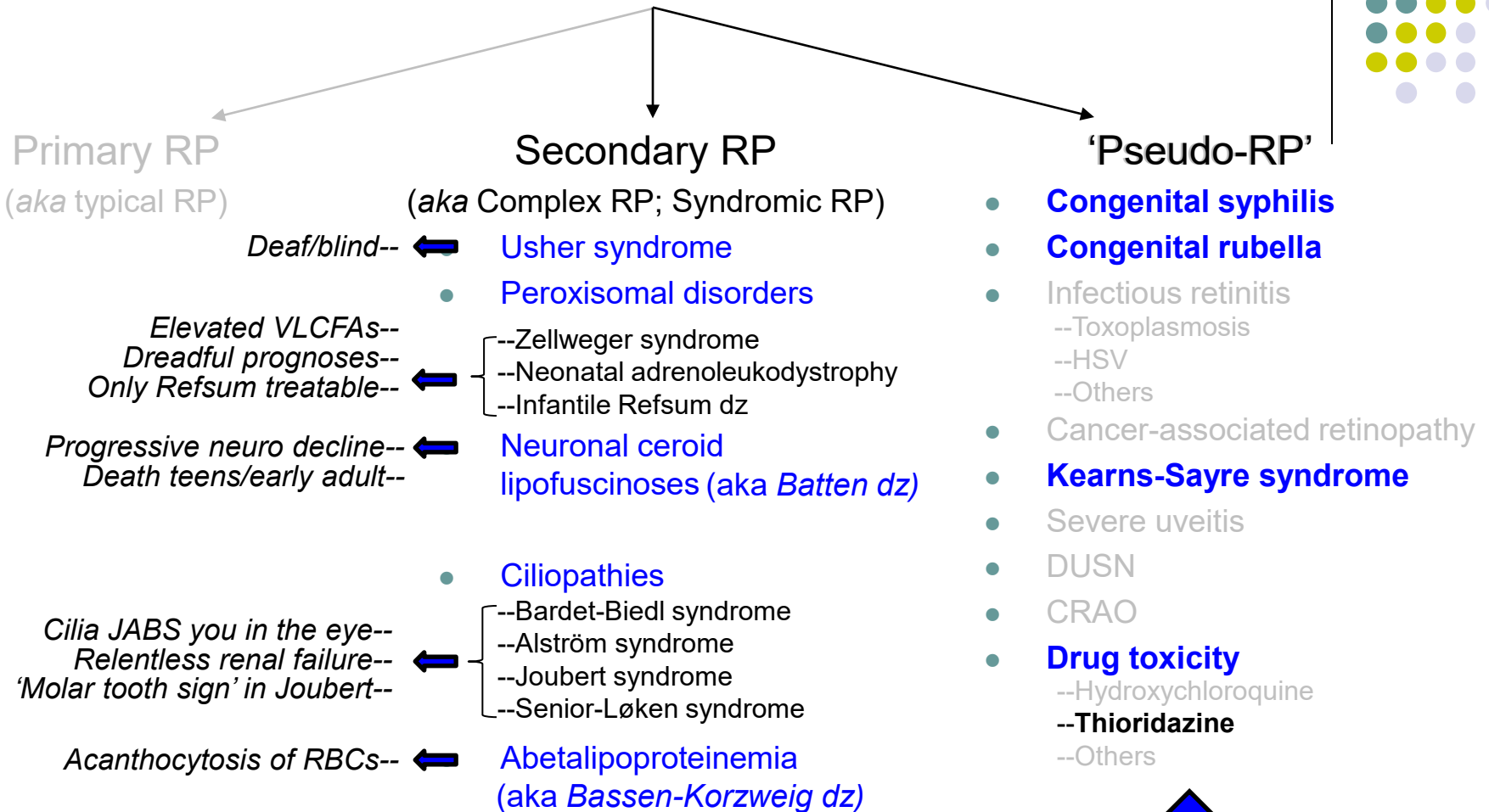
These are my best guesses (emphasis on *guesses*) regarding factoids that should be kept in mind for each. **Toggle!**

DDx for an RP-like Fundus



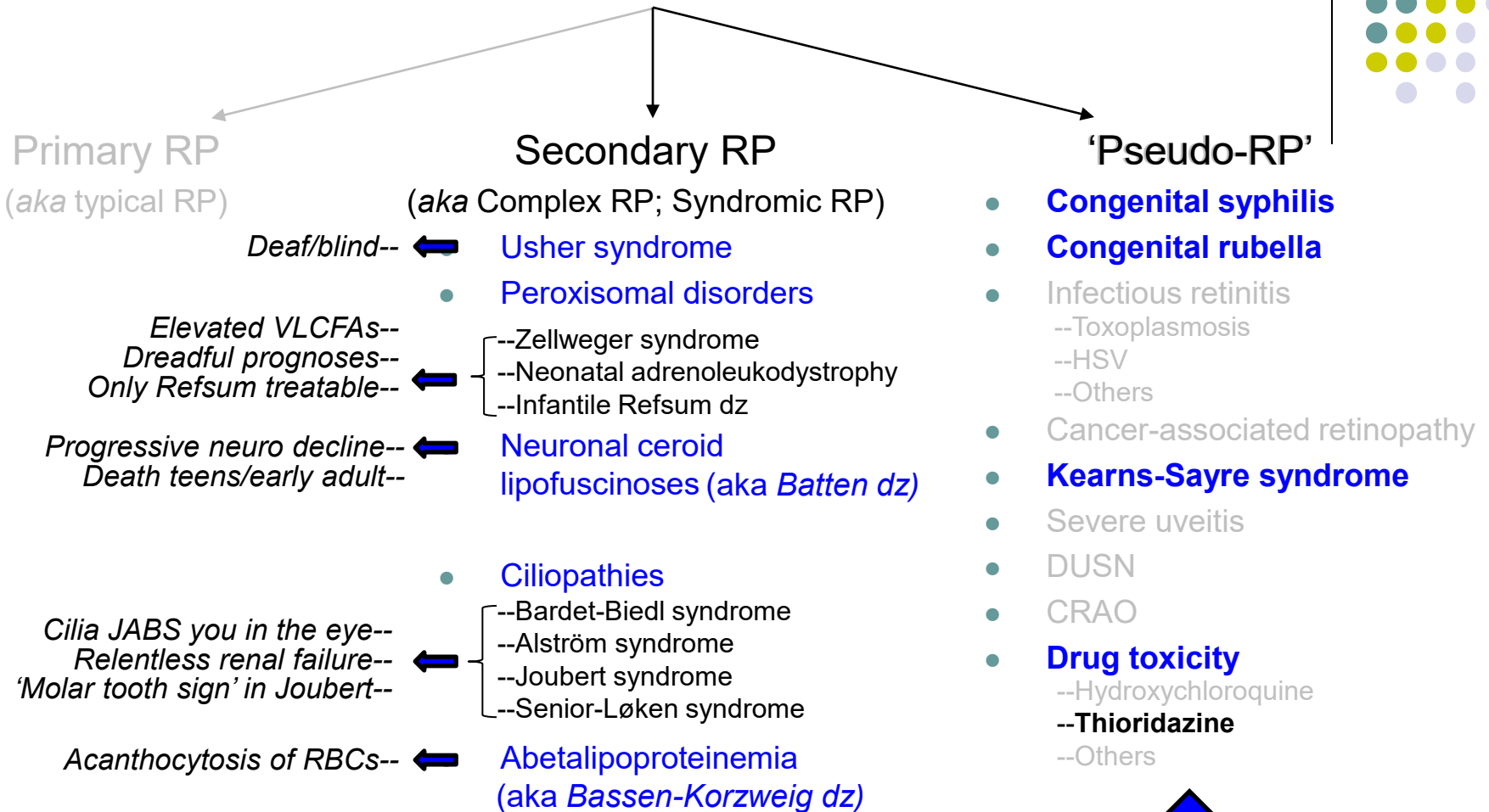
Speaking of guesses...

DDx for an RP-like Fundus



Speaking of guesses... **These** are the causes of *pseudo-RP* I would pay particular attention to.

DDx for an RP-like Fundus



Note: I'm **not** suggesting the other conditions are low-yield topics for the OKAP. Rather, I think they are unlikely to be the correct answer to a question intended to test your knowledge of RP imitators.

Speaking of guesses...**These** are the causes of *pseudo-RP* I would pay particular attention to.