# Q

## Cotton Wool Spots

*What pathologic process results in cotton-wool spots (CWS)?*

# A

## Cotton Wool Spots

*What pathologic process results in cotton-wool spots (CWS)?*

Interruption of the retinal **Blood supply**,
ie, ischemia

# Q

## Cotton Wool Spots

Blood supply

Blood supply

Blood supply

Blood supply

Blood supply

***How many blood supplies does the retina receive?***

Blood supply

Blood supply

Blood supply

Blood supply

Blood supply

Blood supply

Blood supply

Blood supply

# A

## Cotton Wool Spots

**Blood supply**

***How many blood supplies does the retina receive? Two***

**Blood supply**

# Q

## Cotton Wool Spots

**Blood supply:**

***?***

***What are the sources of the retina's two blood supplies?***

**Blood supply:**

***?***

# A

## Cotton Wool Spots

**Blood supply:**
***Central retinal artery***

***What are the sources of the retina's two blood supplies?***

**Blood supply:**
***Choriocapillaris***

# Q

## Cotton Wool Spots

- **Retinal Layers**
  - Internal limiting membrane
  - two words layer
  - two words layer
  - two words layer
  - two words layer
  - two words layer (aka…(one word) layer)
  - two words layer
  - External limiting membrane
  - two/words inner and outer segments
- **RPE**
- **Bruch's membrane**

Blood supply:
*Central retinal artery*

***What are the layers of the retina?***

Blood supply:
*Choriocapillaris*

# A

## Cotton Wool Spots

- **Retinal Layers**
  - Internal limiting membrane
  - Nerve fiber layer
  - Ganglion cell layer
  - Inner plexiform layer
  - Inner nuclear layer
  - Outer plexiform layer (Henle's layer)
  - Outer nuclear layer
  - External limiting membrane
  - Rod/cone inner and outer segments
- **RPE**
- **Bruch's membrane**

Blood supply:
*Central retinal artery*

***What are the layers of the retina?***

Blood supply:
*Choriocapillaris*

# Q

## Cotton Wool Spots

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  - Internal limiting membrane
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- **RPE**
- **Bruch's membrane**

**Blood supply:**
***Central retinal artery***

***Which layers are supplied by each blood supply?***

**Blood supply:**
***Choriocapillaris***

# A

- **Retinal Layers**
  - Internal limiting membrane
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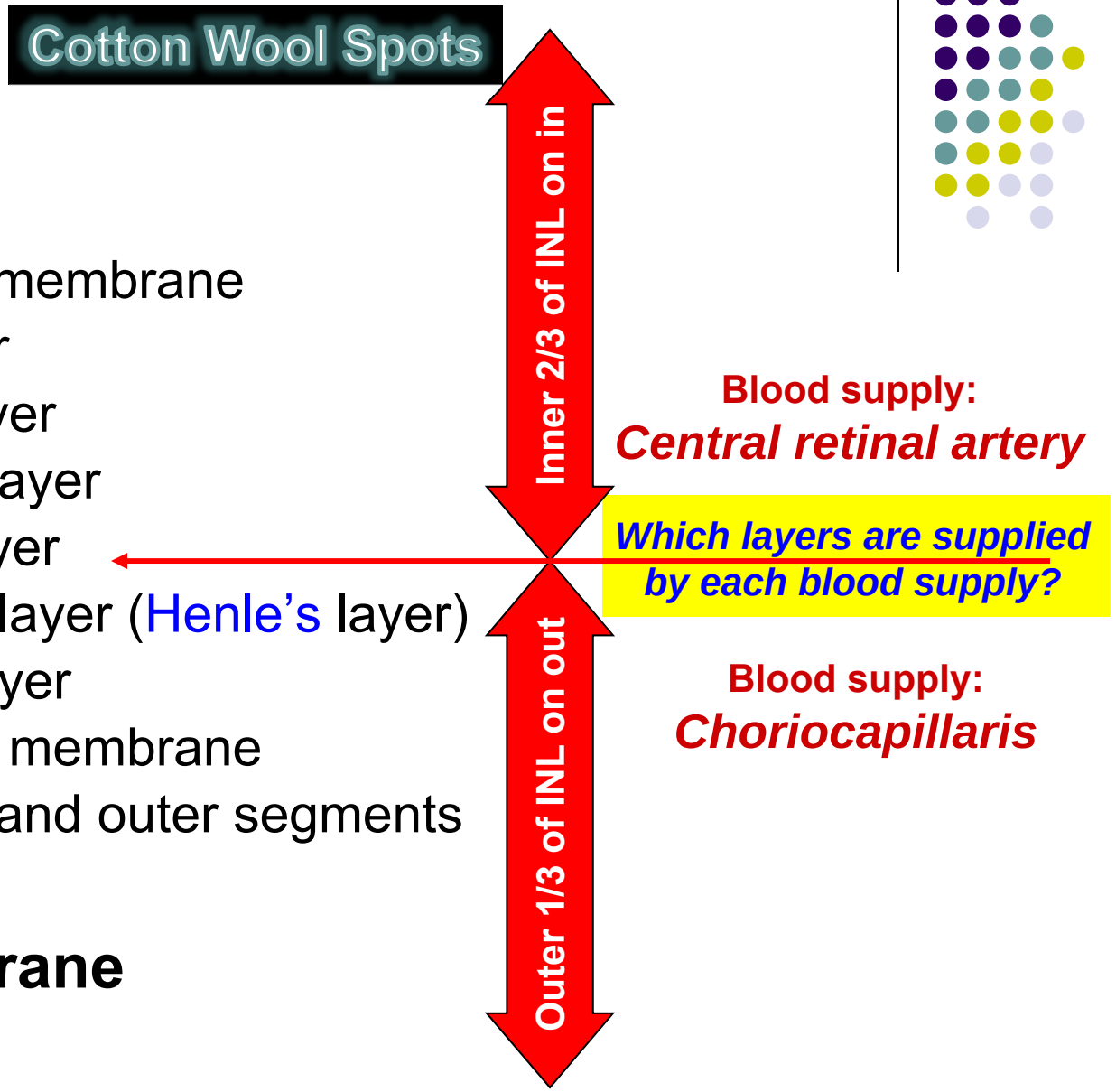

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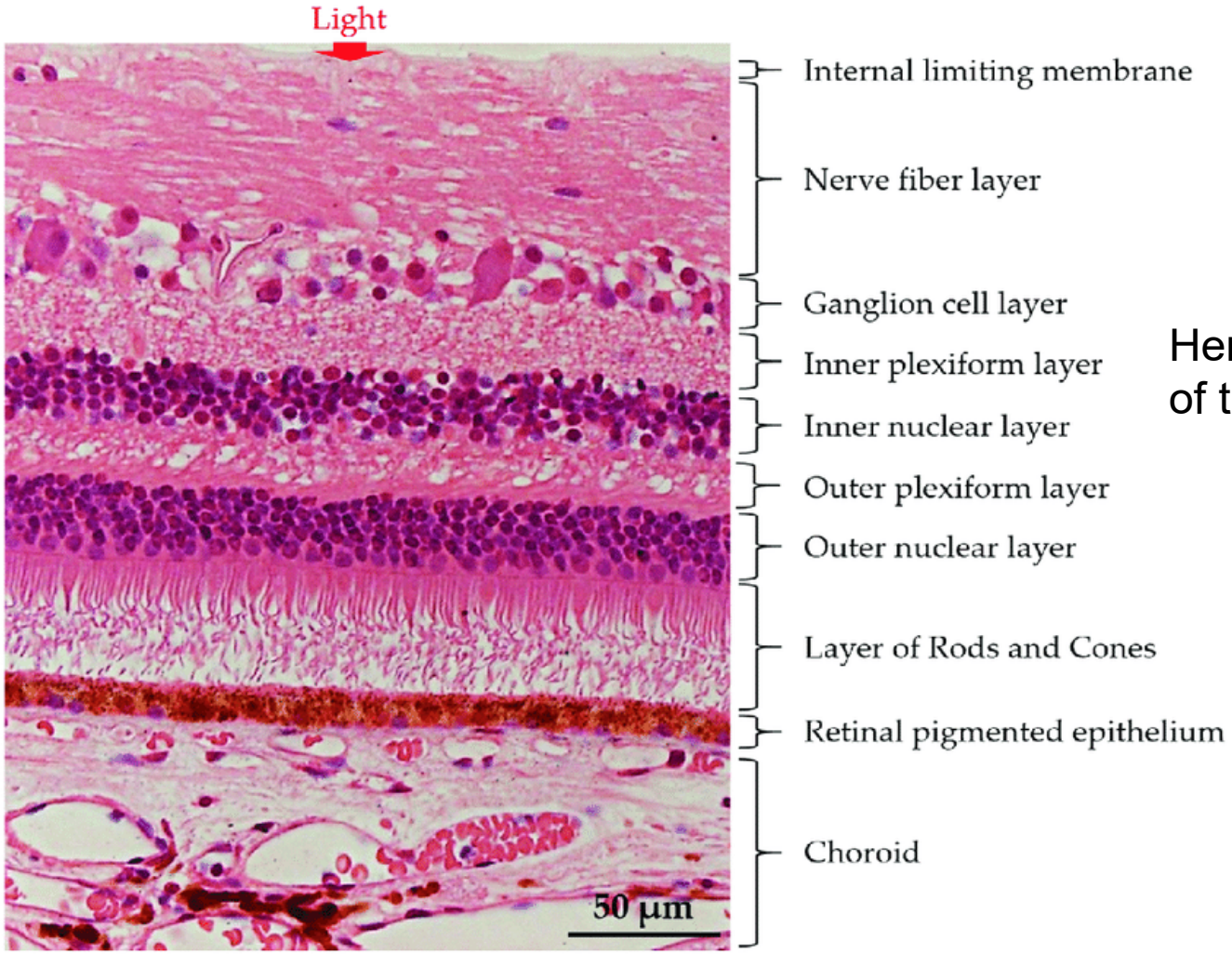
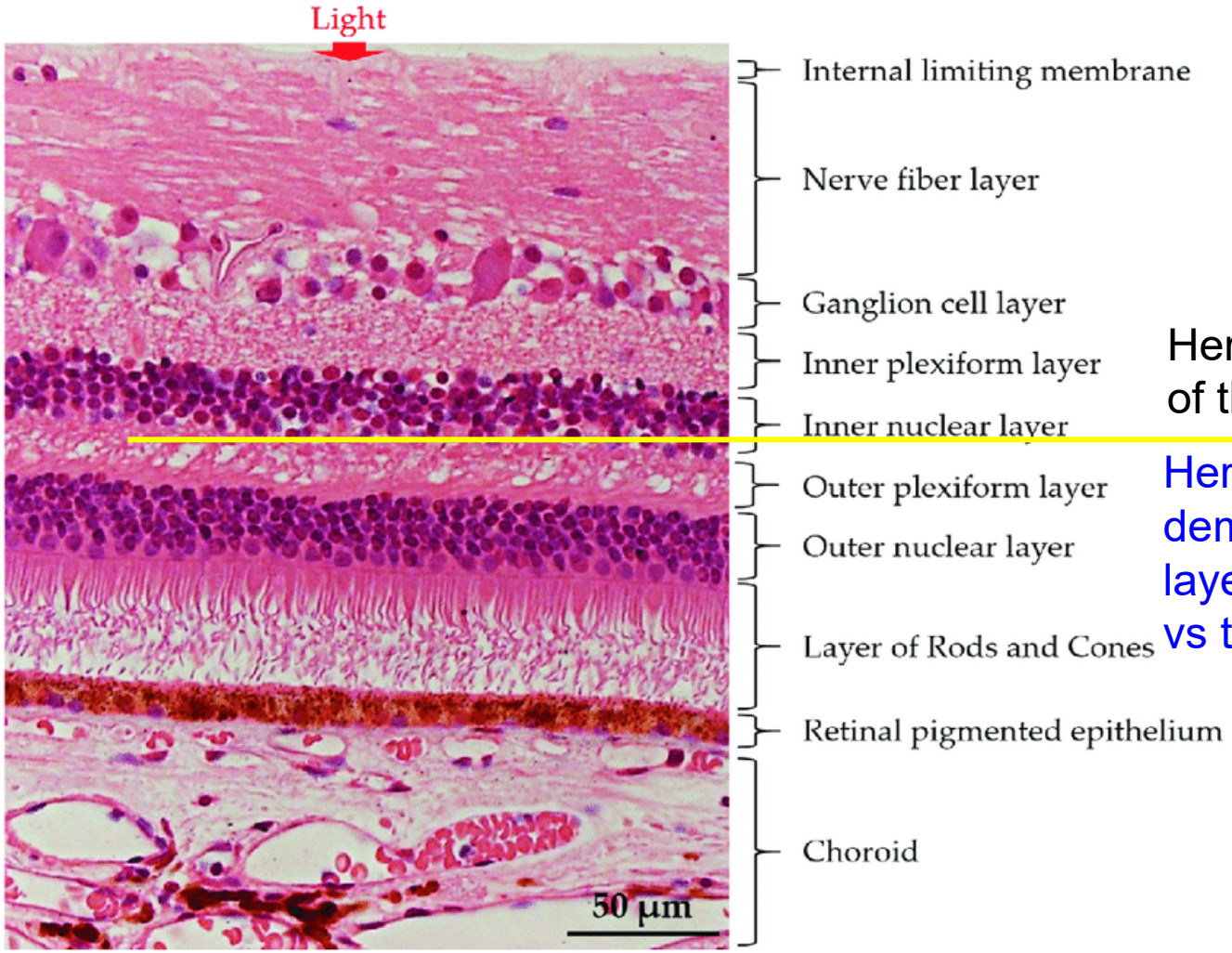



Here is a photomicrograph of the normal human retina

*(No question—proceed when ready)*

# Cotton Wool Spots




Here is a photomicrograph of the normal human retina

Here, approximately, is the demarcation between the layers perfused by the CRA vs the choriocapillaris

*(No question—proceed when ready)*

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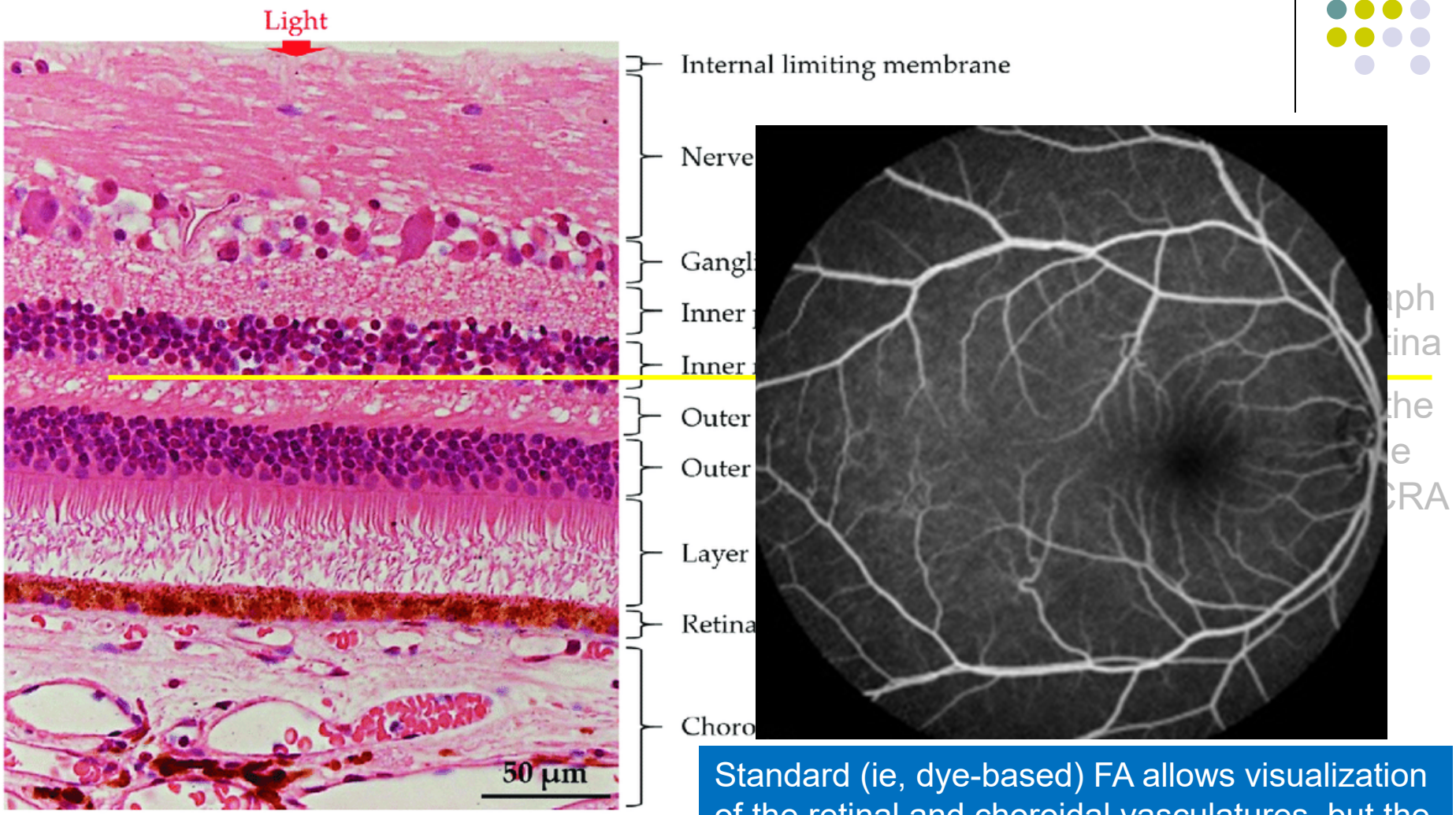


Standard (ie, dye-based) FA allows visualization of the retinal and choroidal vasculatures, but the layers are all superimposed upon one another, making it impossible to distinguish among them

*(No question—proceed when ready)*

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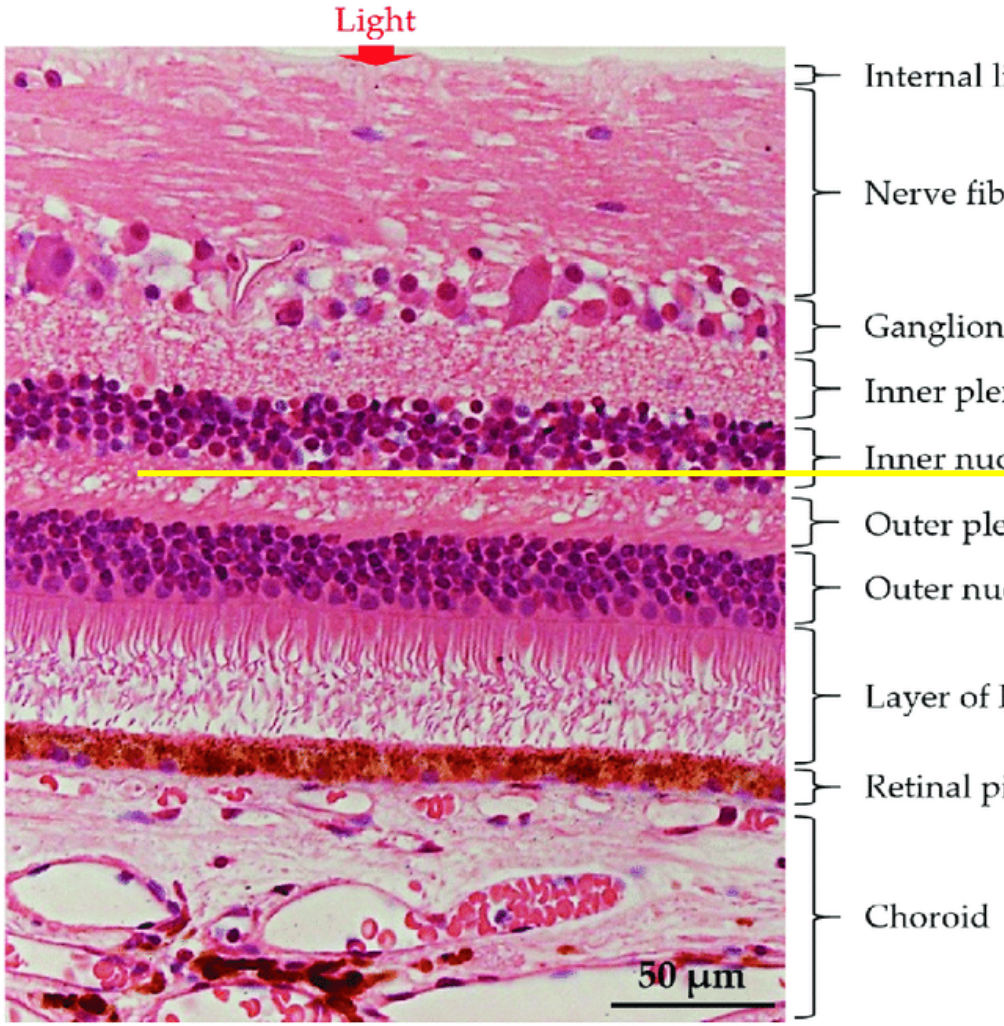
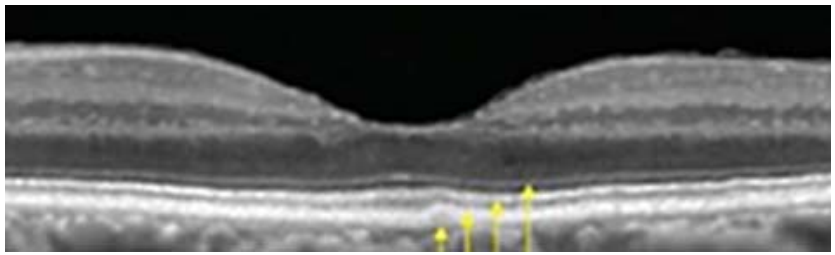



Instead, let's use *en face* OCTA to look at the ultrastructure of the circulatory system (for illustration purposes, in the foveal region)

Here is a photomicrograph of the normal human retina

Here, approximately, is the demarcation between the layers perfused by the CRA vs the choriocapillaris

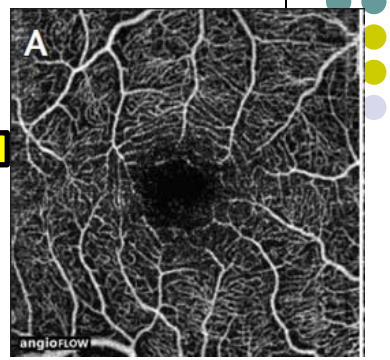


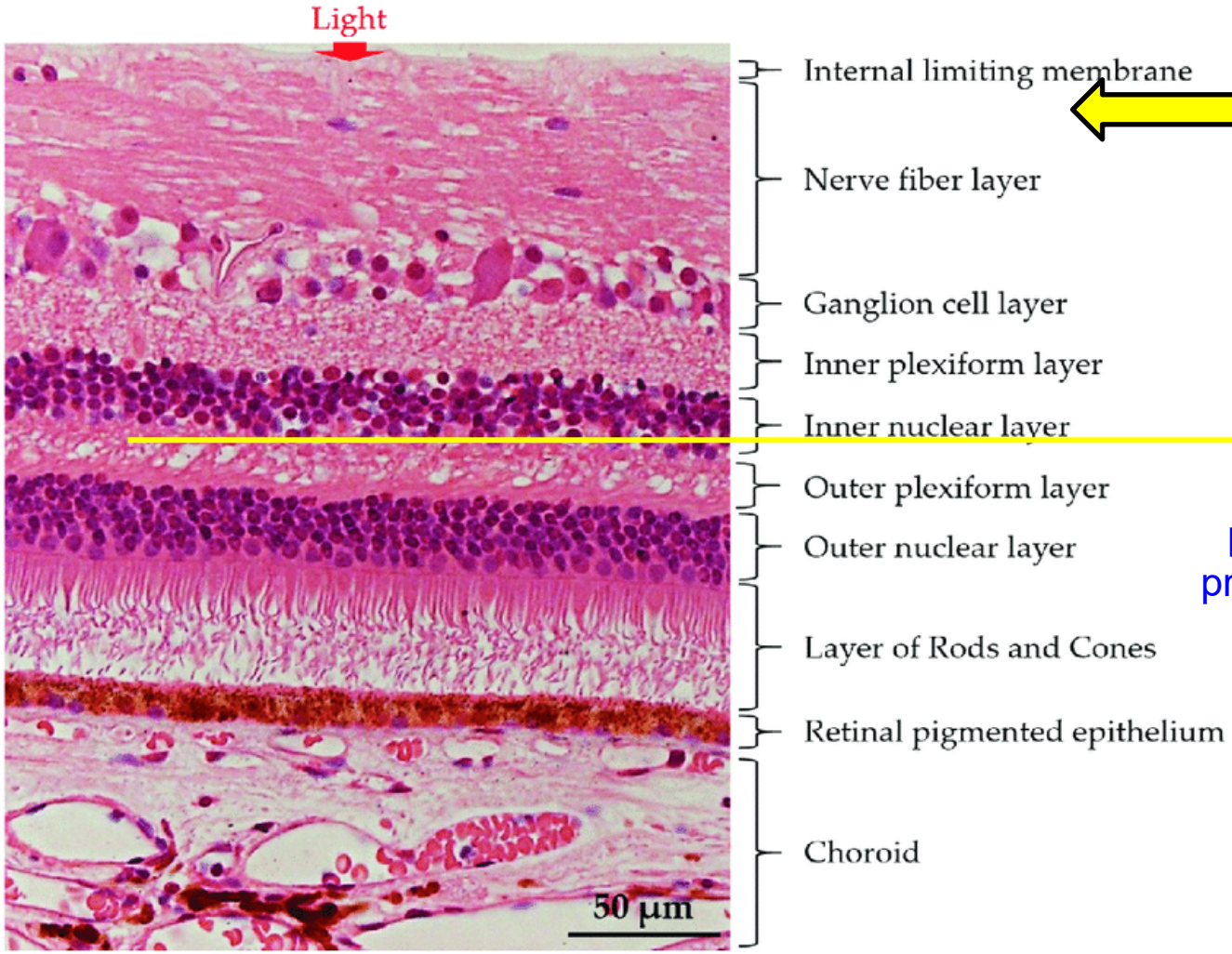
Optical coherence tomography (OCT) through the fovea (cross-sectional, not *en face*)

*(No question—proceed when ready)*

# Cotton Wool Spots

*En face* OCTA



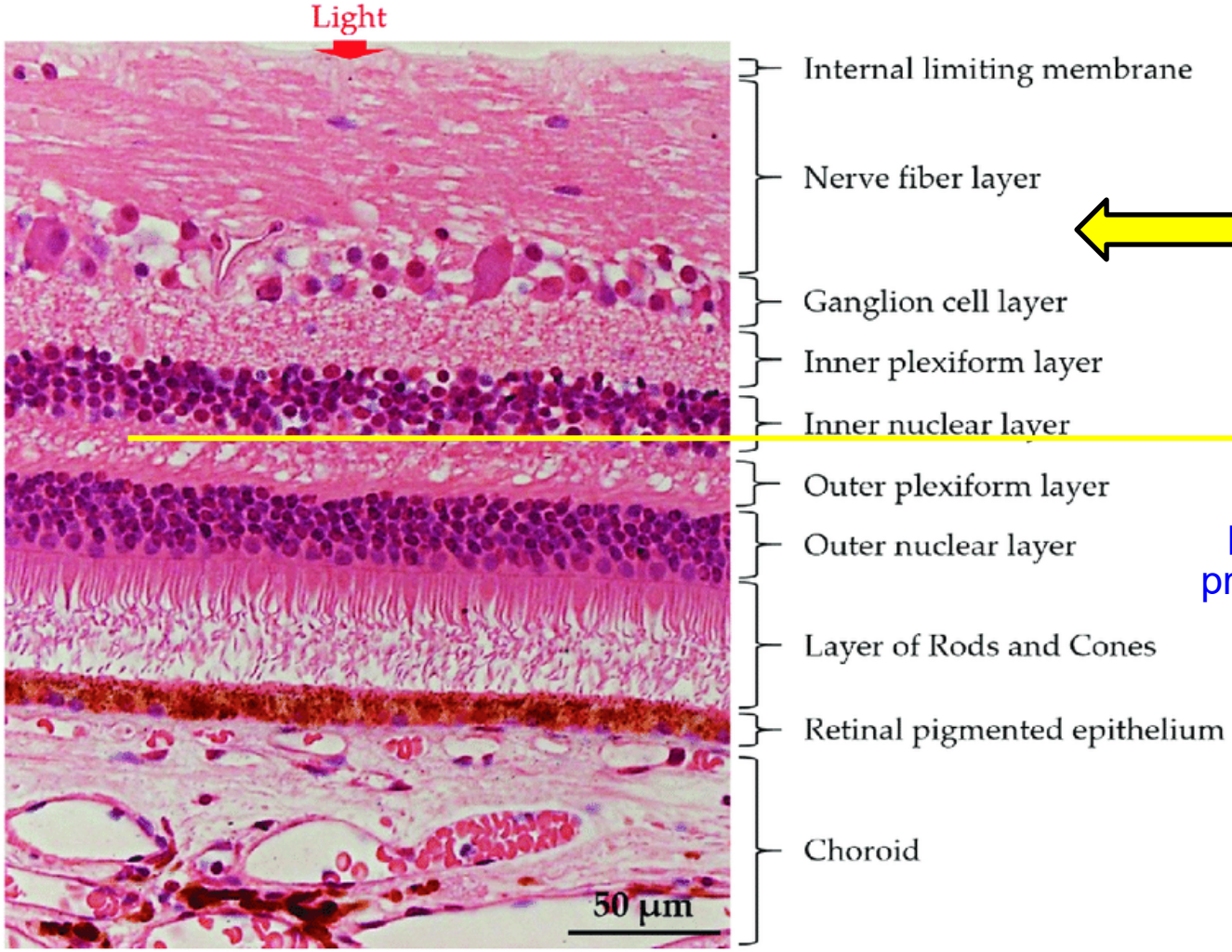



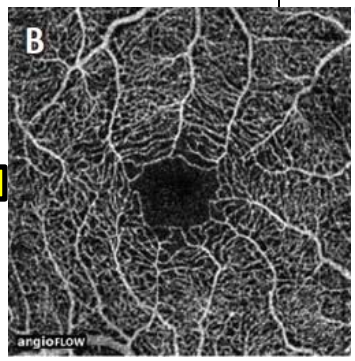

Pics ***A***, *B* and *C* depict the parafoveal vasculature as we progress deeper into the retina

*(No question—proceed when ready)*

# Cotton Wool Spots

## *En face* OCTA




Pics *A*, ***B*** and *C* depict the parafoveal vasculature as we progress deeper into the retina

*(No question—proceed when ready)*

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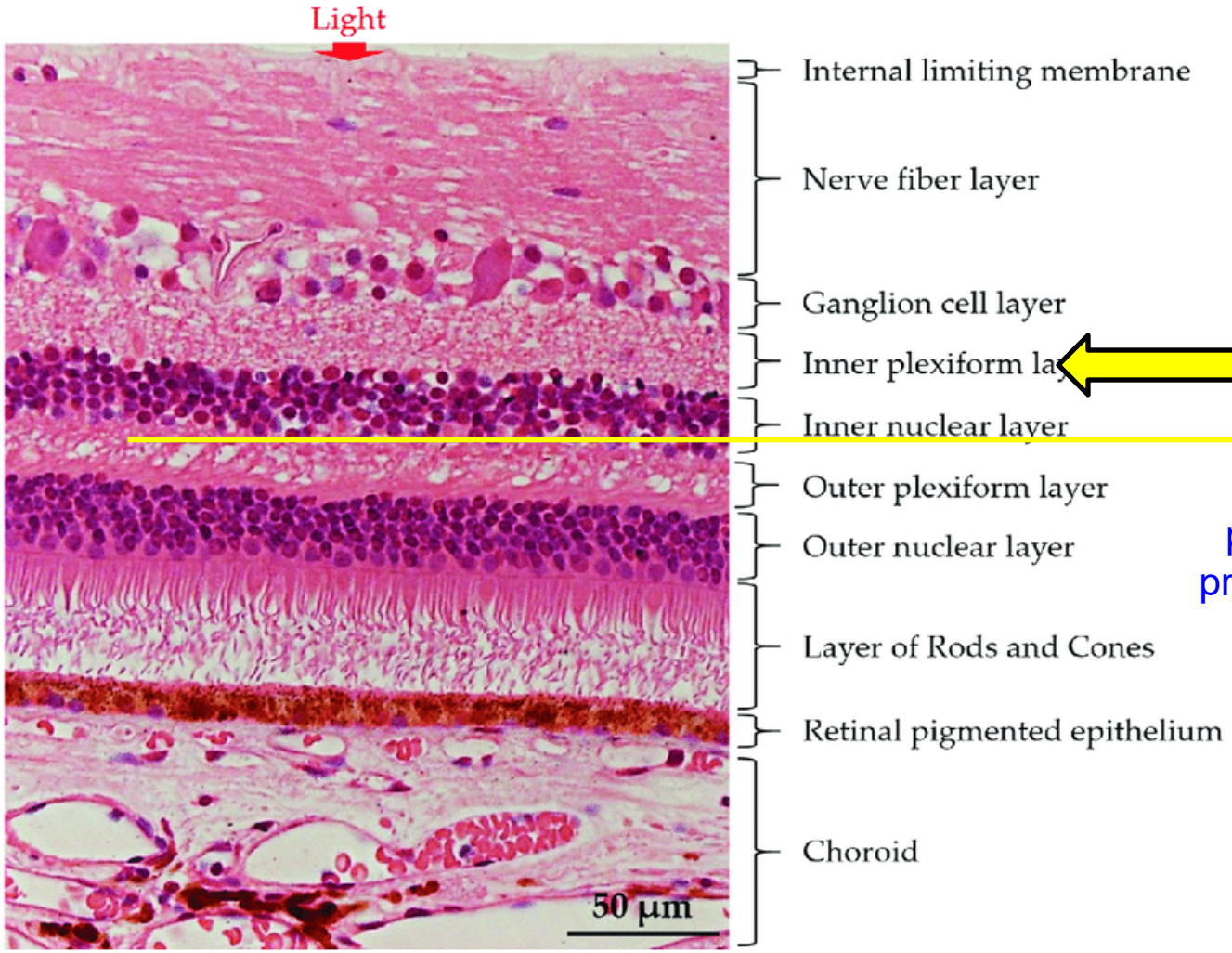
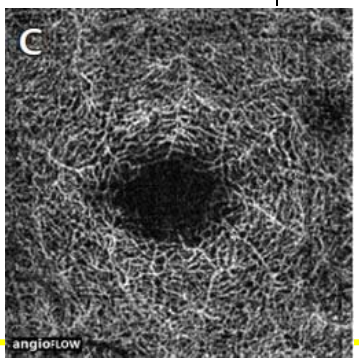
*En face* OCTA



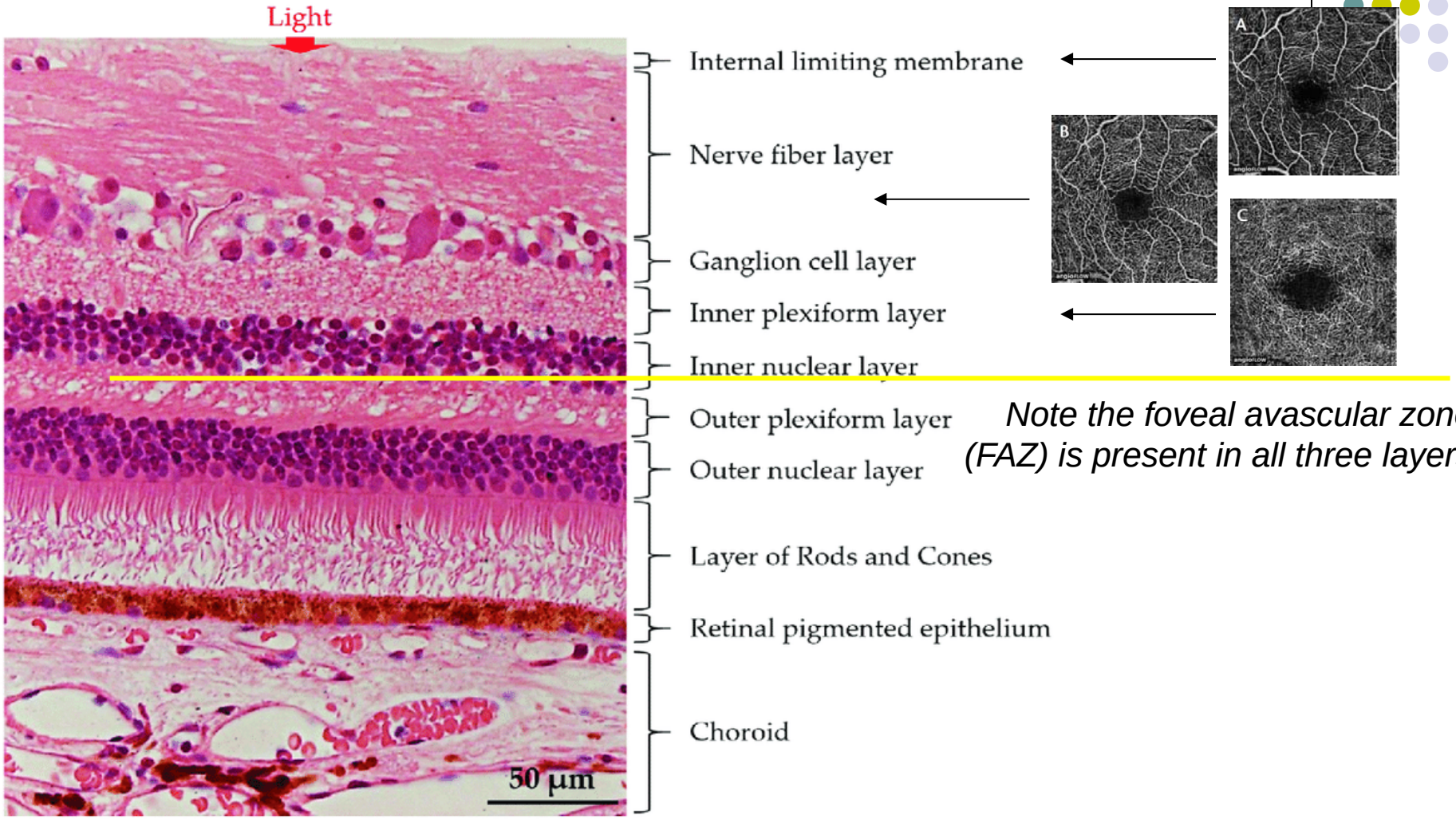




Pics *A*, *B* and ***C*** depict the parafoveal vasculature as we progress deeper into the retina

*(No question—proceed when ready)*

# Cotton Wool Spots

## *En face* OCTA

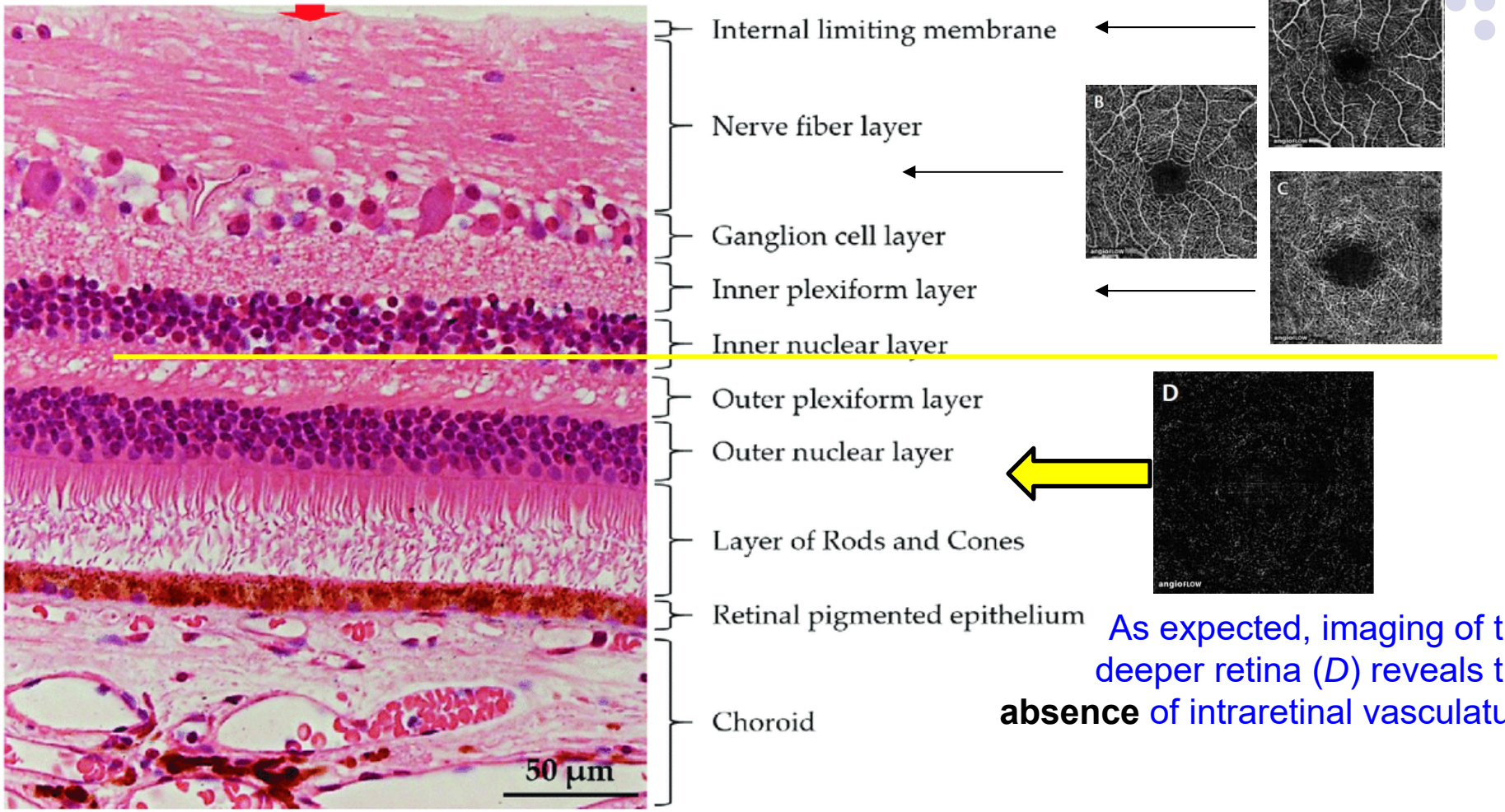



*Note the foveal avascular zone (FAZ) is present in all three layers*

*(No question—proceed when ready)*

# Cotton Wool Spots

## *En face* OCTA

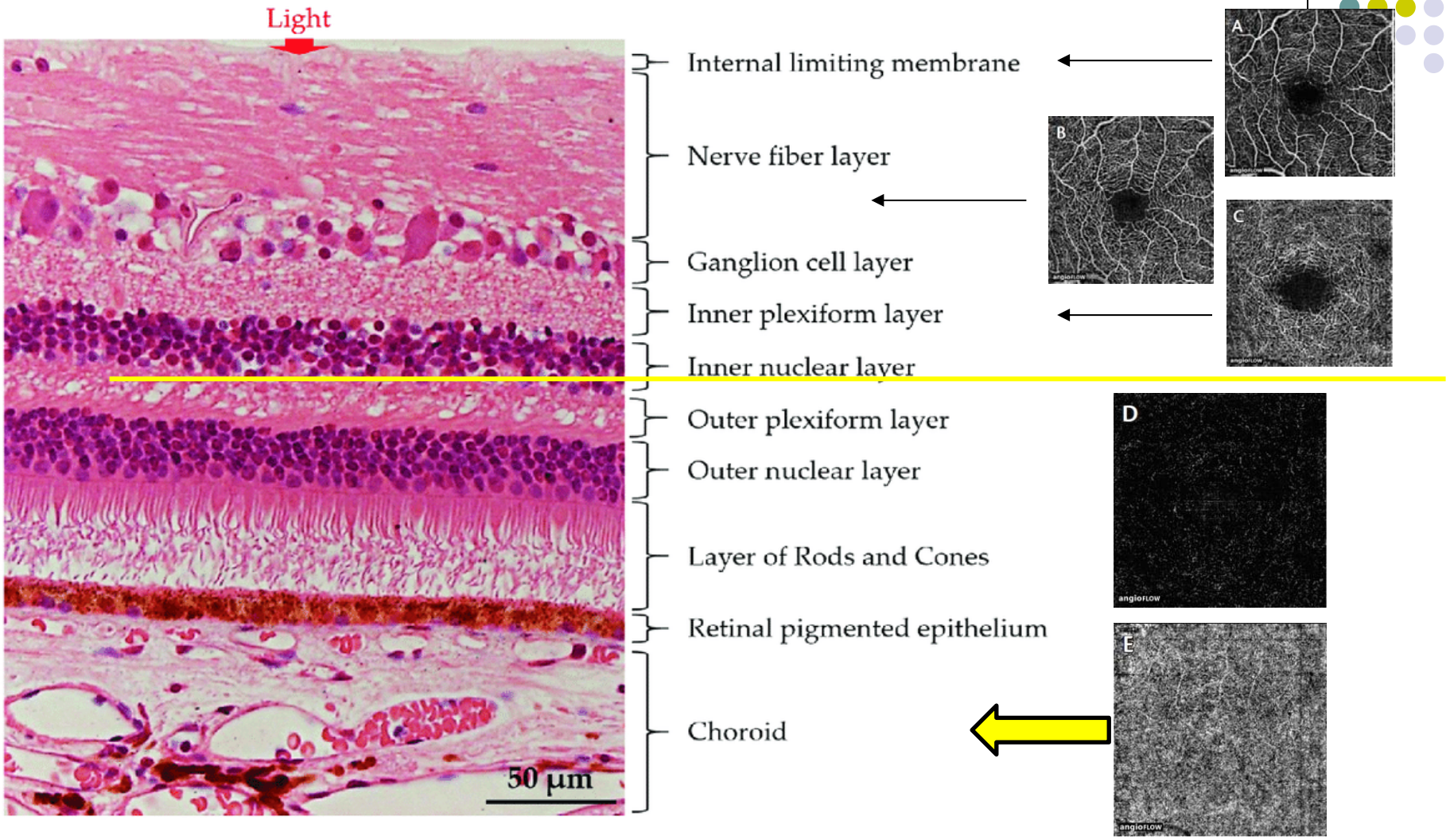



As expected, imaging of the deeper retina (*D*) reveals the **absence** of intraretinal vasculature

*(No question—proceed when ready)*

# Cotton Wool Spots

## *En face* OCTA

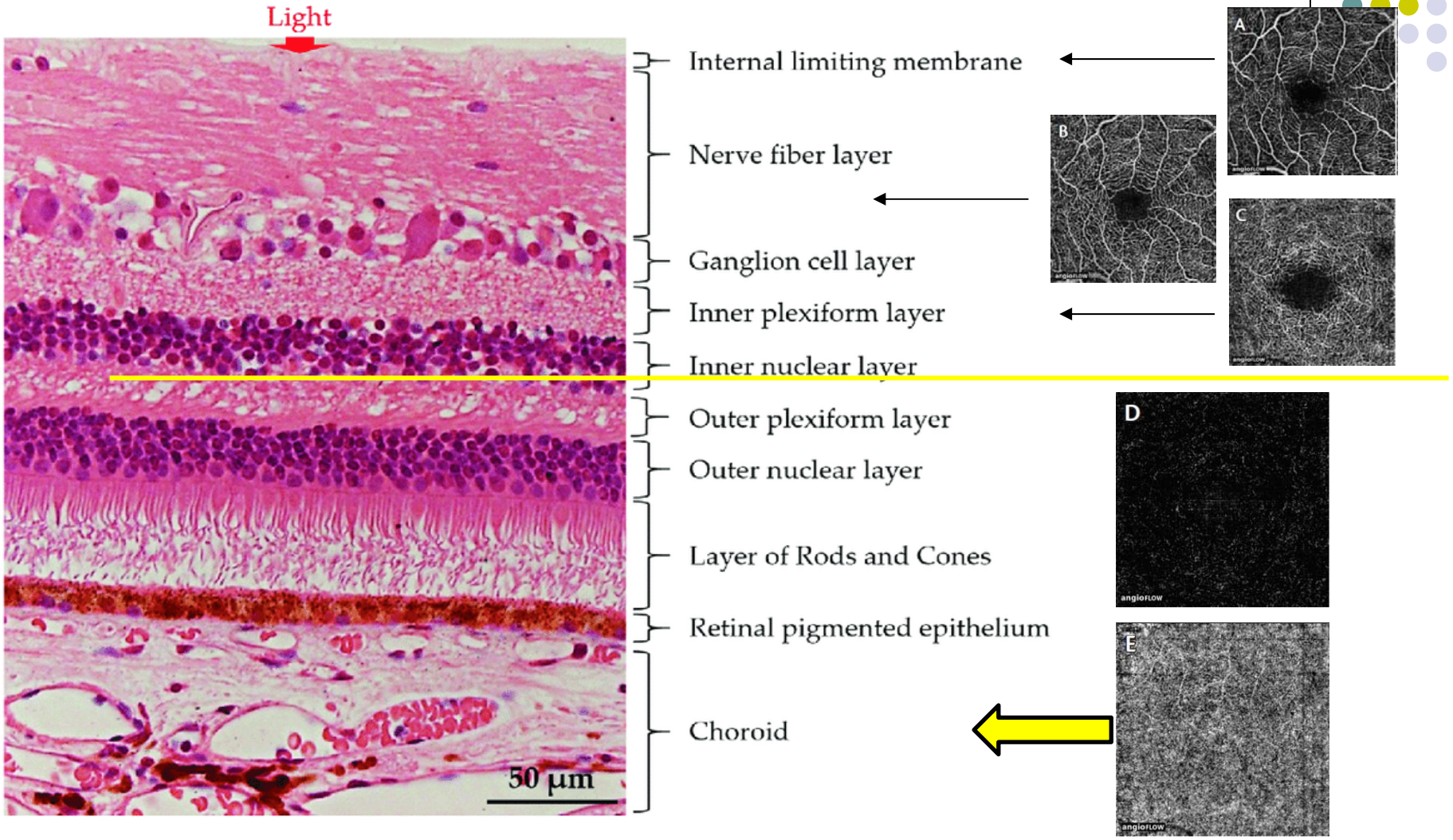



Imaging of the choriocapillaris (*E*) indicates it contains a dense, robust vasculature.

*(No question—proceed when ready)*

# Cotton Wool Spots

*En face* OCTA

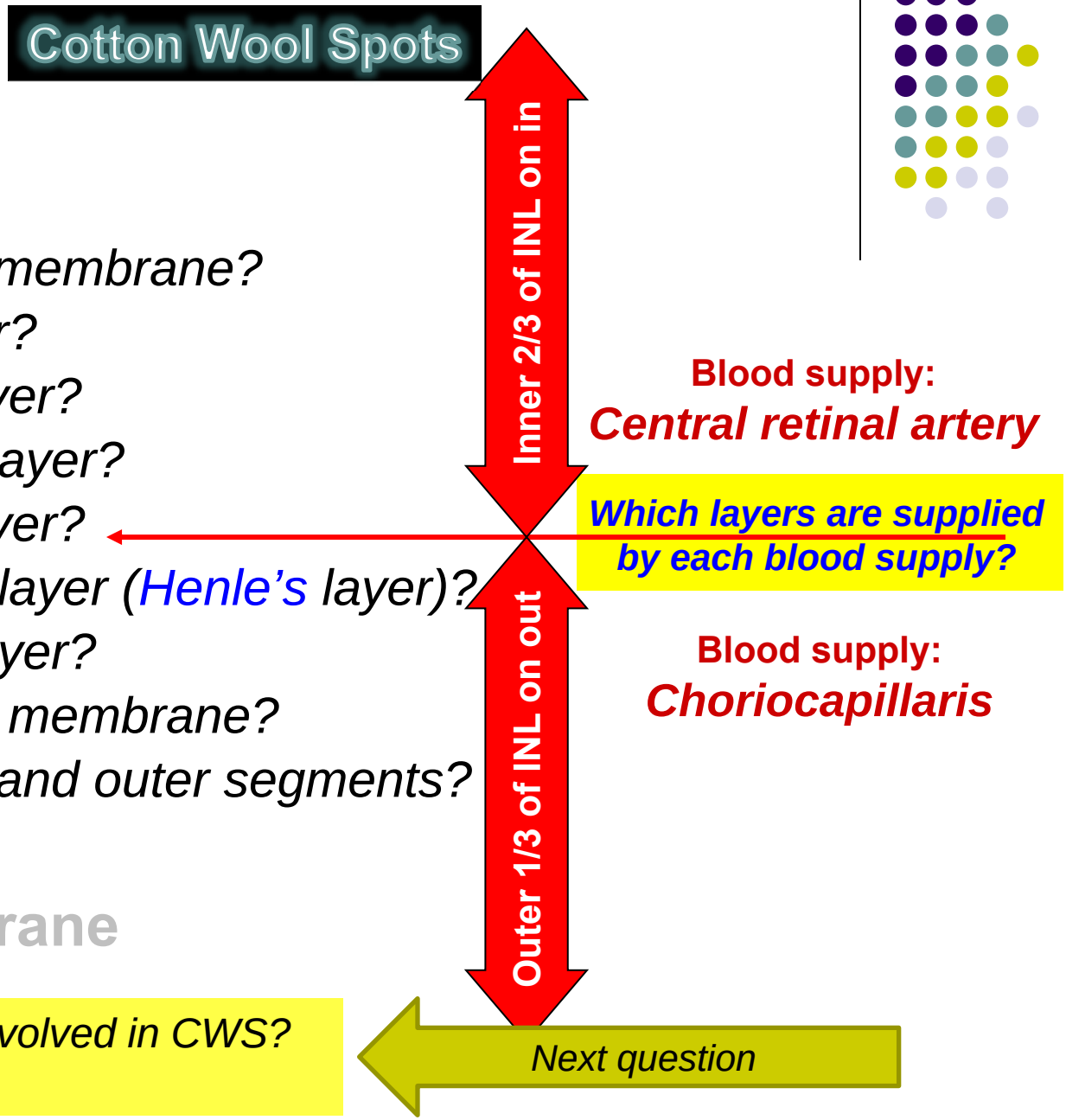



*(No question—proceed when ready)*

Imaging of the choriocapillaris (*E*) indicates it contains a dense, robust vasculature. *As expected, note the* absence *of a void corresponding to the FAZ.*

# Q

- **Retinal Layers**
  - *Internal limiting membrane?*
  - *Nerve fiber layer?*
  - *Ganglion cell layer?*
  - *Inner plexiform layer?*
  - *Inner nuclear layer?*
  - *Outer plexiform layer (Henle's layer)?*
  - *Outer nuclear layer?*
  - *External limiting membrane?*
  - *Rod/cone inner and outer segments?*
- **RPE**
- **Bruch's membrane**



# A

## Cotton Wool Spots

- **Retinal Layers**
  - Internal limiting membrane
  - **Nerve fiber layer**
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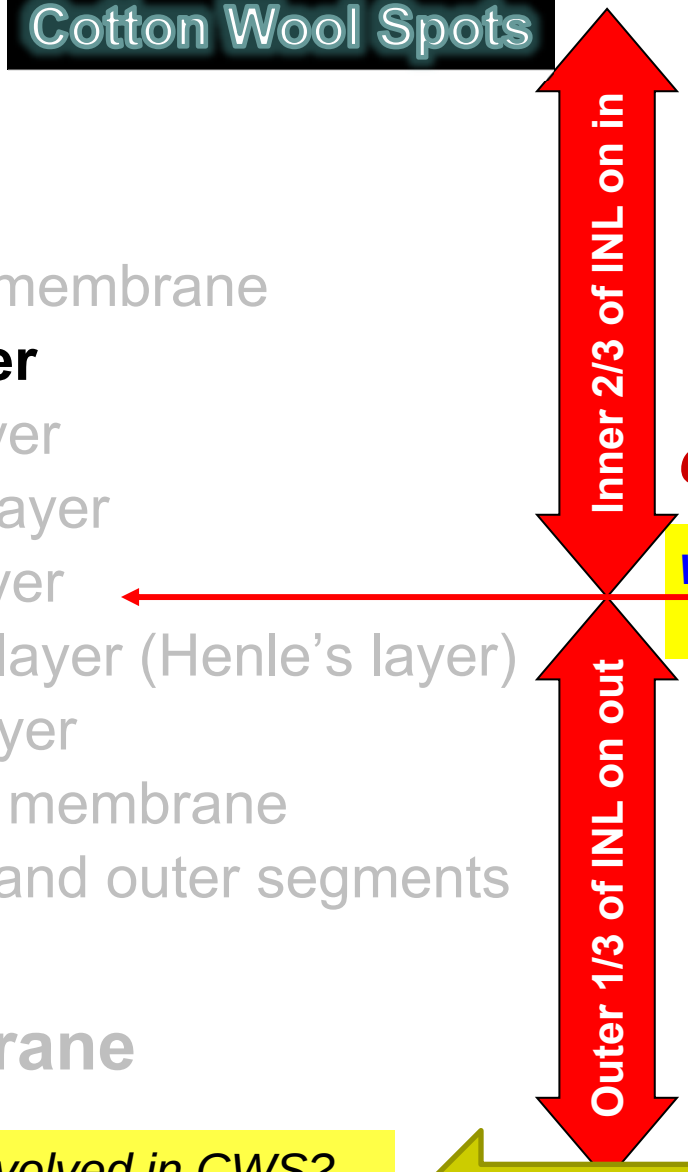



**Blood supply:**
***Central retinal artery***

***Which layers are supplied by each blood supply?***

**Blood supply:**
***Choriocapillaris***

*Which retinal layer is involved in CWS?*
The **nerve fiber layer (NFL)**

*Next question*

# Q

## Cotton Wool Spots

- **Retinal Layers**
  - Internal limiting membrane
  - **Nerve fiber layer**
  - Inner nuclear layer
  - Outer plexiform layer (Henle's layer)
  - Outer nuclear layer
  - External limiting membrane
  - Rod/cone inner and outer segments
- **RPE**
- **Bruch's membrane**

*What does this imply about the etiology of CWS?*

*Which retinal layer is involved in CWS?*
The **nerve fiber layer (NFL)**

**Inner 2/3 of INL on in**

**Blood supply:**
***Central retinal artery***

***Which layers are supplied by each blood supply?***

**Outer 1/3 of INL on out**

**Blood supply:**
***Choriocapillaris***

# A

## Cotton Wool Spots

- **Retinal Layers**
  - Internal limiting membrane
  - **Nerve fiber layer**
  - Inner nuclear layer
  - Outer plexiform layer (Henle's layer)
  - Outer nuclear layer
  - External limiting membrane
  - Rod/cone inner and outer segments
- **RPE**
- **Bruch's membrane**

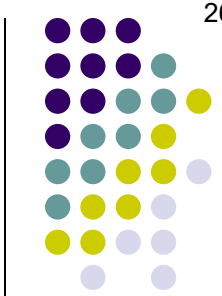
*What does this imply about the etiology of CWS?*
It implies the infarction occurs within branches of the CRA

**Blood supply:**
***Central retinal artery***

*Which retinal layer is involved in CWS?*
The **nerve fiber layer (NFL)**

# Q

## Cotton Wool Spots



Nerve **fiber** layer

*In one word, what sort of structure are the NFL 'fibers'?*

# A

## Cotton Wool Spots

Nerve **fiber** layer

*In one word, what sort of structure are the NFL 'fibers'?*
The fibers are **axons**

# Q

## Cotton Wool Spots

Nerve **fiber** layer

*In one word, what sort of structure are the NFL 'fibers'?*

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*Speaking of axons—to what does the term* axoplasmic flow *refer?*

# A

## Cotton Wool Spots

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*Speaking of axons—to what does the term* axoplasmic flow *refer?*
It refers to the movement of organelles, proteins, lipids, etc, along the length of an axon (ie, to and from the cell body)

# Q

## Cotton Wool Spots

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*To what does the term* axoplasmic stasis *refer?*

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*To what does the term* axoplasmic stasis *refer?*
If axoplasmic flow is interrupted, the material being transported comes to rest and accumulates at the site of the interruption. This is the state of 'axoplasmic stasis.'

# Q

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*What is the relationship between CWS and axoplasmic stasis?*

# A

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*What is the relationship between CWS and axoplasmic stasis?*
Axoplasmic stasis leads to swelling and opacification of the axon at the site of accumulation. If enough axons in an area are similarly affected, the collective appearance of all those swollen/opacified axons results in the ophthalmoscopic finding known as a CWS.

# Q

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*Speaking of ophthalmoscopy—what do CWS look like?*
--Size:
--Color:

# Q/A

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*Speaking of ophthalmoscopy—what do CWS look like?*
--Size: Usually ≤ [redacted] DD
--Color:

# A

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*Speaking of ophthalmoscopy—what do CWS look like?*
--Size: Usually ≤ ¼ DD
--Color:

# Q

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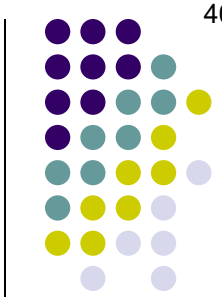
*Speaking of ophthalmoscopy—what do CWS look like?*
--Size: Usually ≤ ¼ DD
--Color: White (is why they are called **cotton** wool spots)

# Cotton Wool Spots

Cotton-wool spots

# Q

## Cotton Wool Spots



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*Do CWS resolve spontaneously?*

*Speaking of ophthalmoscopy—what do CWS look like?*
--Size: Usually ≤ ¼ DD
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*Do CWS resolve spontaneously?*
Yes

*Speaking of ophthalmoscopy—what do CWS look like?*
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# Q

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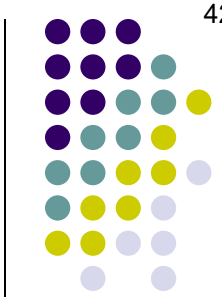

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*Do CWS resolve spontaneously?*
Yes

*How long does it take?*

*Speaking of ophthalmoscopy—what do CWS look like?*
--Size: Usually ≤ ¼ DD
--Color: White (is why they are called **cotton** wool spots)

# A

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*What is the relationship between CWS and axoplasmic stasis?*
Axoplasmic stasis leads to swelling and opacification of the axon at the site of accumulation. If enough axons in an area are similarly affected, the collective appearance of all those swollen/opacified axons results in **the ophthalmoscopic finding known as a CWS**.

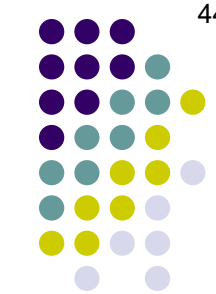
*Do CWS resolve spontaneously?*
Yes

*How long does it take?*
A month or two

*Speaking of ophthalmoscopy—what do CWS look like?*
--Size: Usually ≤ ¼ DD
--Color: White (is why they are called **cotton** wool spots)

# Q

## Cotton Wool Spots



Nerve **fiber** layer

*In one word, what sort of structure are the NFL 'fibers'?*
The fibers are **axons**

*Speaking of axons—to what does the term* axoplasmic flow *refer?*
It refers to the movement of organelles, proteins, lipids, etc, along the length of an axon (ie, to and from the cell body)

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*Do they resolve without sequelae, or with?*

*Do CWS* ***resolve*** *spo -what do CWS look like?*
Yes

called **cotton** wool spots)

*How long does it take?*
A month or two

# A

## Cotton Wool Spots

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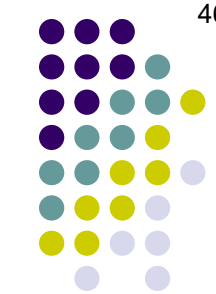

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*Do they resolve without sequelae, or with?*
With

*What is the sequelae?*
The RNFL at the site is a little atrophic/thinned

*Do CWS* ***resolve*** *spo… -what do CWS look like?*
Yes

… called **cotton** wool spots)

*How long does it take?*
A month or two

# Q

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*If axoplasmic flow is interrupted at the ONH, what condition results?*

# A

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*If axoplasmic flow is interrupted at the ONH, what condition results?*
**Disc edema**

# Q

## Cotton Wool Spots

Nerve **fiber** layer

*In one word, what sort of structure are the NFL 'fibers'?*
The fibers are **axons**

*What cells are they the axons of?*

# A

## Cotton Wool Spots

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*What cells are they the axons of?*
Retinal ganglion cells

# Q

## Cotton Wool Spots

Nerve **fiber** layer

*In one word, what sort of structure are the NFL 'fibers'?*
The fibers are **axons**

*What cells are they the axons of?*
Retinal ganglion cells

*Where are the cell bodies of the ganglion cells located?*

# A

## Cotton Wool Spots

- **Retinal Layers**
  - Internal limiting membrane
  - Nerve **fiber** layer
  - **Ganglion cell layer**
  - Inner plexiform layer
  - Inner nuclear layer
  - Outer plexiform layer
  - Outer nuclear layer
  - External limiting membrane
  - Rod/cone inner and outer segments
- **RPE**
- **Bruch's membrane**

*In one word, what sort of structure are the NFL 'fibers'?*
The fibers are **axons**

*What cells are they the axons of?*
Retinal ganglion cells

*Where are the cell bodies of the ganglion cells located?*
In the **ganglion cell layer**

# Q

## Cotton Wool Spots

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*These ganglion-cell axons--where are they headed?*

*lls located?*

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*These ganglion-cell axons--where are they headed?*
To the optic nerve head (ONH)

*Will they synapse at the ONH?*

*lls located?*

- **RPE**
- **Bruch's membrane**

# Q/A

## Cotton Wool Spots

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***What cells are they the axons of?***
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*lls located?*

*These ganglion-cell axons--where are they headed?*
To the optic nerve head (ONH)

*Will they synapse at the ONH?*
No. The ONH contains no synapses; it is simply the aggregate of nerve fibers as they leave the globe via a hole in the sclera called the [two words]

- **RPE**
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# A

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# Q

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*OK, then where* will *they synapse?*

# A

## Cotton Wool Spots

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*OK, then where* will *they synapse?*
Most will synapse in the lateral geniculate nucleus (LGN)

# Q

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*OK, then where will they synapse?*
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*Most? Where will the others synapse, and what are they responsible for?*

# Q/A

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*Most? Where will the others synapse, and what are they responsible for?*
Most of the others are involved in the [three words]; they peel off just prior to reaching the LGN, heading instead to the pretectum of the dorsal midbrain to synapse in the pretectal nuclei

# A

## Cotton Wool Spots

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To the optic nerve hea

***Will they synapse at***
**No**. The ONH contain
as ~~they leave the glob~~

*There is an important clinical entity caused by damage to the pretectal nuclei of the dorsal midbrain. What is its eponymous name?*

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**Parinaud syndrome**

lls located?

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--
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--
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*There is an important clinical entity caused by damage to the pretectal nuclei of the dorsal midbrain. What is its eponymous name?*
**Parinaud syndrome**

*Parinaud syndrome has four classic clinical features. What are they?*
--Light-near dissociation
--Impaired upgaze
--Lid retraction
--Convergence-retraction nystagmus

*There's that word a*
*will the others syna*
*what are they respo*
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**Parinaud syndrome**

*What are the two* noneponymous *names for Parinaud syndrome?*
**1)**
**2)**

*lls located?*

cleus (LGN)

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**Most** of the others are involved in the "pupillary light reflex", they peel off just prior to reaching the LGN, heading instead to the pretectum of the **dorsal midbrain to synapse in the pretectal nuclei**

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*There is an important clinical entity caused by damage to the pretectal nuclei of the dorsal midbrain. What is its eponymous name?*
**Parinaud syndrome**

*What are the two* noneponymous *names for Parinaud syndrome?*
**1) Dorsal midbrain syndrome**
**2) Pretectal syndrome**

*There's that word again. Where will the others synapse, and what are they responsible for?*
The **hypothalamus** , where they are involved in modulating **circadian** activity

**Most** of the others are involved in the "pupillary light reflex", they peel off just prior to reaching the LGN, heading instead to the pretectum of the **dorsal midbrain** **pretectal nuclei**

# Q

## Cotton Wool Spots

*What is the clinical status of most pts with CWS?*

# A

## Cotton Wool Spots

*What is the clinical status of most pts with CWS?*

diabetic

# Q

## Cotton Wool Spots

*What should you do if a* nondiabetic *pt has CWS?*

# A

## Cotton Wool Spots

*What should you do if a* nondiabetic *pt has CWS?*
**Work it up!**

# Cotton Wool Spots

***The rule:***

Work up even 1 cotton-wool spot in a nondiabetic patient!

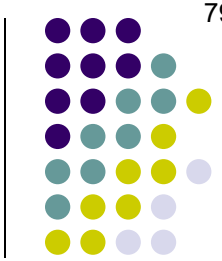
*(No question--proceed when ready)*

# Cotton Wool Spots

- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient.

*(No question--proceed when ready)*

# Cotton Wool Spots



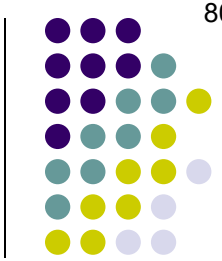
- The following tests constitute a **reasonable battery** in working up a cotton-wool spot in a nondiabetic patient.

  Note: By *reasonable battery* I don't mean that **all** nondiabetic pts with CWS should undergo **all** of the tests. As always, the history, ROS and exam should be used to winnow and motivate any tests pursued.

*(No question--proceed when ready)*

# Q

## Cotton Wool Spots



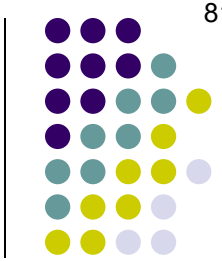
- The following tests constitute a reasonable battery in working up a cotton-wool spot in a **nondiabetic** patient.

***First things first:*** *Check 'em for DM. (Maybe they just don't realize they have it, or are in denial)*

*(No question--proceed when ready)*

# Q

## Cotton Wool Spots



- The following tests constitute a reasonable battery in working up a cotton-wool spot in a **nondiabetic** patient.

***First things first:*** *Check 'em for DM. (Maybe they just don't realize they have it, or are in denial)*

*What percent of 'nondiabetics' with CWS will be found to have elevated blood sugar?*

# A

## Cotton Wool Spots

- The following tests constitute a reasonable battery in working up a cotton-wool spot in a **nondiabetic** patient.

***First things first:*** *Check 'em for DM. (Maybe they just don't realize they have it, or are in denial)*

*What percent of 'nondiabetics' with CWS will be found to have elevated blood sugar?*
One study (quoted by an Academy publication) pegged it at 20%!

# Q

## Cotton Wool Spots

- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - **Sphygnamometry**:
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# A

## Cotton Wool Spots

- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - **Sphygnamometry**: **HTN**
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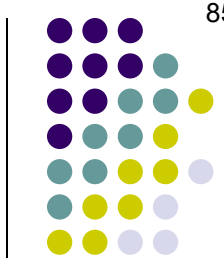
# Q

## Cotton Wool Spots



- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - **Sphygnamometry**: **HTN**

*What percent of 'nonhypertensives' with CWS will be found to have elevated BP?*

# A

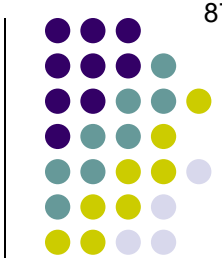
## Cotton Wool Spots

- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - **Sphygnamometry**: **HTN**

*What percent of 'nonhypertensives' with CWS will be found to have elevated BP?*
**50%** (per the same study mentioned previously)

# Q

## Cotton Wool Spots



- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - Sphygnamometry: **HTN**
  - **Echocardiogram**:
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# A

## Cotton Wool Spots

- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - Sphygnamometry: **HTN**
  - **Echocardiogram**: **Cardiac embolic source**
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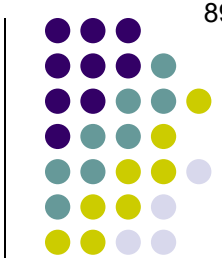
# Q

## Cotton Wool Spots



- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - Sphygnamometry: **HTN**
  - Echocardiogram: **Cardiac embolic source**
  - **Carotid dopplers**:
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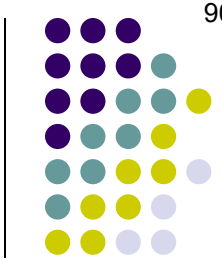
# A

## Cotton Wool Spots



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  - Echocardiogram: **Cardiac embolic source**
  - **Carotid dopplers**: **Carotid embolic source**
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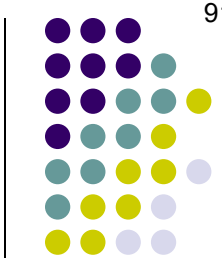
# Q

## Cotton Wool Spots



- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - Sphygnamometry: **HTN**
  - Echocardiogram: **Cardiac embolic source**
  - Carotid dopplers: **Carotid embolic source**
  - **Hgb electrophoresis**:
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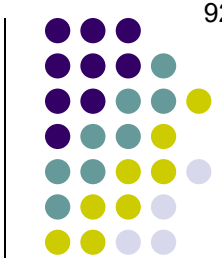
# A

## Cotton Wool Spots



- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - Sphygnamometry: **HTN**
  - Echocardiogram: **Cardiac embolic source**
  - Carotid dopplers: **Carotid embolic source**
  - **Hgb electrophoresis**: **Sickle-cell disease**
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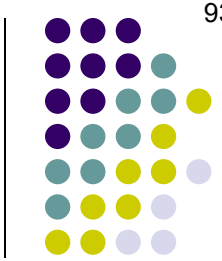
# Q

## Cotton Wool Spots



- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - Sphygnamometry: **HTN**
  - Echocardiogram: **Cardiac embolic source**
  - Carotid dopplers: **Carotid embolic source**
  - Hgb electrophoresis: **Sickle-cell disease**
  - **PMHx for head/neck CA**:
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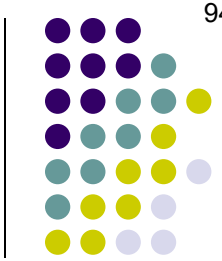
# A

## Cotton Wool Spots



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  - Echocardiogram: **Cardiac embolic source**
  - Carotid dopplers: **Carotid embolic source**
  - Hgb electrophoresis: **Sickle-cell disease**
  - **PMHx for head/neck CA**: **Radiation retinopathy**
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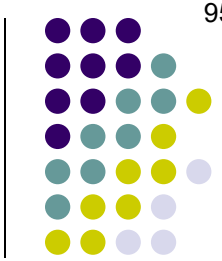
# Q

## Cotton Wool Spots



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  - Hgb electrophoresis: **Sickle-cell disease**
  - PMHx for head/neck CA: **Radiation retinopathy**
  - **ESR, CRP, ANCA**:
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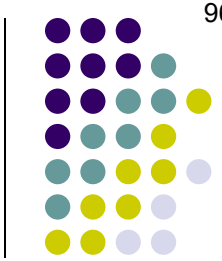
# A

## Cotton Wool Spots



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  - Carotid dopplers: **Carotid embolic source**
  - Hgb electrophoresis: **Sickle-cell disease**
  - PMHx for head/neck CA: **Radiation retinopathy**
  - **ESR, CRP, ANCA**: **Vasculitis**
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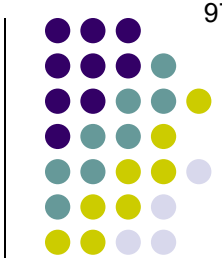
# Q

## Cotton Wool Spots



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  - Carotid dopplers: **Carotid embolic source**
  - Hgb electrophoresis: **Sickle-cell disease**
  - PMHx for head/neck CA: **Radiation retinopathy**
  - ESR, CRP, ANCA: **Vasculitis**
  - **ANA, RF**:
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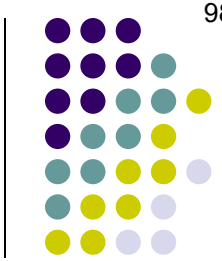
# A

## Cotton Wool Spots



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  - Carotid dopplers: **Carotid embolic source**
  - Hgb electrophoresis: **Sickle-cell disease**
  - PMHx for head/neck CA: **Radiation retinopathy**
  - ESR, CRP, ANCA: **Vasculitis**
  - **ANA, RF**: **Collagen-vascular disease**
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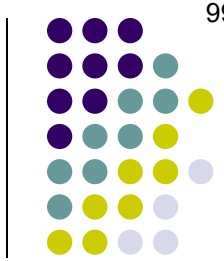
# Q

## Cotton Wool Spots



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  - PMHx for head/neck CA: **Radiation retinopathy**
  - ESR, CRP, ANCA: **Vasculitis**
  - **ANA, RF**: **Collagen-vascular disease**
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  - *To what does the term* collagen-vascular disease *refer?*
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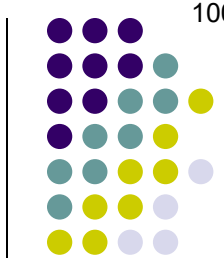
# A

## Cotton Wool Spots



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  - Hgb electrophoresis: **Sickle-cell disease**
  - PMHx for head/neck CA: **Radiation retinopathy**
  - ESR, CRP, ANCA: **Vasculitis**
  - **ANA, RF: Collagen-vascular disease**
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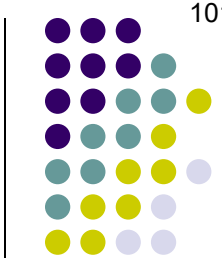
*To what does the term* collagen-vascular disease *refer?*
It is a catch-all (and outdated—more shortly) term for systemic rheumatologic conditions that present with arthralgias, vascular s/s, and skin changes (many other manifestations can occur as well)

# Q

## Cotton Wool Spots



- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - Sphygnamometry: **HTN**

*Why is the term collagen-vascular dz outdated?*

  - ANA, RF: **Collagen-vascular disease**
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*To what does the term collagen-vascular disease refer?*
It is a catch-all (and **outdated**—more shortly) term for systemic rheumatologic conditions that present with arthralgias, vascular s/s, and skin changes (many other manifestations can occur as well)

# A

## Cotton Wool Spots

- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - Sphygnamometry: **HTN**

*Why is the term collagen-vascular dz outdated?*
It was once thought that the causal nexus of these conditions was found in the tissue that manifests them; ie, that these conditions were **primary** disorders of collagen ('connective') and vascular tissues. However, we now know that it is derangements of the **immune system** that are responsible for these conditions—connective and vascular tissue are simply the locations at which the immune derangements declare themselves. Because the term *collagen-vascular dz* (and the related *connective-tissue dz*) reflect a (mis)understanding of the pathology involved, they are no longer preferred.

  - ANA, RF: **Collagen-vascular disease**
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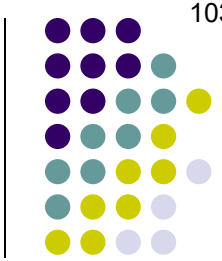
*To what does the term collagen-vascular disease refer?*
It is a catch-all (and **outdated**—more shortly) term for systemic rheumatologic conditions that present with arthralgias, vascular s/s, and skin changes (many other manifestations can occur as well)

# Q

## Cotton Wool Spots



- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - Sphygnamometry: **HTN**

*Why is the term collagen-vascular dz outdated?*
It was once thought that the causal nexus of these conditions was found in the tissue that manife**y** disorders of collagen ('connective') and vascul**angements of the immune system** that are respor**cular tissue are simply the locations at** which . Because the term *collagen-vascular dz* (and the related *connective-tissue dz*) reflect a (mis)understanding of the pathology involved, they a**no longer preferred**.

*OK then, if 'collagen-vascular disease ' and 'connective-tissue disease' are outdated, what is the preferred term?*

  - ANA, RF: **Collagen-vascular disease**
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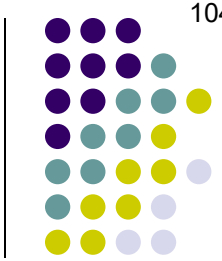
*To what does the term collagen-vascular disease refer?*
It is a catch-all (and **outdated**—more shortly) term for systemic rheumatologic conditions that present with arthralgias, vascular s/s, and skin changes (many other manifestations can occur as well)

# A

## Cotton Wool Spots



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*OK then, if 'collagen-vascular disease ' and 'connective-tissue disease' are outdated, what is the preferred term?*
'Systemic rheumatic disease'

  - ANA, RF: **Collagen-vascular disease**
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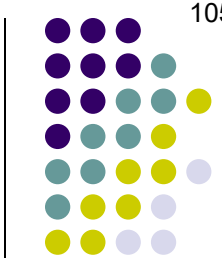
*To what does the term collagen-vascular disease refer?*
It is a catch-all (and **outdated**—more shortly) term for systemic rheumatologic conditions that present with arthralgias, vascular s/s, and skin changes (many other manifestations can occur as well)

# Q

## Cotton Wool Spots



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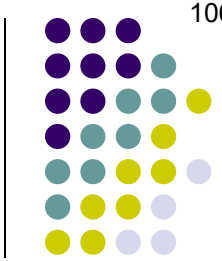
'Systemic rheumatic disease'

  - ANA, RF: **Collagen-vascular disease**
  -
  - and skin changes (many other manifestations can occur as well)

*When you hear the terms 'collagen-vascular disease' and 'cotton-wool spots' in the same sentence, one disease should immediately come to mind. What is it?*

# A

## Cotton Wool Spots



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*OK then, if 'collagen-vascular disease ' and 'connective-tissue disease' are outdated, what is the preferred term?*
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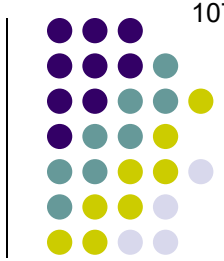
  - and skin changes (many other manifestations can occur as well)

*When you hear the terms 'collagen-vascular disease' and 'cotton-wool spots' in the same sentence, one disease should immediately come to mind. What is it?*
**Systemic lupus erythematosus**

# Q

## Cotton Wool Spots



- *Who is the classic lupus pt?*

le battery in
abetic patient.
*h?*

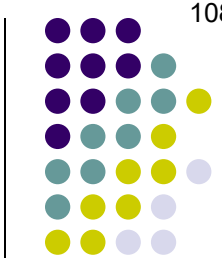
thy

*When you hear the terms 'collagen-vascular disease' and 'cotton-wool spots' in the same sentence, one disease should immediately come to mind. What is it?*

**Systemic lupus erythematosus**

# Q/A

## Cotton Wool Spots



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  A M v F

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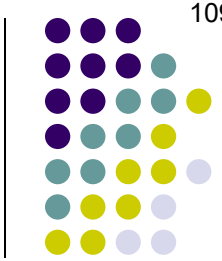
**Systemic lupus erythematosus**

# Q/A

Cotton Wool Spots



- *Who is the classic lupus pt?*
  A woman of stage of life

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abetic patient.
*h?*

thy

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**Systemic lupus erythematosus**

# A

## Cotton Wool Spots

- *Who is the classic lupus pt?*
  A woman of childbearing age

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*When you hear the terms 'collagen-vascular disease' and 'cotton-wool spots' in the same sentence, one disease should immediately come to mind. What is it?*
**Systemic lupus erythematosus**

# Q

## Cotton Wool Spots

*Who is the classic lupus pt?*
A woman of childbearing age

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thy

*When you hear the terms 'collagen-vascular disease' and 'cotton-wool spots' in the same sentence, one disease should immediately come to mind. What is it?*
**Systemic lupus erythematosus**

# Q/A

## Cotton Wool Spots

*Who is the classic lupus pt?*
A woman of childbearing age

*Is there a racial predilection?*
Yes, [redacted] and [redacted] women are at greater risk than are [redacted] women

*(three different ethnicities)*

*When you hear the terms 'collagen-vascular disease' and 'cotton-wool spots' in the same sentence, one disease should immediately come to mind. What is it?*
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# A

## Cotton Wool Spots

*Who is the classic lupus pt?*
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Yes, black and Hispanic women are at greater risk than are white women

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# Q

## Cotton Wool Spots

- *Who is the classic lupus pt?*
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  Yes, black and Hispanic women are at greater risk than are white women

  *What proportion of lupus pts manifest retinal findings?*

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# A

## Cotton Wool Spots

*Who is the classic lupus pt?*
A woman of childbearing age

*Is there a racial predilection?*
Yes, black and Hispanic women are at greater risk than are white women

*What proportion of lupus pts manifest retinal findings?*
About 3-30%

*When you hear the terms 'collagen-vascular disease' and 'cotton-wool spots' in the same sentence, one disease should immediately come to mind. What is it?*
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# Q

## Cotton Wool Spots

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*What retinal findings may occur?*

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# A

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*What retinal findings may occur?*
Occlusive events: Asymptomatic cotton wool spots
if 'lucky,' an infarcted macula if not

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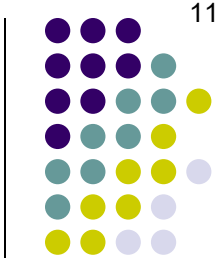
# Cotton Wool Spots



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About 3-30%

*What retinal findings may occur?*
Occlusive events: Asymptomatic **cotton wool spots**
if 'lucky,' an infarcted macula if not

*CWS are* **the** *classic manifestation of lupus retinopathy!*

*(No question—proceed when ready)*

*When you hear the terms 'collagen-vascular disease' and 'cotton-wool spots' in the same sentence, one disease should immediately come to mind. What is it?*
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# Cotton Wool Spots

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A woman of childbearing age

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Yes, black and Hispanic women are at greater risk than are white women

*What proportion of lupus pts manifest retinal findings?*
About **3-30%**

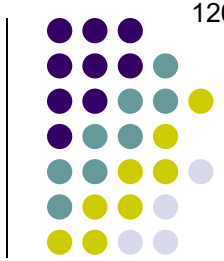
Note: This range represents a compromise between inconsistencies in the *BCSC* series:
--Rate of lupus retinopathy per the *Retina* book: 3-10%
--Rate per the *Uveitis* book: 3-29%
(I rounded to *30* to make it easier to remember)

*(No question—proceed when ready)*

*When you hear the terms 'collagen-vascular disease' and 'cotton-wool spots' in the same sentence, one disease should immediately come to mind. What is it?*
**Systemic lupus erythematosus**

# Q

## Cotton Wool Spots



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*Why is lupus-associated retinal arteritis an ominous finding?*

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**Systemic lupus erythematosus**

# A

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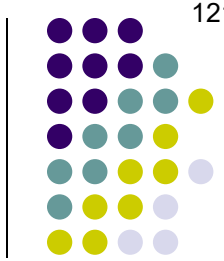

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It heralds CNS and/or renal involvement with the disease, and carries a high risk of mortality

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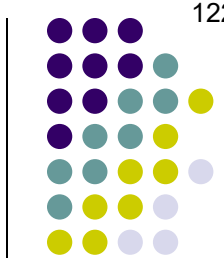

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*Given its dire systemic significance, how should lupus-associated retinal arteritis be managed?*

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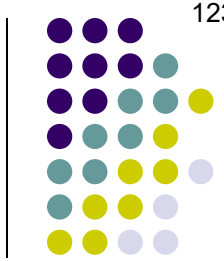

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*Given its dire systemic significance, how should lupus-associated retinal arteritis be managed?*
With the big dogs: Plasmapheresis + IV cyclophosphamide acutely

*When you hear the terms 'collagen-vascular disease' and 'cotton-wool spots' in the same sentence, one disease should immediately come to mind. What is it?*
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# Q

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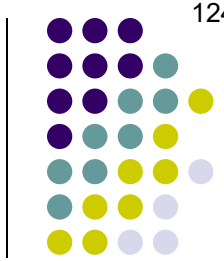

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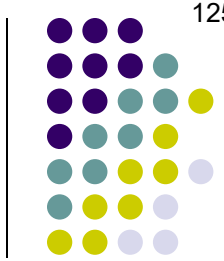

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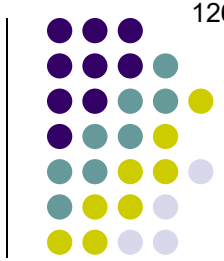

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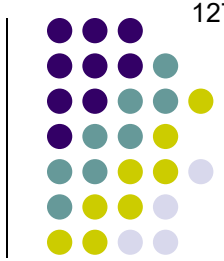

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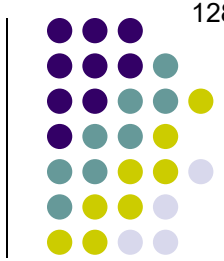

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*Can procainamide-induced SLE cause CWS?*

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# Q/A

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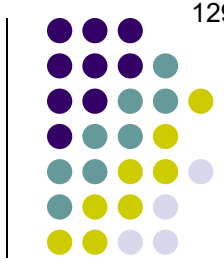

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Procainamide

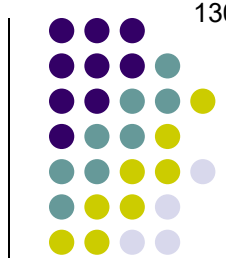
*Generally speaking, what sort of drug is it?*
An anti-arrhythmic

*Can procainamide-induced SLE cause CWS?*
You betcha. It also can cause
resulting in severe vision loss

two words

# A

## Cotton Wool Spots



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# Q

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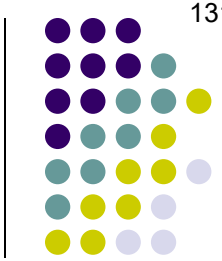

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  - Hgb electrophoresis: **Sickle-cell disease**
  - PMHx for head/neck CA: **Radiation retinopathy**
  - ESR, CRP, ANCA: **Vasculitis**
  - ANA, RF: **Collagen-vascular disease**
  - **CBC with diff**:
  -
  -
  -

# A

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# Q

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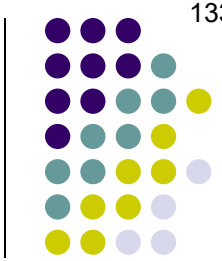

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  -
  -

# A

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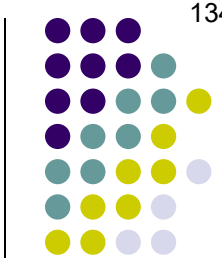

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  - **ELISA**: **HIV**
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# Q

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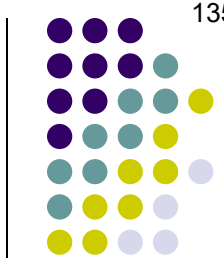

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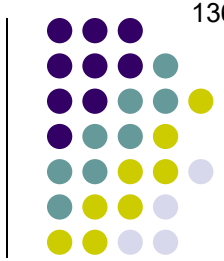

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  - **ELISA**: **HIV**

# Q

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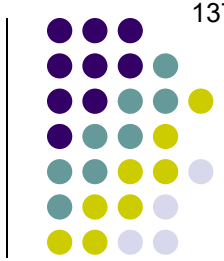

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    *What is the appearance of HIV retinopathy?*
  - **ELISA**: **HIV**

# A

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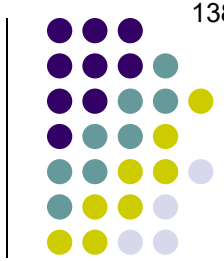

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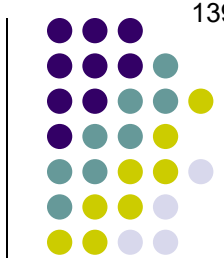

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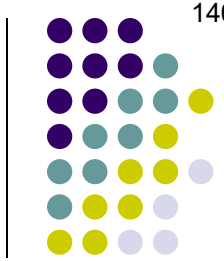

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    *What is the appearance of HIV retinopathy?*
    Cotton-wool spots in the posterior pole +/- MAs and DBH

    *What is the pathophysiology?*
    Arteriolar occlusion→focal ischemia→disruption of axoplasmic flow→CWS
  - **ELISA**: **HIV**

# Q

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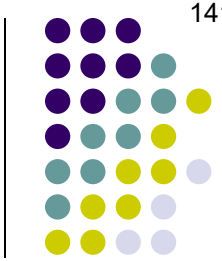

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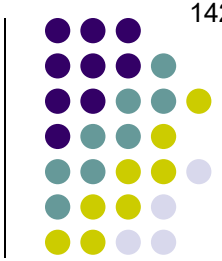
  - Carotid dopplers: **Carotid embolic source**
  - Hgb electrophoresis: **Sickle-cell disease**
  - PMHx for head/neck CA: **Radiation retinopathy**
  - ESR, CRP, ANCA: **Vasculitis**
  - ANA, RF: **Collagen-vascular disease**
  - CBC with diff: **Leukemia; severe anemia**
  - ELISA: **HIV**
  - **Hx of compressive chest trauma:**
  -

# A

## Cotton Wool Spots



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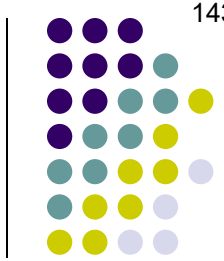
# Q

## Cotton Wool Spots



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  - ELISA: **HIV**
  - **Hx of compressive chest trauma: Purtscher's retinopathy**
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# A

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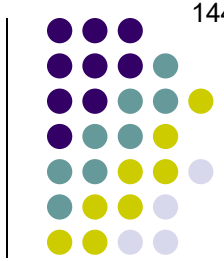

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*What is the classic DFE appearance in Purtscher's retinopathy?*
Multiple peripapillary CWS surrounding a relatively normal-appearing ONH (disc edema may be present). Additional areas of retinal whitening are usually present, as are small intraretinal hemorrhages.

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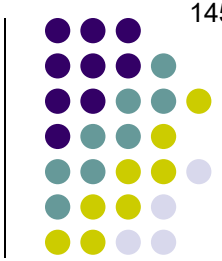

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# A

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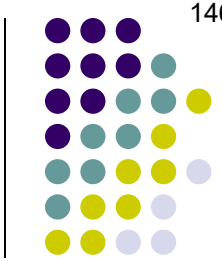

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# Q

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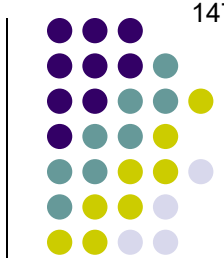

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*There are other 'classic clinical scenarios' that get mentioned in this context. What are they?*

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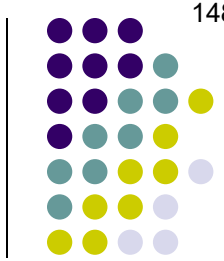

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# Q

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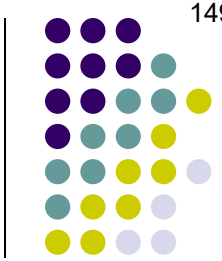

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*Wadda ya mean, 'these don't cause Purtscher's'? Everyone knows they do. What's the deal?*

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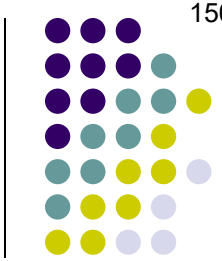

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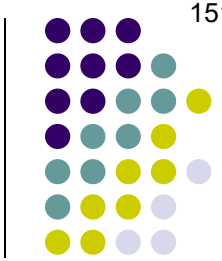

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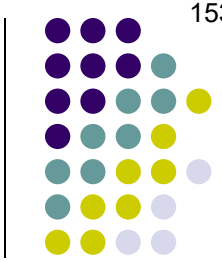

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# Q/A

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activation→ aggregation→
→

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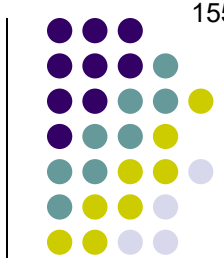

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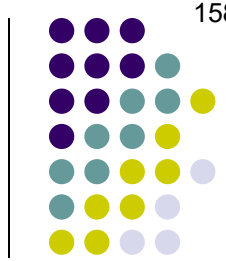

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*Aggregates of what sort of immune cells for the emboli?*

# A

## Cotton Wool Spots

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*What is the pathologic process underlying Purtscher's?*
activation→ granulocyte aggregation→ leukoembolization → occlusion of small retinal arterioles

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# Q

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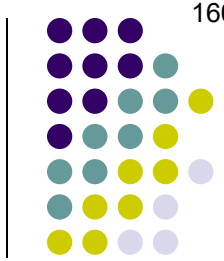

*And lastly: Activation of which aspect of the immune system begins the cascade?*

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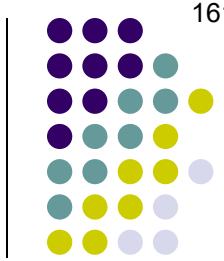
**Purtscher's retinopathy**

# A

## Cotton Wool Spots



*And lastly: Activation of which aspect of the immune system begins the cascade?*
**The complement system**

*What is the pathologic process underlying Purtscher's?*
Complement activation→ granulocyte aggregation→ leukoembolization → occlusion of small retinal arterioles

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*Aggregates of what sort of immune cells for the emboli?*
**Granulocytes**

- ELISA: **HIV**
- **Hx of compressive chest trauma:** **Purtscher's retinopathy**
-

Q

Cotton Wool Spots

*Circling back to 'additional areas of retinal whitening.' Isn't this the same thing as CWS?*

- *What is the classic CWS appearance in Purtscher's retinopathy?*
  Multiple peripapillary CWS surrounding a relatively normal-appearing ONH (disc edema may be present). Additional areas of **retinal whitening** are usually present, as are small intraretinal hemorrhages.

  *What is the classic clinical scenario?*
  An acute hx of compressive trauma to the chest (it can occur in the context of head trauma as well)

- ELISA: **HIV**
- **Hx of compressive chest trauma: Purtscher's retinopathy**
-

Q

Cotton Wool Spots

*Circling back to 'additional areas of retinal whitening.' Isn't this the same thing as CWS?*
No. This is referring to two words, polygonal-shaped areas of retinal whitening found in the peripapillary area and macula.

*What is the classic CWS appearance in Purtscher's retinopathy?*
Multiple peripapillary CWS surrounding a relatively normal-appearing ONH (disc edema may be present). Additional areas of **retinal whitening** are usually present, as are small intraretinal hemorrhages.

*What is the classic clinical scenario?*
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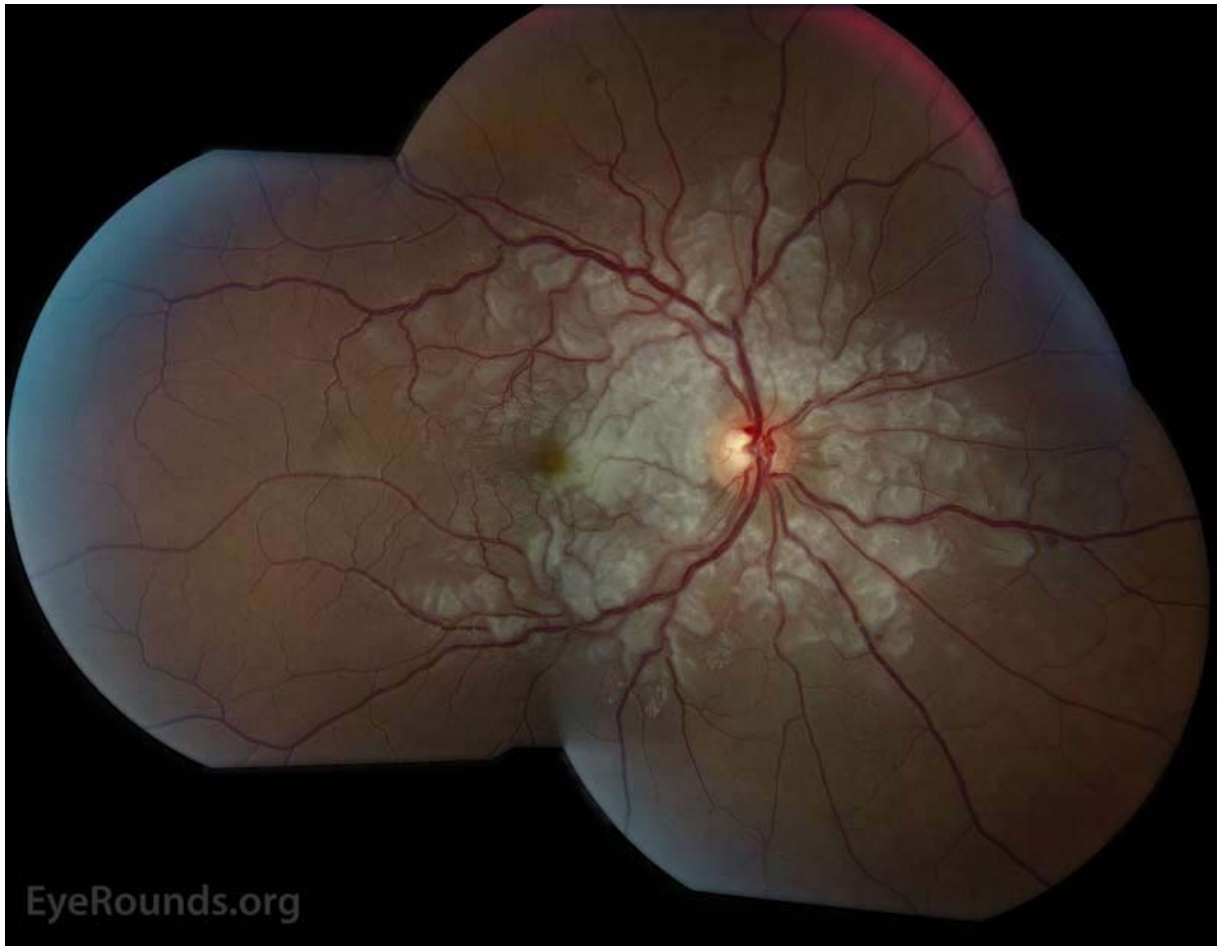
# Cotton Wool Spots




Purtscher flecken

Q

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*What is the mechanism by which Purtscher flecken form?*

*What is the classic OCT appearance in Purtscher's retinopathy?*
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*Occlusion…that's what causes CWS. Do Purtscher flecken and CWS differ in any meaningful way?*

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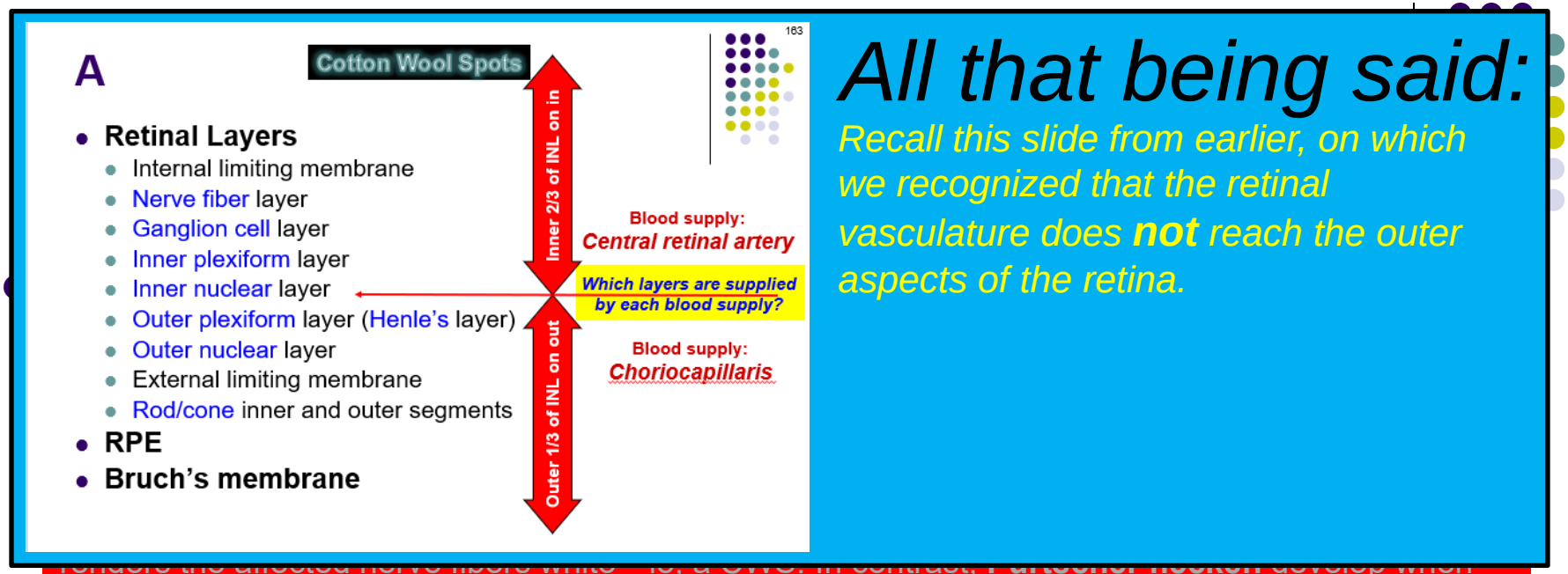


# *All that being said:*

*Recall this slide from earlier, on which we recognized that the retinal vasculature does **not** reach the outer aspects of the retina.*

occlusion occurs at the ***capillary*** level of retinal circulation. **These vessels are located deeper in the retina**, and thus their occlusion doesn't affect the retina nerve fiber layer--so no CWS.

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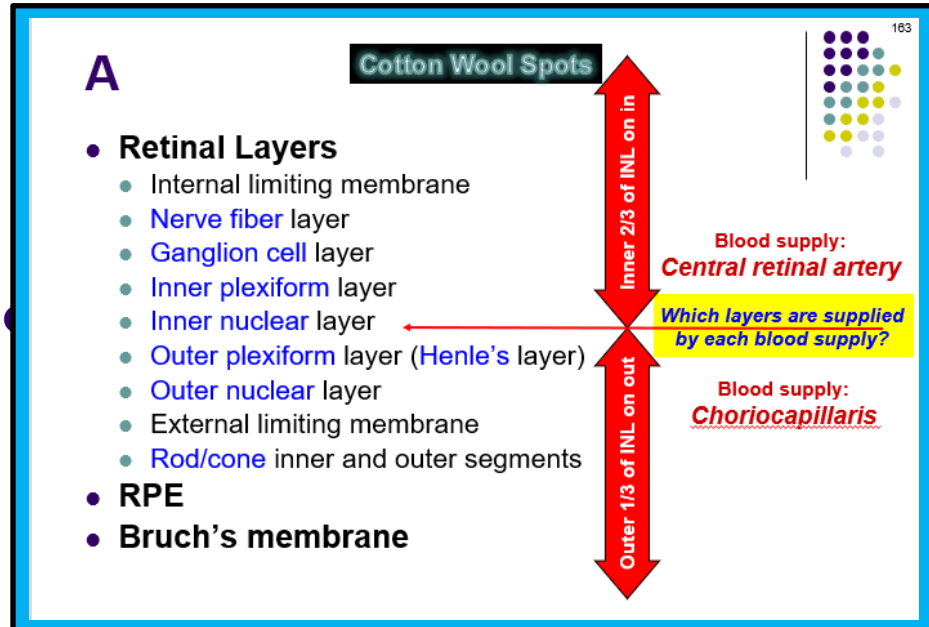
- **fjcghmcgh**




# *All that being said:*

*Recall this slide from earlier, on which we recognized that the retinal vasculature does **not** reach the outer aspects of the retina.* The point being, when we say Purtscher flecken are related to 'vessels located deeper in the retina,' bear in mind that *deeper* is a relative term, and that the involved retina is actually **centrally** positioned.

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**Cotton-wool spots**

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# Cotton-Wool Spots

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No. This is referring to ***Purtscher flecken*** , polygonal-shaped areas of retinal whitening found in the peripapillary area and macula.

*How can Purtscher flecken and CWS be differentiated at DFE?*
CWS have indistinct borders, and obscure vessels running through them.

- *What is the mechanism by which Purts*
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*Occlusion…that's what causes CWS. B*
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# A

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*How can Purtscher flecken and CWS be differentiated at DFE?*
CWS have indistinct borders, and obscure vessels running through them. In contrast, Purtscher flecken are more sharply demarcated and do **not** obscure adjacent vessels--in fact, a 'clear zone' appears between vessels and the flecken.

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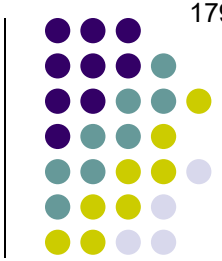
# Q

## Cotton Wool Spots



- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - Sphygnamometry: **HTN**
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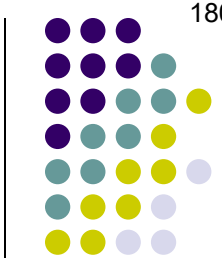
  - Carotid dopplers: **Carotid embolic source**
  - Hgb electrophoresis: **Sickle-cell disease**
  - PMHx for head/neck CA: **Radiation retinopathy**
  - ESR, CRP, ANCA: **Vasculitis**
  - ANA, RF: **Collagen-vascular disease**
  - CBC with diff: **Leukemia; severe anemia**
  - ELISA: **HIV**
  - Hx of compressive chest trauma: **Purtscher's retinopathy**
  - **Hx of viral hepatitis:**

# A

## Cotton Wool Spots



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# Q

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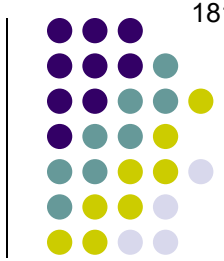

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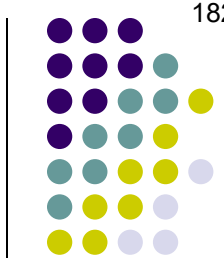
*Which interferon formulation are we talking about here?*

# A

## Cotton Wool Spots



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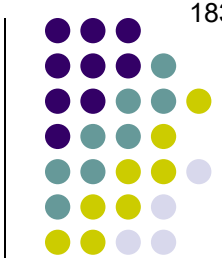
*Which interferon formulation are we talking about here?*
Interferon alfa-2a

# Q

## Cotton Wool Spots



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*Do CWS present in isolation?*

# A

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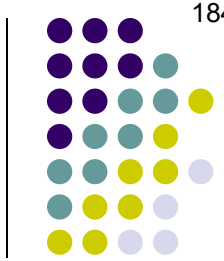

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*Do CWS present in isolation?*
No, they are often accompanied by retinal hemorrhages

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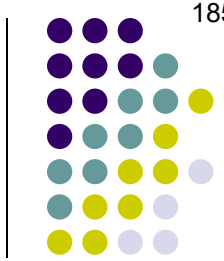

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*Is interferon retinopathy a common finding in interferon pts?*

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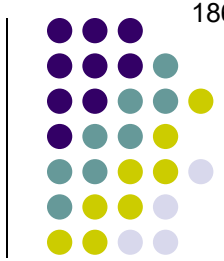

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Interferon alfa-2a

*Do CWS present in isolation?*
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*Is interferon retinopathy a common finding in interferon pts?*
Yes--estimates vary widely, but run no lower than about 20%

# Q

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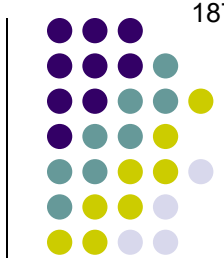

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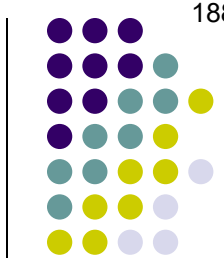
Yes--estimates vary widely, but run no lower than about 20%

*How is it managed?*

# A

## Cotton Wool Spots



- The following tests constitute a reasonable battery in working up a cotton-wool spot in a nondiabetic patient. *What disease is being ruled out with each?*
  - Sphygnamometry: **HTN**
  - Echocardiogram: **Cardiac embolic source**
  - Carotid dopp
  - Hgb electrop
  - PMHx for he
  - ESR, CRP, A
  - ANA, RF: **Co**
  - CBC with diff
  - ELISA: **HIV**
  - Hx of compressive chest trauma: **Purtscher's retinopathy**
  - **Hx of viral hepatitis: Interferon retinopathy**

*Which interferon formulation are we talking about here?*
Interferon alfa-2a

*Do CWS present in isolation?*
No, they are often accompanied by retinal hemorrhages

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*How is it managed?*
If mild, by lowering the dose; if severe, by stopping the drug

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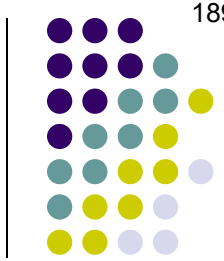

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***Remember: Work-up even one CWS in a non-DM patient!***

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No, they are often accompanied by retinal hemorrhages

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*How is it managed?*
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