Before you begin: This is a big topic, and big topics beget big slide-sets. There’s a natural break just past the halfway mark (slide 374ish); I placed a *break time!* slide at that point to mark it.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

What proportion of Americans 65+ have ARMD?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

What proportion of Americans 65+ have ARMD?

10%
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations

*What proportion of Americans 65+ have ARMD? 75+?*
10%
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

What proportion of Americans 65+ have ARMD? 75+?
10%. 25%!
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

*What proportion of Americans 65+ have ARMD? 75+?*
10%. 25%!

*Speaking of demographics: Is ARMD risk related to ethnicity?*
Yes, [highlighted text] have the highest risk and [highlighted text] the lowest.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

What proportion of Americans 65+ have ARMD? 75+?
10%. 25%!

Speaking of demographics: Is ARMD risk related to ethnicity?
Yes, whites have the highest risk and AAs the lowest.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

*What proportion of Americans 65+ have ARMD? 75+?*
10%. 25%!

*Speaking of demographics: Is ARMD risk related to ethnicity?*
Yes, whites have the highest risk and AAs the lowest; and fall in-between
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

What proportion of Americans 65+ have ARMD? 75+?
10%. 25%!

Speaking of demographics: Is ARMD risk related to ethnicity?
Yes, whites have the highest risk and AAs the lowest; Asians and Hispanics fall in-between.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

What are the other ARMD risk factors?

- Family history;
- Female;
- Light iris color;
- Age;
- Anglo (ie, white ethnicity);
- Smoking;
- Sun exposure;
- Hyperopia;
- Hypercholesterolemia;
- High CRP;

The mnemonic is…
Age-related macular degeneration is the #1 cause of blindness in adults age **50+** in resource-rich nations

**Age** is the strongest risk factor for ARMD

What are the other ARMD risk factors?

- Family history;  
- Female;  
- Light iris color;  
- Age;  
- Anglo (ie, white ethnicity);  
- Smoking;  
- Sun exposure;  
- Hyperopia;  
- Hypercholesterolemia;  
- High CRP

The mnemonic is…**FLASH**
• Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations
• **Age** is the strongest risk factor for ARMD

**What are the other ARMD risk factors?**
- **F**amily history; **F**emale
- **L**ight iris color
- **A**ge; **A**nglo (ie, white ethnicity)
- **S**moking; **S**un exposure
- **H**yperopia; **H**ypercholesterolemia; **H**igh CRP

The mnemonic is…**FLASH**

(two F’s)
(another A)
(two S’s)
(three H’s)
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations

**Age** is the strongest risk factor for ARMD

*What are the other ARMD risk factors?*

- Family history; **Female**
- Light iris color
- **Age; Anglo** (ie, white ethnicity)
- Smoking; **Sun** exposure
- Hyperopia; **Hypercholesterolemia; High CRP**

*Of the modifiable ones, which is most impactful?*
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. **Age** is the strongest risk factor for ARMD.

**What are the other ARMD risk factors?**
- **Family history; Female**
- **Light iris color**
- **Age; Anglo (ie, white ethnicity)**
- **Smoking; Sun exposure**
- **Hyperopia; Hypercholesterolemia; High CRP**

*Of the modifiable ones, which is most impactful?* Smoking
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

**Age** is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

Drusen are aggregates of material within the outer-retinal space.

What are drusen?

Drusen are made up of proteins and lipids—detritus shed by photoreceptors, mainly.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**

Aggregates of material within the outer-retinal space.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- Drusen are categorized by their **size**.
- Drusen are categorized by their **boundaries**.
- Drusen are categorized by the **retinal layer** in which they’re located.
Age-related macular degeneration is the #1 cause of blindness in adults age \( \geq 50 \) in resource-rich nations.

**What are drusen?**
Aggregates of material within the outer-retinal space

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly

**How are drusen categorized?**
There are several ways:

- Drusen are categorized by their **size**
- Drusen are categorized by the **retinal layer** in which they’re located
- Drusen are categorized by their **boundaries**
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- Drusen are categorized by their **size**:
  - ?
  - ?
  - ?
  - ?

- Drusen are categorized by the **retinal layer** in which they’re located.

- Drusen are categorized by their **boundaries**.
Age-related macular degeneration is the #1 cause of blindness in adults age **50+** in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of **drusen** in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

*Drusen are categorized by their size:*
  --Small
  --Intermediate
  --Large
  --Drusenoid PED

*Drusen are categorized by the retinal layer in which they’re located*

*Drusen are categorized by their boundaries*
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly.

How are drusen categorized?
There are several ways:

Drusen are categorized by their size:
- Small: <63 μm diameter
- Intermediate
- Large
- Drusenoid PED

Drusen are categorized by the retinal layer in which they're located.

Drusen are categorized by their boundaries.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly.

How are drusen categorized?
There are several ways:

Drusen are categorized by their size:
- Small: <63 μm diameter
- Intermediate
- Large
- Drusenoid PED

Drusen are categorized by the retinal layer in which they’re located.

Drusen are categorized by their boundaries.
Small drusen
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Drusen are categorized by their size:**
  - Small: <63 μm diameter
  - Intermediate:
  - Large
  - Drusenoid PED

- **Drusen are categorized by the retinal layer in which they're located**

- **Drusen are categorized by their boundaries**
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Drusen are categorized by their size:**
  - **Small:** <63 μm diameter
  - **Intermediate:** 63–124
  - **Large**
  - **Drusenoid PED**

- **Drusen are categorized by the retinal layer in which they’re located**

- **Drusen are categorized by their boundaries**
Intermediate drusen
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly.

How are drusen categorized?
There are several ways:

Drusen are categorized by their size:
--Small: <63 μm diameter
--Intermediate: 63–124
--Large: ≥125
--Drusenoid PED

Drusen are categorized by the retinal layer in which they’re located.

Drusen are categorized by their boundaries.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Drusen are categorized by their size:**
  - Small: <63 μm diameter
  - Intermediate: 63–124
  - Large: ≥125
  - Drusenoid PED

- **Drusen are categorized by the retinal layer in which they’re located**

- **Drusen are categorized by their boundaries**
Large drusen
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Size:**
  - Small: <63 μm diameter
  - Intermediate: 63–124
  - Large: ≥125

- **Boundaries**

- **Retinal layer** in which they’re located

*How the heck are you supposed to know the size of a druse in microns?*

Drusen are categorized by their **boundaries**.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

*Drusen are categorized by their size:*
- *Small:* <63 µm diameter
- *Intermediate:* 63–124
- *Large:* ≥125

*Drusen are categorized by the retinal layer in which*:

*How the heck are you supposed to know the size of a druse in microns?*
By comparing it to the size of a retinal vein as it crosses the border of the ONH (their diameter is about 124 µm there, and thus make a convenient reference).

*Drusen are categorized by their boundaries*
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly.

How are drusen categorized?
There are several ways:

- Drusen are categorized by their size:
  - Small: <63 µm diameter
  - Intermediate: 63–124
  - Large: ≥125

- Drusen are categorized by the retinal layer in which they occur.

om the heck are you supposed to know the size of a druse in microns?
By comparing it to the size of a retinal vein as it crosses the border of the ONH.

Drusen are categorized by their boundaries.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- Drusen are categorized by their **size**:
  - Small: <63 µm diameter
  - Intermediate: 63–124
  - Large: ≥125

- Drusen are categorized by the **retinal layer in which** they’re located.

**How the heck are you supposed to know the size of a druse in microns?**
By comparing it to the size of a retinal vein as it crosses the border of the ONH (their diameter is about there, and thus make a convenient reference).
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly.

How are drusen categorized?
There are several ways:

- Drusen are categorized by their size:
  - Small: <63 μm diameter
  - Intermediate: 63–124
  - Large: ≥125

- Drusen are categorized by the retinal layer in which they’re located.

- Drusen are categorized by their boundaries.

How the heck are you supposed to know the size of a druse in microns? By comparing it to the size of a retinal vein as it crosses the border of the ONH (their diameter is about 124 μm there, and thus make a convenient reference).
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Drusen are categorized by their size:**
  - Small: <63 μm diameter
  - Intermediate: 63–124
  - Large: ≥125
  - Drusenoid PED:

- **Drusen are categorized by the retinal layer in which they’re located**

- **Drusen are categorized by their boundaries**
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

*Drusen are categorized by their size:*
  --Small: <63 μm diameter
  --Intermediate: 63–124
  --Large: ≥125
  --Drusenoid PED: >350

*Drusen are categorized by the retinal layer in which they’re located*

*Drusen are categorized by their boundaries*
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly

How are drusen categorized?

There are several ways:

- **Small**: <63 μm diameter
- **Intermediate**: 63–124
- **Large**: ≥125
- **Drusenoid PED**: >350

In this context, what does PED stand for?

**Pigment epithelium detachment**

What does it mean to say the RPE is 'detached'?
It means the RPE is no longer in direct contact with its basement membrane, or that the RPE/basement membrane complex is separated from the underlying structure.

Why is it a big deal if the RPE is separated from its BM, or deeper structures?
Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris. Thus, a PED can lead to RPE dysfunction, death and atrophy. This in turn can lead to photoreceptor dysfunction, death and atrophy, which results in vision loss.

There are three basic forms of PED—what are the other two? Each is identifiable via the appearance of the sub-RPE space on OCT. What is this appearance for each?

- **Drusenoid**: Uniformly hyperreflective
- **Serous/hemorrhagic**: Solid with 'clefts'
- **Fibrovascular**: Sub-RPE space 'empty'
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly.

How are drusen categorized?

- **Small**: <63 μm diameter
- **Intermediate**: 63–124
- **Large**: ≥125
- **Drusenoid PED**: >350

Drusen are categorized by their size:
- **Small**: <63 μm diameter
- **Intermediate**: 63–124
- **Large**: ≥125
- **Drusenoid PED**: >350

In this context, what does PED stand for?
Pigment epithelium detachment.

Drusen are categorized by their boundaries:

Drusen are categorized by the retinal layer in which they’re located.

In this context, what does PED stand for?
Pigment epithelium detachment.

Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris. Thus, a PED can lead to RPE dysfunction, death and atrophy. This in turn can lead to photoreceptor dysfunction, death and atrophy, which results in vision loss.

There are three basic forms of PED—what are the other two? Each is identifiable via the appearance of the sub-RPE space on OCT. What is this appearance for each?

- **Drusenoid**: Uniformly hyperreflective
- **Serous/hemorrhagic**: Solid with ‘clefts’
- **Fibrovascular**: Sub-RPE space ‘empty’
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly

What are drusen categorized by?

In this context, what does PED stand for?
Pigment epithelium detachment

What does it mean to say the RPE is ‘detached’?
Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris. Thus, a PED can lead to RPE dysfunction, death and atrophy. This in turn can lead to photoreceptor dysfunction, death and atrophy, which results in vision loss.

There are three basic forms of PED—what are the other two? Each is identifiable via the appearance of the sub-RPE space on OCT. What is this appearance for each?

--Drusenoid: Uniformly hyperreflective
--Serous/hemorrhagic: Solid with ‘clefts’
--Fibrovascular: Sub-RPE space ‘empty’
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Size**:
  - Small: <63 μm diameter
  - Intermediate: 63–124
  - Large: ≥125
  - Drusenoid PED: >350

- **Boundaries**
- **Retinal layer** in which they’re located

**In this context, what does PED stand for?**
Pigment epithelium detachment.

**What does it mean to say the RPE is ‘detached’?**
It means the RPE is no longer in direct contact with its basement membrane, or that the RPE/basement membrane complex is separated from the underlying structure.

Drusen are categorized by:
- Small: <63 μm
d- Intermediate: 63–124
- Large: ≥125
- Drusenoid PED: >350
Drusen

Drusenoid-ish

Drusenoid PED

Coalescence of large soft drusen over time to form a drusenoid PED with increasing accumulation of vitelliform material (red arrow) and overlying pigmentary changes, as seen on color fundus photograph (CFP) and OCT.

OCT: Drusenoid PED
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Small**: <63 μm diameter
- **Intermediate**: 63–124
- **Large**: ≥125
- **Drusenoid PED**: >350

**In this context, what does PED stand for?**
Pigment epithelium detachment

**What does it mean to say the RPE is ‘detached’?**
It means the RPE is no longer in direct contact with its basement membrane, or that the RPE/basement membrane complex is separated from the underlying structure.

**Why is it a big deal if the RPE is separated from its BM, or deeper structures?**
Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris. Thus, a PED can lead to RPE dysfunction, death and atrophy. This in turn can lead to photoreceptor dysfunction, death and atrophy, which results in vision loss.

**There are three basic forms of PED—what are the other two?**
Each is identifiable via the appearance of the sub-RPE space on OCT. What is this appearance for each?

- **Drusenoid**: Uniformly hyperreflective
- **Serous/hemorrhagic**: Solid with ‘clefts’
- **Fibrovascular**: Sub-RPE space ‘empty’
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly.

What are drusen categorized by?

- **Size:**
  - Small: <63 μm diameter
  - Intermediate: 63–124
  - Large: ≥125
  - Drusenoid PED: >350

- **Boundaries**
- **Retinal layer** in which they’re located.

In this context, what does PED stand for?
Pigment epithelium detachment.

What does it mean to say the RPE is ‘detached’?
It means the RPE is no longer in direct contact with its basement membrane, or that the RPE/basement membrane complex is separated from the underlying structure.

Why is it a big deal if the RPE is separated from its BM, or deeper structures?
Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris. Thus, a PED can lead to RPE dysfunction, death and atrophy. This in turn can lead to photoreceptor dysfunction, death and atrophy, which results in vision loss.

There are three basic forms of PED—what are the other two? Each is identifiable via the appearance of the sub-RPE space on OCT. What is this appearance for each?
- **Drusenoid:** Uniformly hyperreflective
- **Serous/hemorrhagic:** Solid with ‘clefts’
- **Fibrovascular:** Sub-RPE space ‘empty’.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen? Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material? Proteins and lipids—detritus shed by photoreceptors, mainly.

How are drusen categorized? There are several ways:

- **Small**: <63 μm diameter
- **Intermediate**: 63–124
- **Large**: ≥125
- **Drusenoid PED**: >350

Drusen are categorized by the retinal layer in which they’re located.

In this context, what does PED stand for? Pigment epithelium detachment.

What does it mean to say the RPE is ‘detached’? It means the RPE is no longer in direct contact with its basement membrane, or that the RPE/basement membrane complex is separated from the underlying structure.

Why is it a big deal if the RPE is separated from its BM, or deeper structures? Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly.

Drusen are categorized by their size:
- Small: <63 μm diameter
- Intermediate: 63–124
- Large: ≥125
- Drusenoid PED: >350

Drusen are categorized by their boundaries.

Drusen are categorized by the retinal layer in which they’re located.

In this context, what does PED stand for?
Pigment epithelium detachment.

What does it mean to say the RPE is ‘detached’?
It means the RPE is no longer in direct contact with its basement membrane, or that the RPE/basement membrane complex is separated from the underlying structure.

Why is it a big deal if the RPE is separated from its BM, or deeper structures?
Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris. Thus, a PED can lead to RPE dysfunction, death and atrophy. This in turn can lead to photoreceptor dysfunction, death and atrophy, resulting in vision loss.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly.

Drusen are categorized by:
- Size:
  - Small: <63 μm diameter
  - Intermediate: 63–124
  - Large: ≥125
  - Drusenoid PED: >350

Drusen are categorized by their boundaries:
- Depending on the retinal layer in which they're located.

In this context, what does PED stand for?
Pigment epithelium detachment.

What does it mean to say the RPE is ‘detached’?
It means the RPE is no longer in direct contact with its basement membrane, or that the RPE/basement membrane complex is separated from the underlying structure.

Why is it a big deal if the RPE is separated from its BM, or deeper structures?
Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris. Thus, a PED can lead to RPE dysfunction, death, and atrophy. This in turn can lead to photoreceptor dysfunction, death, and atrophy, resulting in vision loss.

There are three basic forms of PED—what are the other two?
- Drusenoid
- ?
- ?
Age-related macular degeneration (ARMD) is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Size:**
  - Small: $< 63$ μm diameter
  - Intermediate: $63 - 124$
  - Large: $≥ 125$
  - Drusenoid PED: $> 350$

- **Boundaries:**
  - Drusen are categorized by the retinal layer in which they're located.

**In this context, what does PED stand for?**
Pigment epithelium detachment.

**What does it mean to say the RPE is ‘detached’?**
It means the RPE is no longer in direct contact with its basement membrane, or that the RPE/basement membrane complex is separated from the underlying structure.

**Why is it a big deal if the RPE is separated from its BM, or deeper structures?**
Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris. Thus, a PED can lead to RPE dysfunction, death and atrophy. This in turn can lead to photoreceptor dysfunction, death and atrophy, resulting in vision loss.

**There are three basic forms of PED—what are the other two?**

- Drusenoid
- Serous
- Fibrovascular
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. 

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly.

What does it mean to say the RPE is ‘detached’?
It means the RPE is no longer in direct contact with its basement membrane, or that the RPE/basement membrane complex is separated from the underlying structure.

Why is it a big deal if the RPE is separated from its BM, or deeper structures?
Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris. Thus, a PED can lead to RPE dysfunction, death and atrophy. This in turn can lead to photoreceptor dysfunction, death and atrophy, resulting in vision loss.

There are three basic forms of PED—what are the other two? Each is identifiable via the appearance of the sub-RPE space on OCT. What is this appearance for each?
--Drusenoid: ?
--Serous
--Fibrovascular
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly.

How are drusen categorized?
There are several ways:

- Small: <63 μm diameter
- Intermediate: 63–124
- Large: ≥125
- Drusenoid PED: >350

In this context, what does PED stand for?
Pigment epithelium detachment.

What does it mean to say the RPE is ‘detached’?
It means the RPE is no longer in direct contact with its basement membrane, or that the RPE/basement membrane complex is separated from the underlying structure.

Why is it a big deal if the RPE is separated from its BM, or deeper structures?
Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris. Thus, a PED can lead to RPE dysfunction, death and atrophy. This in turn can lead to photoreceptor dysfunction, death and atrophy, resulting in vision loss.

There are three basic forms of PED—what are the other two? Each is identifiable via the appearance of the sub-RPE space on OCT. What is this appearance for each?

- Drusenoid: Uniformly hyperreflective
- Serous
- Fibrovascular
Drusenoid PEDs have a uniform (aka ‘homogenous’), mildly hyper-reflective interior
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**In this context, what does PED stand for?**
Pigment epithelium detachment.

**What does it mean to say the RPE is ‘detached’?**
It means the RPE is no longer in direct contact with its basement membrane, or that the RPE/basement membrane complex is separated from the underlying structure.

**Why is it a big deal if the RPE is separated from its BM, or deeper structures?**
Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris. Thus, a PED can lead to RPE dysfunction, death and atrophy. This in turn can lead to photoreceptor dysfunction, death and atrophy, resulting in vision loss.

**There are three basic forms of PED—what are the other two?** Each is identifiable via the appearance of the sub-RPE space on OCT. What is this appearance for each?

--- Drusenoid: Uniformly hyperreflective
--- Serous: ?
--- Fibrovascular

**Drusen are categorized by their size:**
- Small: <63 µm diameter
- Intermediate: 63–124
- Large: ≥125
- Drusenoid PED: >350

**Drusen are categorized by their boundaries:**
- In this context, what does PED stand for? Pigment epithelium detachment.

**Drusen are categorized by the retinal layer in which they’re located:**
- Why is it a big deal if the RPE is separated from its BM, or deeper structures?
- In this context, what does PED stand for? Pigment epithelium detachment.
- What does it mean to say the RPE is ‘detached’?
- Why is it a big deal if the RPE is separated from its BM, or deeper structures?
- There are three basic forms of PED—what are the other two? Each is identifiable via the appearance of the sub-RPE space on OCT. What is this appearance for each?
- Drusenoid: Uniformly hyperreflective
- Serous: ?
- Fibrovascular
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

Drusen are categorized by their size:
- **Small:** <63 μm diameter
- **Intermediate:** 63–124
- **Large:** ≥125
- **Drusenoid PED:** >350

Drusen are categorized by their boundaries:

Drusen are categorized by the retinal layer in which they’re located.

In this context, what does PED stand for?
Pigment epithelium detachment.

**What does it mean to say the RPE is ‘detached’?**
It means the RPE is no longer in direct contact with its basement membrane, or that the RPE/basement membrane complex is separated from the underlying structure.

**Why is it a big deal if the RPE is separated from its BM, or deeper structures?**
Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris. Thus, a PED can lead to RPE dysfunction, death and atrophy. This in turn can lead to photoreceptor dysfunction, death and atrophy, resulting in vision loss.

**There are three basic forms of PED—what are the other two?** Each is identifiable via the appearance of the sub-RPE space on OCT. What is this appearance for each?
- **Drusenoid:** Uniformly hyperreflective
- **Serous:** Sub-RPE space ‘empty’
- **Fibrovascular**
Serous PEDs are seen on OCT as areas of smooth, sharply demarcated, dome-shaped RPE elevation, typically overlying a homogenously hyporeflective space.
Age-related macular degeneration is the #1 cause of blindness in adults age **50+** in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Small**: <63 μm diameter
- **Intermediate**: 63–124
- **Large**: ≥125
- **Drusenoid PED**: >350

**In this context, what does PED stand for?**
Pigment epithelium detachment.

**What does it mean to say the RPE is ‘detached’?**
It means the RPE is no longer in direct contact with its basement membrane, or that the RPE/basement membrane complex is separated from the underlying structure.

**Why is it a big deal if the RPE is separated from its BM, or deeper structures?**
Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris. Thus, a PED can lead to RPE dysfunction, death and atrophy. This in turn can lead to photoreceptor dysfunction, death and atrophy, resulting in vision loss.

**There are three basic forms of PED—what are the other two?**
Each is identifiable via the appearance of the sub-RPE space on OCT. What is this appearance for each?

- **Drusenoid**: Uniformly hyperreflective
- **Serous**: Sub-RPE space ‘empty’
- **Fibrovascular**: ?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**In this context, what does PED stand for?**
Pigment epithelium detachment.

**What does it mean to say the RPE is ‘detached’?**
It means the RPE is no longer in direct contact with its basement membrane, or that the RPE/basement membrane complex is separated from the underlying structure.

**Why is it a big deal if the RPE is separated from its BM, or deeper structures?**
Recall that the RPE plays an indispensable role in the health of the photoreceptors. Recall further that the RPE meets its metabolic needs via blood supplied by the underlying choriocapillaris. Thus, a PED can lead to RPE dysfunction, death and atrophy. This in turn can lead to photoreceptor dysfunction, death and atrophy, resulting in vision loss.

**There are three basic forms of PED—what are the other two?** Each is identifiable via the appearance of the sub-RPE space on OCT. What is this appearance for each?

--Drusenoid: Uniformly hyperreflective
--Serous: Sub-RPE space ‘empty’
--Fibrovascular: Solid with ‘clefts’
Fibrovascular PEDs appear to be filled with solid layers of material of medium reflectivity separated by hyporeflective clefts.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

- **Age** is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Drusen are categorized by their size:**
  - Small: <63 μm diameter
  - Intermediate: 63–124
  - Large: ≥125
  - Drusenoid PED: >350

- **Drusen are categorized by the retinal layer in which they’re located**

- **Drusen are categorized by their boundaries:**
  - ?
  - ?
  - ?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Drusen are categorized by their size:**
  - Small: <63 μm diameter
  - Intermediate: 63–124
  - Large: ≥125
  - Drusenoid PED: >350

- **Drusen are categorized by the retinal layer in which they’re located**

- **Drusen are categorized by their boundaries:**
  - Hard
  - Soft
  - Confluent
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly.

How are drusen categorized?
There are several ways:

Drusen are categorized by their **size**:
- Small: <63 μm diameter
- Intermediate: 63–124
- Large: ≥125
- Drusenoid PED: >350

Drusen are categorized by their **boundaries**:
- Hard: ?
- Soft
- Confluent

Which are described as being…

Drusen are categorized by the retinal layer in which they’re located.
Age-related macular degeneration (ARMD) is the #1 cause of blindness in adults age 50+ in resource-rich nations.

**Age** is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of **drusen** in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly

**How are drusen categorized?**
There are several ways:

**Drusen are categorized by their size:**
- **Small**: <63 μm diameter
- **Intermediate**: 63–124
- **Large**: ≥125
- **Drusenoid PED**: >350

**Drusen are categorized by the retinal layer in which they’re located**

**Drusen are categorized by their boundaries:**
- **Hard**: Discrete, well demarcated
- **Soft**
- **Confluent**

**Which are described as being…**
Hard drusen
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly

**How are drusen categorized?**
There are several ways:

*Drusen are categorized by their size:*
- Small: <63 μm diameter
- Intermediate: 63–124
- Large: ≥125
- Drusenoid PED: >350

*Drusen are categorized by their boundaries:*
- Hard: Discrete, well demarcated
- Soft: ?
- Confluent

*Drusen are categorized by the retinal layer in which they’re located*

Which are described as being...
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

*Drusen are categorized by their size:*
  --Small: <63 μm diameter
  --Intermediate: 63–124
  --Large: ≥125
  --Drusenoid PED: >350

*Drusen are categorized by their boundaries:*
  --Hard: Discrete, well demarcated
  --Soft: Amorphous, poorly demarcated
  --Confluent

*Drusen are categorized by the retinal layer in which they’re located*
Soft drusen
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Drusen are categorized by their size:**
  - Small: <63 μm diameter
  - Intermediate: 63–124
  - Large: ≥125
  - Drusenoid PED: >350

- **Drusen are categorized by their boundaries:**
  - Hard: Discrete, well demarcated
  - Soft: Amorphous, poorly demarcated
  - Confluent: ?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

*Drusen are categorized by their size:*
--- Small: <63 μm diameter
--- Intermediate: 63–124
--- Large: ≥125
--- Drusenoid PED: >350

*Drusen are categorized by their boundaries:*
--- Hard: Discrete, well demarcated
--- Soft: Amorphous, poorly demarcated
--- Confluent: Contiguous drusen without clear boundaries

--- Which are described as being...
A, Color fundus photograph shows soft, confluent, large drusen in a patient with ARMD. B, Corresponding SD-OCT of the soft drusen. C, Autofluorescence image of an eye with areas of confluent drusen.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Drusen are categorized by their size:**
  - **Small:** <63 μm diameter
  - **Intermediate:** 63–124
  - **Large:** ≥125
  - **Drusenoid PED:** >350

- **Drusen are categorized by the retinal layer in which they’re located**

- **Drusen are categorized by their boundaries:**
  - **Hard:** Discrete, well demarcated
  - **Soft:** Amorphous, poorly demarcated
  - **Confluent:** Contiguous drusen without clear boundaries

Which type(s) carry a greater risk of dz progression?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

**Drusen are categorized by their size:**
- **Small:** <63 μm diameter
- **Intermediate:** 63–124
- **Large:** ≥125
- **Drusenoid PED:** >350

**Drusen are categorized by the retinal layer in which they’re located**

**Drusen are categorized by their boundaries:**
- **Hard:** Discrete, well demarcated
- **Soft:** Amorphous, poorly demarcated
- **Confluent:** Contiguous drusen without clear boundaries

Which type(s) carry a greater risk of dz progression?
Soft for sure, and probably confluent as well.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

**Drusen are categorized by their size:**
- **Small:** <63 μm diameter
- **Intermediate:** 63–124
- **Large:** ≥125
- **Drusenoid PED:** >350

**Drusen are categorized by the retinal layer in which they're located:**
- --?
- --?
- --?

**Drusen are categorized by their boundaries:**
- **Hard:** Discrete, well demarcated
- **Soft:** Amorphous, poorly demarcated
- **Confluent:** Contiguous drusen without clear boundaries
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen? Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material? Proteins and lipids—detritus shed by photoreceptors, mainly.

How are drusen categorized? There are several ways:

Drusen are categorized by their size:
- Small: <63 μm diameter
- Intermediate: 63–124
- Large: ≥125
- Drusenoid PED: >350

Drusen are categorized by the retinal layer in which they're located:
- Basal
- Reticular

Drusen are categorized by their boundaries:
- Hard: Discrete, well demarcated
- Soft: Amorphous, poorly demarcated
- Confluent: Contiguous drusen without clear boundaries
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly

**How are drusen categorized?**
There are several ways:

- **Drusen are categorized by their size:**
  - Small: <63 μm diameter
  - Intermediate: 63–124
  - Large: ≥125
  - Drusenoid PED: >350

- **Drusen are categorized by the retinal layer in which they’re located:**
  - Basal laminar
  - Basal linear
  - Reticular pseudodrusen

- **Drusen are categorized by their boundaries:**
  - Hard: Discrete, well demarcated
  - Soft: Amorphous, poorly demarcated
  - Confluent: Contiguous drusen without clear boundaries
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

**Age** is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of **drusen** in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Drusen are categorized by their retinal layer in which they're located:**
  - Basal laminar: ?
  - Basal linear: ?
  - Reticular pseudodrusen: ?

- **Drusen are categorized by their size:**
  - Small: <63 μm diameter
  - Intermediate: 63–124
  - Large: ≥125
  - Drusenoid PED: >350

- **Drusen are categorized by their boundaries:**
  - Hard: Discrete, well demarcated
  - Soft: Amorphous, poorly demarcated
  - Confluent: Contiguous drusen without clear boundaries

Before identifying the location for each drusen, let’s review the anatomy of the outer retina.
But first:

What are the five layers of Bruch’s membrane?

1) (Start here)
2)
3)
4)
5)

Bruch’s membrane

Innermost

Outermost
But first:

What are the five layers of Bruch’s membrane?

1) two words of RPE

Innermost

Outermost
But first:

What are the five layers of Bruch’s membrane?

(Nota: This line represents the RPE basement membrane)

1) **Basement membrane** of RPE

Bruch’s membrane

- 1)
- 2)
- 3)
- 4)
- 5)

Innermost

Outermost
But first:

What are the five layers of Bruch’s membrane?

1) Baseline membrane of RPE
2) (next)
But first:

What are the five layers of Bruch’s membrane?

1) Basement membrane of RPE
2) Inner collagenous layer
3) One word
4) Innermost
5) Outermost
But first:

What are the five layers of Bruch’s membrane?

1) **Basement membrane** of RPE
2) Inner **collagenous** layer
3) (etc)
4)
5)
**But first:**

What are the five layers of Bruch’s membrane?

1) **Basement membrane** of RPE
2) **Inner collagenous** layer
3) **diff one word** layer
4) 
5) 

*Innermost*

*Outermost*
But first:

What are the five layers of Bruch’s membrane?

1) Basement membrane of RPE
2) Inner collagenous layer
3) Elastic layer
4) 
5) 

Innermost

Outermost
But first:

What are the five layers of Bruch’s membrane?

1) **Basement membrane** of RPE
2) Inner **collagenous** layer
3) **Elastic** layer
4) Outer **layer**
5) **one familiar word**

**Innermost**

**Outermost**
But first:

What are the five layers of Bruch's membrane?

1) **Basement membrane** of RPE
2) Inner **collagenous** layer
3) **Elastic** layer
4) Outer **collagenous** layer
5) 

Innermost → Bruch's membrane → Outermost
But first:

What are the five layers of Bruch’s membrane?

1) Basement membrane of RPE
2) Inner collagenous layer
3) Elastic layer
4) Outer collagenous layer
5) two familiar words of choriocapillaris
But first:

What are the five layers of Bruch’s membrane?

1) **Basement membrane** of RPE
2) Inner **collagenous** layer
3) **Elastic** layer
4) Outer **collagenous** layer
5) **Basement membrane** of choriocapillaris

(Note: This line represents the c’capillaris basement membrane)
What are the five layers of Bruch’s membrane?

1) Basement membrane of RPE
2) Inner collagenous layer
3) Elastic layer
4) Outer collagenous layer
5) Basement membrane of choriocapillaris

But first:

What (non-Bruch’s) structure goes here?

0) ?

ARMD
What are the five layers of Bruch’s membrane?

0) RPE cells
1) Basement membrane of RPE
2) Inner collagenous layer
3) Elastic layer
4) Outer collagenous layer
5) Basement membrane of choriocapillaris

What (non-Bruch’s) structure goes here? The RPE cells themselves
What are the five layers of Bruch’s membrane?

0) RPE cells

1) Basement membrane of RPE
2) Inner collagenous layer
3) Elastic layer
4) Outer collagenous layer
5) Basement membrane of choriocapillaris

So, the basal plasma membranes of the RPE cells…
What are the five layers of Bruch’s membrane?

1) **Basement membrane of RPE**
2) **Inner collagenous layer**
3) **Elastic layer**
4) **Outer collagenous layer**
5) **Basement membrane of choriocapillaris**

But first:

0) **RPE cells**

So, the basal plasma membranes of the RPE cells... *sit directly on their BM* (as you would expect)
What are the five layers of Bruch’s membrane?

0) **RPE cells**

1) **Basement membrane of RPE**

2) **Inner collagenous layer**

3) **Elastic layer**

4) **Outer collagenous layer**

5) **Basement membrane of choriocapillaris**

**Foreshadowing alert:** Another name for the basal plasma membrane of a cell is ‘basal lamina’.
What are the five layers of Bruch's membrane?

1. Basement membrane of RPE
2. Inner collagenous layer
3. Elastic layer
4. Outer collagenous layer
5. Basement membrane of choriocapillaris

But first:

- RPE cells
- RPE cells

What (non-RPE) structures go here?
What are the five layers of Bruch’s membrane?

- Layer 1: Basement membrane of RPE
- Layer 2: Inner collagenous layer
- Layer 3: Elastic layer
- Layer 4: Outer collagenous layer
- Layer 5: Basement membrane of choriocapillaris

But first:

- Layer -1: Photoreceptor outer segments
- Layer 0: RPE cells

What (non-RPE) structures go here?
The photoreceptor outer segments
What are the five layers of Bruch’s membrane?

1) Basement membrane of RPE
2) Inner collagenous layer
3) Elastic layer
4) Outer collagenous layer
5) Basement membrane of choriocapillaris

But first:

What cell type is this?

ARMD
What are the five layers of Bruch's membrane?

- 1) Basement membrane of RPE
- 2) Inner collagenous layer
- 3) Elastic layer
- 4) Outer collagenous layer
- 5) Basement membrane of choriocapillaris

What cell type is this?

0) RPE cells

-1) PR outer segs

-2) Bipolar cells

But first:

1) PR outer segs

0) RPE cells

1) Basement membrane of RPE

2) Inner collagenous layer

3) Elastic layer

4) Outer collagenous layer

5) Basement membrane of choriocapillaris

ARMD
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen?
Aggregates of material within the outer-retinal space

What sorts of substances constitute the material?
Proteins and lipids—detritus shed by photoreceptors, mainly

How are drusen categorized?
There are several ways:

Drusen are categorized by their size:
--Small: <63 μm diameter
--Intermediate: 63–124
--Large: ≥125
--Drusenoid PED: >350

Drusen are categorized by the retinal layer in which they're located:
--Basal laminar?
--Basal linear
--Reticular pseudodrusen

Drusen are categorized by their boundaries:
--Hard: Discrete, well demarcated
--Soft: Amorphous, poorly demarcated
--Confluent: Contiguous drusen without clear boundaries
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. 

**What are drusen?**
Aggregates of material within the outer-retinal space

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly

**How are drusen categorized?**
There are several ways:

**Drusen are categorized by their size:**
- **Small**: <63 μm diameter
- **Intermediate**: 63–124
- **Large**: ≥125
- **Drusenoid PED**: >350

**Drusen are categorized by the retinal layer in which they're located:**
- **Basal laminar**: Between RPE cells and their BM
- **Basal linear**
- **Reticular pseudodrusen**

**Drusen are categorized by their boundaries:**
- **Hard**: Discrete, well demarcated
- **Soft**: Amorphous, poorly demarcated
- **Confluent**: Contiguous drusen without clear boundaries
What are the five layers of Bruch’s membrane?

1) Basement membrane of RPE
2) Inner collagenous layer
3) Elastic layer
4) Outer collagenous layer
5) Basement membrane of choriocapillaris

But first:

-2) Bipolar cells
-1) PR outer segs
0) RPE cells RPE cells

basal laminar drusen
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Drusen are categorized by their size:**
  - Small: <63 μm diameter
  - Intermediate: 63–124
  - Large: ≥125
  - Drusenoid PED: >350

- **Drusen are categorized by the retinal layer in which they’re located:**
  - Basal laminar: Between RPE cells and their BM
  - Basal linear: ?
  - Reticular pseudodrusen

- **Drusen are categorized by their boundaries:**
  - Hard: Discrete, well demarcated
  - Soft: Amorphous, poorly demarcated
  - Confluent: Contiguous drusen without clear boundaries
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

What are drusen? Aggregates of material within the outer-retinal space.

What sorts of substances constitute the material? Proteins and lipids—detritus shed by photoreceptors, mainly.

How are drusen categorized? There are several ways:

**Drusen are categorized by their size:**
- Small: <63 μm diameter
- Intermediate: 63–124
- Large: ≥125
- Drusenoid PED: >350

**Drusen are categorized by the retinal layer in which they’re located:**
- Basal laminar: Between RPE cells and their BM
- Basal linear: Within inner aspect of Bruchs membrane
- Reticular pseudodrusen

**Drusen are categorized by their boundaries:**
- Hard: Discrete, well demarcated
- Soft: Amorphous, poorly demarcated
- Confluent: Contiguous drusen without clear boundaries
What are the five layers of Bruch’s membrane?

1. Basement membrane of RPE
2. Inner collagenous layer
3. Elastic layer
4. Outer collagenous layer
5. Basement membrane of choriocapillaris

But first:

0) RPE cells

-1) PR outer segs

-2) Bipolar cells

Bipolar cells are located just inside the PR outer segments, which are external to the RPE cells.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

**Drusen are categorized by their size:**
- **Small:** <63 μm diameter
- **Intermediate:** 63–124
- **Large:** ≥125
- **Drusenoid PED:** >350

**Drusen are categorized by the retinal layer in which they’re located:**
- **Basal laminar:** Between RPE cells and their BM
- **Basal linear:** Within inner aspect of Bruch’s membrane
- **Reticular pseudodrusen:** ?

**Drusen are categorized by their boundaries:**
- **Hard:** Discrete, well demarcated
- **Soft:** Amorphous, poorly demarcated
- **Confluent:** Contiguous drusen without clear boundaries
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

- **Drusen are categorized by their size:**
  - **Small:** <63 μm diameter
  - **Intermediate:** 63–124 μm
  - **Large:** ≥125 μm
  - **Drusenoid PED:** >350 μm

- **Drusen are categorized by the retinal layer in which they’re located:**
  - **Basal laminar:** Between RPE cells and their BM
  - **Basal linear:** Within inner aspect of Bruchs membrane
  - **Reticular pseudodrusen:** Between the apical surface of the RPE cells and the overlying photoreceptors

- **Drusen are categorized by their boundaries:**
  - **Hard:** Discrete, well demarcated
  - **Soft:** Amorphous, poorly demarcated
  - **Confluent:** Contiguous drusen without clear boundaries
What are the five layers of Bruch’s membrane?

1) Basement membrane of RPE
2) Inner collagenous layer
3) Elastic layer
4) Outer collagenous layer
5) Basement membrane of choriocapillaris

But first:

0) RPE cells
-1) PR outer segs
-2) Bipolar cells

Reticular pseudodrusen

ARMD
Reticular pseudodrusen: Classic distribution in the superior macula
Reticular pseudodrusen can be seen as multiple areas of granular hyperreflectivity between the RPE and photoreceptors.
Age-related macular degeneration (ARMD) is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

**What are drusen?**
Aggregates of material within the outer-retinal space.

**What sorts of substances constitute the material?**
Proteins and lipids—detritus shed by photoreceptors, mainly.

**How are drusen categorized?**
There are several ways:

**Drusen are categorized by their size:**
- **Small:** <63 μm diameter
- **Intermediate:** 63–124 μm
- **Large:** ≥125 μm
- **Drusenoid PED:** >350 μm

**Drusen are categorized by the retinal layer in which they're located:**
- **Basal laminar:** Between RPE cells and their BM
- **Basal linear:** Within inner aspect of Bruch's membrane
- **Reticular pseudodrusen:** Between the apical surface of the RPE cells and the overlying photoreceptors

**Circling back to drusenoid PEDs for a moment…**

**Drusen are categorized by their boundaries:**
- **Hard:** Discrete, well demarcated
- **Soft:** Amorphous, poorly demarcated
- **Confluent:** Contiguous drusen without clear boundaries
But first: What are the five layers of Bruch's membrane?

0) RPE cells

1) Basement membrane of RPE

2) Inner collagenous layer

3) Elastic layer

4) Outer collagenous layer

5) Basement membrane of choriocapillaris

So now we can see how basal laminar drusen, if extensive enough, can cause a drusenoid PED.

-2) Bipolar cells

-1) PR outer segs
Likewise, we can see that extensive basal linear drusen can also producing a drusenoid PED.
-2) **Bipolar cells**

**But first:**

-1) **PR outer segs**

0) **RPE cells RPE cells**

However, *reticular pseudodrusen* do not separate the RPE from Bruch’s, so they cannot cause a PED

1) **Basement membrane** of RPE

2) **Inner collagenous layer**

3) **Elastic layer**

4) **Outer collagenous layer**

5) **Basement membrane** of choriocapillaris

**RPE cells RPE cells**
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations

**Age** is the strongest risk factor for ARMD

The clinical hallmark of ARMD is the presence of **drusen** in the macula

There are two types: [insert type 1] and [insert type 2]
Age-related macular degeneration (ARMD) is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: Nonexudative and exudative.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative**

*By what two other names are each condition commonly known?*

**Nonexudative:** ?

Exudative
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative**.

*By what two other names are each condition commonly known?*

**Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD

**Exudative**: ?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

By what two other names are each condition commonly known?

- Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
- Exudative: Neovascular ARMD; ‘wet’ ARMD
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?
--?
--?
--?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations

Age is the strongest risk factor for ARMD

The clinical hallmark of ARMD is the presence of drusen in the macula

There are two types: **Nonexudative** and **exudative**

By what two other names are each condition commonly known?

- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?

-- Drusen
-- RPE changes
-- Geographic atrophy
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative ARMD.

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD

Exudative: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?

- Drusen
- RPE changes

*We have already discussed drusen, and will look at RPE change in detail a little later in the set.*

--Geographic atrophy
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. 

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative ARMD.

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?
--Drusen
--RPE changes
--Geographic atrophy

What is geographic atrophy (GA)?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?
--Drusen
--RPE changes
--Geographic atrophy

What is geographic atrophy (GA)?
It is one of forms of advanced ARMD.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative**.

By what two other names are each condition commonly known?

**Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
**Exudative**: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?
--Drusen
--RPE changes
**Geographic atrophy**

What is geographic atrophy (GA)?
It is one of two forms of advanced ARMD.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: Nonexudative and exudative.

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?
--Drusen
--RPE changes
--Geographic atrophy

What is geographic atrophy (GA)?
It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.
Geographic atrophy (GA)
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and Exudative ARMD.

By what two other names are each condition commonly known?

*Nonexudative*: Nonneovascular ARMD; ‘dry’ ARMD

*Exudative*: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?

--Drusen
--RPE changes
--Geographic atrophy

What is geographic atrophy (GA)?

It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

*How large must the area of atrophy be to qualify as GA?*

By definition, it must have a diameter of at least 175 µm.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. **Age** is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: **Nonexudative** and **exudative**

By what two other names are each condition commonly known?

**Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
**Exudative**: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?

--Drusen
--RPE changes
--**Geographic atrophy**

What is geographic atrophy (GA)?
It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

How large must the area of atrophy be to qualify as GA?
By definition, it must have a diameter of at least 175 µm.
Age-related macular degeneration (ARMD) is the #1 cause of blindness in adults age 50+ in resource-rich nations.

- **Age** is the strongest risk factor for ARMD.
- The clinical hallmark of ARMD is the presence of drusen in the macula.
- There are two types: **Nonexudative** and **exudative** ARMD.

**By what two other names are each condition commonly known?**

- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

**What are the three hallmark findings in nonexudative ARMD?**

- Drusen
- RPE changes
- **Geographic atrophy**

**What is geographic atrophy (GA)?**

It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

**What is its typical pattern of progression?**
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative** ARMD.

By what two other names are each condition commonly known?

- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?
- Drusen
- RPE changes
- **Geographic atrophy**

What is geographic atrophy (GA)?

It is one of the two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

What is its typical pattern of progression?

It starts in the perifoveal region, expanding over time to eventually involve the foveal center.
Progression of GA over a 2.5 year period. Note the characteristic perifoveal→foveal center pattern.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: Nonexudative and exudative ARMD.

By what two other names are each condition commonly known?

**Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD

**Exudative**: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?

--Drusen

--RPE changes

--Geographic atrophy

What is geographic atrophy (GA)?

It is one of the two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

What does GA look like on...

**FA?**

--A well-circumscribed area of hyperfluorescence

**Autofluorescence?**

--Dense hypoautofluorescence with a ring of hypofluorescence

**OCT?**

--RPE loss; thinning/loss of the outer retinal layers
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations

Age is the strongest risk factor for ARMD

The clinical hallmark of ARMD is the presence of drusen in the macula

There are two types: **Nonexudative** and **exudative**

**By what two other names are each condition commonly known?**

- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

**What are the three hallmark findings in nonexudative ARMD?**

- Drusen
- RPE changes
- **Geographic atrophy**

**What is geographic atrophy (GA)?**

It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

**What does GA look like on…**

**FA?** A well-circumscribed area of hypo- vs hyperfluorescence

**Autofluorescence?** Dense hypoautofluorescence with a ring of hypofluorescence

**OCT?** RPE loss; thinning/loss of the outer retinal layers
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative** ARMD.

By what two other names are each condition commonly known?

**Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD

**Exudative**: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?

-- Drusen
-- RPE changes
-- **Geographic atrophy**

What is geographic atrophy (GA)?

It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

What does GA look like on...

**FA?** A well-circumscribed area of hyperfluorescence

**Autofluorescence?** Dense hypoautofluorescence with a ring of hypofluorescence

**OCT?** RPE loss; thinning/loss of the outer retinal layers

Eventually involves the foveal center.
Geographic atrophy in ARMD: FA
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

Nonexudative:
- Nonneovascular ARMD; 'dry' ARMD

Exudative:
- Neovascular ARMD; 'wet' ARMD

What are the three hallmark findings in non-exudative ARMD?
- Drusen
- RPE changes
- Geographic atrophy

What is geographic atrophy (GA)?
It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

What is its typical pattern of progression?
It starts in the perifoveal region, expanding over time to eventually involve the foveal center.

Speaking generally: What are the four causes of hyperfluorescence on FA?
- Drusen
- RPE changes
- Geographic atrophy
- Window defect

What does GA look like on FA?
A well-circumscribed area of hyperfluorescence

What does GA look like on Autofluorescence?
Dense hypoautofluorescence with a ring of hypofluorescence

What does GA look like on OCT?
RPE loss; thinning/loss of the outer retinal layers
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

Nonexudative ARMD: Nonneovascular ARMD; 'dry' ARMD

Exudative ARMD: Neovascular ARMD; 'wet' ARMD

What are the three hallmark findings in nonexudative ARMD?
--Drusen
--RPE changes
--Geographic atrophy

Geographic atrophy (GA) is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

What is its typical pattern of progression?
It starts in the perifoveal region, expanding over time to eventually involve the foveal center.

Speaking generally: What are the four causes of hyperfluorescence on FA?
--Pooling
--Leaking
--Staining
--Window defect
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula.

By what two other names are each condition commonly known?

- Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
- Exudative: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?

- Drusen
- RPE changes
- Geographic atrophy

What is geographic atrophy (GA)?

It is one of ‘two’ forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

What is its typical pattern of progression?

It starts in the perifoveal region, expanding over time to eventually involve the foveal center.

Speaking generally: What are the four causes of hyperfluorescence on FA?

- Pooling?
- Leaking?
- Staining?
- Window defect?

Which one of these accounts for the hyperfluorescence of GA?

- Geographic atrophy

What does GA look like on…

**FA?** A well-circumscribed area of hyperfluorescence
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula.

Nonexudative ARMD: Nonneovascular ARMD; 'dry' ARMD

Exudative ARMD: Neovascular ARMD; 'wet' ARMD

What are the three hallmark findings in nonexudative ARMD?
- Drusen
- RPE changes
- Geographic atrophy

What does geographic atrophy (GA) look like on...
- FA? A well-circumscribed area of hyperfluorescence
- Autofluorescence? Dense hypoautofluorescence with a ring of hypofluorescence
- OCT? RPE loss; thinning/loss of the outer retinal layers

Speaking generally: What are the four causes of hyperfluorescence on FA?
- Pooling
- Leaking
- Staining
- Window defect

Which one of these accounts for the hyperfluorescence of GA?
- Window defect

Geographic atrophy (GA) is one of 'two' forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

Eventually, involves the foveal center...
Geographic atrophy. A, Fundus photo. B, On fluorescein angiography, there is a “window defect” during the early frames with transmission of choroidal fluorescence. C, Note the absence of leakage in later frames.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: **Nonexudative** and **exudative** ARMD.

*By what two other names are each condition commonly known?*

**Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD

**Exudative**: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?

--- Drusen

--- RPE changes

--- Geographic atrophy

What is geographic atrophy (GA)?

It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

What does GA look like on…

**FA?** A well-circumscribed area of hyperfluorescence

**Autofluorescence?**

--- Dense hypoautofluorescence with a ring of hypofluorescence

**OCT?**

--- RPE loss; thinning/loss of the outer retinal layers

--- Eventually involves the inner retina
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative ARMD.

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?

-- Drusen
-- RPE changes
-- Geographic atrophy

What is geographic atrophy (GA)?
It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

What does GA look like on...
FA? A well-circumscribed area of hyperfluorescence
Autofluorescence? Dense hypo- vs hyperfluorescence with a ring of hypo- vs hyperfluorescence

Eventually involves the foveal center.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?

--Drusen
--RPE changes
--Geographic atrophy

What is geographic atrophy (GA)?

It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

What does GA look like on…

FA? A well-circumscribed area of hyperfluorescence

Autofluorescence? Dense hypofluorescence with a ring of hyperautofluorescence

Eventually involves the foveal center.
FAF: Normal retina for comparison

FAF: GA

ARMD
Geographic atrophy (GA). Top, Color fundus photographs of right (left panel) and left (right panel) eyes, demonstrating advanced GA. Bottom, Corresponding autofluorescent images of GA in the same patient with atrophic AMD. The areas of RPE atrophy are hypoautofluorescent (dark gray or black), the areas of “sick” RPE are hyperautofluorescent (brighter than background), and the areas of healthy RPE are gray.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations

**Age** is the strongest risk factor for ARMD

The clinical hallmark of ARMD is the presence of drusen in the macula

There are two types: **Nonexudative** and **exudative**

**By what two other names are each condition commonly known?**

- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

**What are the three hallmark findings in nonexudative ARMD?**

- Drusen
- RPE changes
- **Geographic atrophy**

**What does GA look like on…**

**FA?** A well-circumscribed area of hyperfluorescence

**Autofluorescence?** Dense hypoautofluorescence with a ring of hyperautofluorescence

**OCT?** Eventually involve the fovea.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative**.

**By what two other names are each condition commonly known?**

- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

**What are the three hallmark findings in nonexudative ARMD?**

- Drusen
- RPE changes
- **Geographic atrophy**

**What is geographic atrophy (GA)?**

It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

**What does GA look like on…**

- **FA?** A well-circumscribed area of hyperfluorescence
- **Autofluorescence?** Dense hypoautofluorescence with a ring of hyperautofluorescence
- **OCT?** RPE loss; thinning/loss of the outer retinal layers
OCT over the fovea in a patient with non-exudative AMD and geographic atrophy. There is loss of outer retinal layers and RPE.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative**

By what two other names are each condition commonly known?

**Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD

**Exudative**: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?

--Drusen
--RPE changes
--Geographic atrophy

What is geographic atrophy (GA)?

It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

What is its typical pattern of progression?

It starts in the perifoveal region, expanding over time to eventually involve the foveal center.

What is the other form that defines advanced ARMD?

The presence of neovascularization.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: Nonexudative and exudative ARMD.

By what two other names are each condition commonly known?
- Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
- Exudative: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?
- Drusen
- RPE changes
- Geographic atrophy

What is geographic atrophy (GA)? It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

What is its typical pattern of progression? It starts in the perifoveal region, expanding over time to eventually involve the foveal center.

What is the other form that defines advanced ARMD? The presence of neovascularization.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

There are two types: nonexudative and exudative.

**Nonexudative ARMD**: Defined by the presence of small drusen, intermediate drusen, and geographic atrophy.

**Exudative ARMD**: Defined by the presence of neovascularization.

**By what two other names are each condition commonly known?**

- **Nonexudative**: Nonneovascular ARMD; 'dry' ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

**What are the three hallmark findings in nonexudative ARMD?**

- Drusen
- RPE changes
- Geographic atrophy

**What is geographic atrophy (GA)?**

It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

**What is its typical pattern of progression?**

It starts in the perifoveal region, expanding over time to eventually involve the foveal center.

**What is the other form that defines advanced ARMD?**

The presence of neovascularization.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **nonexudative** and **exudative** ARMD.

**Nonexudative** ARMD:

- Drusen
- RPE changes
- Geographic atrophy

**Exudative** ARMD: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD? 

- Drusen
- RPE changes
- **Geographic atrophy**

What is **geographic atrophy** (GA)?

It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

What is its typical pattern of progression?

It starts in the perifoveal region, expanding over time to eventually involve the foveal center.

What is the other form that defines advanced ARMD?

The presence of neovascularization.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+. The presence of drusen is strongly related to the risk of ARMD.

What about early and intermediate ARMD—how are they defined?

**Early ARMD:** Defined by the presence of small drusen +/- a “few” intermediate drusen

**Intermediate ARMD:** ?

**Advanced ARMD:** Defined by the presence of either geographic atrophy or a neovascular membrane

What are the three hallmark findings in nonexudative ARMD?

--- Drusen
--- RPE changes
--- Geographic atrophy

What is geographic atrophy (GA)?

It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

What is its typical pattern of progression?

It starts in the perifoveal region, expanding over time to eventually involve the foveal center.

What is the other form that defines advanced ARMD?

The presence of neovascularization

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD

Exudative: Neovascular ARMD; ‘wet’ ARMD

There are two types: **nonexudative** and **exudative**
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

The clinical hallmark of ARMD is the presence of drusen.

There are two types: **Nonexudative** and **Exudative**.

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

What are the three hallmark findings in nonexudative ARMD?

--- Drusen
--- RPE changes
--- Geographic atrophy

What is Geographic atrophy?

It is one of two forms of advanced ARMD. It is characterized by a sharply defined area in the posterior pole manifesting atrophy of the RPE, the overlying photoreceptors, and the underlying choriocapillaris.

What is its typical pattern of progression?

It starts in the perifoveal region, expanding over time to eventually involve the foveal center.

What is the other form that defines advanced ARMD?

The presence of neovascularization.

What about early and intermediate ARMD—how are they defined?

Early ARMD: Defined by the presence of small drusen +/- a “few” intermediate drusen
Intermediate ARMD: Characterized by extensive intermediate drusen, or the presence of any large drusen
Advanced ARMD: Defined by the presence of either geographic atrophy or a neovascular membrane.
ARMD

- Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations
- **Age** is the strongest risk factor for ARMD
- The clinical hallmark of ARMD is the presence of drusen in the macula
- There are two types: **Nonexudative** and **exudative**

By what two other names are each condition commonly known?

- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

*Time to tackle exudative ARMD. But before doing so, we need to review the vascular supply of the retina*
- 1) PR outer segs
- 2) Bipolar cells
0) RPE cells RPE cells
1) Basement membrane of RPE
2) Inner collagenous layer
3) Elastic layer
4) Outer collagenous layer
5) Basement membrane of choriocapillaris
6) What structure is this?

But first:

What is the innermost layer of Bruch’s membrane?
What are the five layers of Bruch’s membrane?

- Basement membrane of RPE
- Inner collagenous layer
- Elastic layer
- Outer collagenous layer
- Basement membrane of choriocapillaris
- Choriocapillaris
What are the five layers of Bruch's membrane?

- 0) RPE cells RPE cells
- 1) PR outer segs
- 2) Bipolar cells
- 3) Elastic layer
- 4) Outer collagenous layer
- 5) Basement membrane of choriocapillaris
- 6) Choriocapillaris
- 7) ?

What structure is this?

Innermost: Basement membrane of RPE
Outermost: Basement membrane of choriocapillaris

But first:
- 0) RPE cells RPE cells
What are the five layers of Bruch’s membrane?

- Basement membrane of RPE
- Inner collagenous layer
- Elastic layer
- Outer collagenous layer
- Basement membrane of choriocapillaris

But first:
- PR outer segs
- Bipolar cells
- RPE cells

Innermost: RPE cells

Outermost: Choriocapillaris

What structure is this? The choroid
What are the five layers of Bruch’s membrane?

1. Basement membrane of RPE
2. Inner collagenous layer
3. Elastic layer
4. Outer collagenous layer
5. Basement membrane of choriocapillaris

What is the deepest retinal layer in which branches of the retinal vasculature can be found?

- PR outer segs
- 0) RPE cells RPE cells
- 1) Bipolar cells
- 2) RPE cells
- 3) Inner nuclear layer (INL)
- 4) Retinal vessels
- 5) Choriocapillaris
- 6) Choroid
- 7) Choroid
What are the five layers of Bruch’s membrane?

- 1) Basement membrane of RPE
- 2) Inner collagenous layer
- 3) Elastic layer
- 4) Outer collagenous layer
- 5) Basement membrane of choriocapillaris

Retinal vessels

But first:

0) RPE cells

- 1) PR outer segs

What is the deepest retinal layer in which branches of the retinal vasculature can be found?
The inner nuclear layer (INL)

- 2) Bipolar cells

What is the deepest retinal layer in which branches of the retinal vasculature can be found?
The inner nuclear layer (INL)
What are the five layers of Bruch's membrane?

1) Basement membrane of RPE
2) Inner collagenous layer
3) Elastic layer
4) Outer collagenous layer
5) Basement membrane of choriocapillaris
6) Choriocapillaris
7) Choroid

So, the retinal vessels supply the inner retinal layers...
What are the five layers of Bruch's membrane?

- Basement membrane of RPE
- Inner collagenous layer
- Elastic layer
- Outer collagenous layer
- Basement membrane of choriocapillaris

But first:

- PR outer segs
- RPE cells

So, the retinal vessels supply the inner retinal layers... Whereas the choroid/choriocapillaris supply the outer retina and RPE.
- Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.
- **Age** is the strongest risk factor for ARMD.
- The clinical hallmark of ARMD is the presence of drusen in the macula.
- There are two types: **Nonexudative** and **exudative** ARMD.

**Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD

**Exudative**: Neovascular ARMD; ‘wet’ ARMD

*What does it mean to say ARMD is ‘exudative’?*
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative** ARMD.

**By what two other names are each condition commonly known?**

- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

**What does it mean to say ARMD is ‘exudative’?**

It means a neovascular membrane, (almost always choroidal in origin) is present.
Age-related macular degeneration (ARMD) is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: Nonexudative and exudative ARMD.

By what two other names are each condition commonly known?
Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

What does it mean to say ARMD is ‘exudative’?
It means a neovascular membrane, (almost always choroidal in origin) is present.
Age-related macular degeneration (ARMD) is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: Nonexudative and exudative.

By what two other names are each condition commonly known? Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD Exudative: Neovascular ARMD; ‘wet’ ARMD

What does it mean to say ARMD is ‘exudative’? It means a neovascular membrane, (almost always choroidal in origin) is present.

What vessels give rise to the neovascular membrane?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

By what two other names are each condition commonly known?
- Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
- Exudative: Neovascular ARMD; ‘wet’ ARMD

What does it mean to say ARMD is ‘exudative’?
It means a neovascular membrane, (almost always choroidal in origin) is present.

What vessels give rise to the neovascular membrane?
The choriocapillaris (with one exception, to be discussed later)
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative**.

**By what two other names are each condition commonly known?**

- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

**What does it mean to say ARMD is ‘exudative’?**

It means a neovascular membrane, (almost always choroidal in origin) is present.

**What vessels give rise to the neovascular membrane?**

The choriocapillaris (with one exception, to be discussed later).

**What will a pt c/o if a CNVM develops?**

Blurry vision, metamorphopsia and/or a paracentral scotoma.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative ARMD.

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD

Exudative: Neovascular ARMD; ‘wet’ ARMD

What does it mean to say ARMD is ‘exudative’?
It means a neovascular membrane, (almost always choroidal in origin) is present.

What vessels give rise to the neovascular membrane?
The choriocapillaris (with one exception, to be discussed later).

What will a pt c/o if a CNVM develops?
Blurry vision, metamorphopsia and/or a paracentral scotoma.
Age-related macular degeneration is the #1 cause of blindness in adults age **50+** in resource-rich nations

*Age* is the strongest risk factor for ARMD

The clinical hallmark of ARMD is the presence of **drusen** in the macula

There are two types: **Nonexudative** and **exudative**

*By what two other names are each condition commonly known?*

**Nonexudative:** Nonneovascular ARMD; ‘dry’ ARMD

**Exudative:** Neovascular ARMD; ‘wet’ ARMD

*Three types of neovascular membranes occur in ARMD—what are they called?*

---?

---?

---?

*Blurry vision, metamorphopsia and/or a paracentral scotoma*
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: Nonexudative and exudative.

By what two other names are each condition commonly known?
- Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
- Exudative: Neovascular ARMD; ‘wet’ ARMD

Three types of neovascular membranes occur in ARMD—what are they called?
- Type 1
- Type 2
- Type 3

Blurry vision, metamorphopsia and/or a paracentral scotoma
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: **Nonexudative** and **exudative**.

By what two other names are each condition commonly known?

- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

Three types of neovascular membranes occur in ARMD—what are they called? **What are the defining features of each?**

--- Type 1: ?
--- Type 2
--- Type 3

Blurry vision, metamorphopsia and/or a paracentral scotoma.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: Nonexudative and exudative.

By what two other names are each condition commonly known? Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD. Exudative: Neovascular ARMD; ‘wet’ ARMD.

Three types of neovascular membranes occur in ARMD—what are they called? What are the defining features of each?--Type 1: CNVM originates from the choriocapillaris and extends into Bruch’s membrane and/or the sub-RPE space.

--Type 2

--Type 3: Blurry vision, metamorphopsia and/or a paracentral scotoma.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative**

By what two other names are each condition commonly known?
- Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
- Exudative: Neovascular ARMD; ‘wet’ ARMD

Three types of neovascular membranes occur in ARMD—what are they called?

What are the defining features of each?
- Type 1: CNVM originates from the choriocapillaris and extends into Bruchs membrane and/or the sub-RPE space
- Type 2
- Type 3

Blurry vision, metamorphopsia and/or a paracentral scotoma
-2) Bipolar cells

-1) PR outer segs

0) RPE cells

Bruch's membrane

1) Inner collagenous layer

2) Inner collagenous layer

3) Elastic layer

4) Outer collagenous layer

5) Basement membrane of choriocapillaris

6) Choriocapillaris

7) Choroid

Type 1 with the CNVM in Bruchs membrane
What are the five layers

1) Basement membrane of RPE
2) Inner collagenous layer
3) Elastic layer
4) Outer collagenous layer
5) Basement membrane of choriocapillaris

Type 1 with the CNVM in the sub-RPE space

-2) Bipolar cells

-1) PR outer segs

0) RPE cells

1) Basement membrane of RPE
2) Inner collagenous layer
3) Elastic layer
4) Outer collagenous layer
5) Basement membrane of choriocapillaris
6) Choriocapillaris
7) Choroid
Type 1 CNVM with hyperreflective material visible in the PED. Note that the RPE can be seen to ride above the lesion.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: **Nonexudative** and **exudative**.

**Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD

**Exudative**: Neovascular ARMD; ‘wet’ ARMD

By what two other names are each condition commonly known?
- Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
- Exudative: Neovascular ARMD; ‘wet’ ARMD

Three types of neovascular membranes occur in ARMD—what are they called? *What are the defining features of each?*

--Type 1: CNVM originates from the choriocapillaris and extends into Bruch’s membrane and/or the sub-RPE space
--Type 2: ?
--Type 3: Blurry vision, metamorphopsia and/or a paracentral scotoma
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

By what two other names are each condition commonly known?
Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

Three types of neovascular membranes occur in ARMD—what are they called? What are the defining features of each?

--Type 1: CNVM originates from the choriocapillaris and extends into Bruch’s membrane and/or the sub-RPE space
--Type 2: CNVM originates from the choriocapillaris and extends into the sub-retinal space (ie, just above the RPE)
--Type 3 NVM arises from the deep capillary plexus of the retina and grows toward the RPE

Blurry vision, metamorphopsia and/or a paracentral scotoma
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

- **Age** is the strongest risk factor for ARMD.
- The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative**.

By what two other names are each condition commonly known?
- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

Three types of neovascular membranes occur in ARMD—what are they called? *What are the defining features of each?*

---
- **Type 1**: CNVM originates from the choriocapillaris and extends into Bruch's membrane and/or the sub-RPE space.
- **Type 2**: CNVM originates from the choriocapillaris and extends into the sub-retinal space.
- **Type 3**: Blurry vision, metamorphopsia and/or a paracentral scotoma.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD

Exudative: Neovascular ARMD; ‘wet’ ARMD

Three types of neovascular membranes occur in ARMD—what are they called?

What are the defining features of each?

--Type 1: CNVM originates from the choriocapillaris and extends into Bruch’s membrane and/or the sub-RPE space

--Type 2: CNVM originates from the choriocapillaris and extends into the sub-retinal space (ie, just above the RPE)

--Type 3: Blurry vision, metamorphopsia and/or a paracentral scotoma
What are the five layers of Bruch's membrane?

1. Basement membrane of RPE
2. Inner collagenous layer
3. Elastic layer
4. Outer collagenous layer
5. Basement membrane of choriocapillaris

Type 2 with the CNVM in the sub-retinal space
Type 2 CNVM located above the RPE with subretinal fluid (SRF) adjacent to the lesion. Note the RPE can be seen below the lesion.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative ARMD.

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

Three types of neovascular membranes occur in ARMD—what are they called? What are the defining features of each?

--Type 1: CNVM originates from the choriocapillaris and extends into Bruch's membrane and/or the sub-RPE space
--Type 2: CNVM originates from the choriocapillaris and extends into the sub-retinal space (ie, just above the RPE)
--Type 3: ?

Blurry vision, metamorphopsia and/or a paracentral scotoma
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations
Age is the strongest risk factor for ARMD
The clinical hallmark of ARMD is the presence of drusen in the macula
There are two types: **Nonexudative** and **exudative**

*By what two other names are each condition commonly known?*
Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

*Three types of neovascular membranes occur in ARMD—what are they called? What are the defining features of each?*
--Type 1: CNVM originates from the choriocapillaris and extends into Bruch's membrane and/or the sub-RPE space
--Type 2: CNVM originates from the choriocapillaris and extends into the sub-retinal space (ie, just above the RPE)
--Type 3: NVM arises from the deep capillary plexus of the retina and grows down toward the RPE

Blurry vision, metamorphopsia and/or a paracentral scotoma
What are the five layers of Bruch’s membrane?

1) Basement membrane of RPE
2) Inner collagenous layer
3) Elastic layer
4) Outer collagenous layer
5) Basement membrane of choriocapillaris

Type 3 with the NVM growing down from retinal vessels
What are the five layers of Bruch’s membrane?

- 1) PR outer segs
- 2) Bipolar cells
- 3) Retinal vessels
- 4) Type 3 with the NVM growing down from retinal vessels
- 5) Choriocapillaris
- 6) RPE cells
- 7) Choroid

- 1) Basement membrane of RPE
- 2) Inner collagenous layer
- 3) Elastic layer
- 4) Outer collagenous layer
- 5) Basement membrane of choriocapillaris
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative**

By what two other names are each condition commonly known?

- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

What does it mean to say ARMD is ‘exudative’?

It means a neovascular membrane, (almost always choroidal in origin) is present.

What vessels give rise to the neovascular membrane?

- **The choriocapillaris** (with one exception, to be discussed later)
- **Type 3**: NVM arises from the deep capillary plexus of the retina

What will a pt c/o if a CNVM develops?

Blurry vision, metamorphopsia and/or a paracentral scotoma.

Three types of neovascular membranes occur in ARMD—what are they called? What are the defining features of each?

- **Type 1**: CNVM originates from the choriocapillaris and extends into Bruch's membrane and/or the sub-RPE space
- **Type 2**: CNVM originates from the choriocapillaris and extends into the sub-retinal space (i.e., just above the RPE)
- **Type 3**: NVM arises from the deep capillary plexus of the retina and grows down toward the RPE

Type 3 is the exception to the statement ‘CNVM originate in the choriocapillaris’ mentioned a few slides ago.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative** ARMD.

**By what two other names are each condition commonly known?**

- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

**Three types of neovascular membranes (NVM) can occur**: What are the defining features of each?

---

- **Type 1**: CNVM originates from the choriocapillaris and extends into Bruch membrane and/or the sub-RPE space
- **Type 2**: CNVM originates from the choriocapillaris and extends into the sub-retinal space (ie, just above the RPE)
- **Type 3**: NVM arises from the deep capillary plexus of the retina and grows down toward the RPE

**Of the three, which occurs most frequently in ARMD?**

Type 1

**Type 2 CNVM is strongly associated with what condition (it’s not ARMD)?**

Ocular histoplasmosis

**By what other name is Type 3 known?**

Retinal angiomatous proliferation (RAP)
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: **Nonexudative** and **exudative**

**By what two other names are each condition commonly known?**
- Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
- Exudative: Neovascular ARMD; ‘wet’ ARMD

**What does it mean to say ARMD is ‘exudative’?**
It means a neovascular membrane, (almost always choroidal in origin) is present.

**What vessels give rise to the neovascular membrane?**
The choriocapillaris (with one exception, to be discussed later).

**What will a pt c/o if a CNVM develops?**
Blurry vision, metamorphopsia and/or a paracentral scotoma.

**Three types of neovascular membranes occur in ARMD—what are they called and what are the defining features of each?**
- **Type 1**: CNVM originates from the choriocapillaris and extends into Bruch’s membrane and/or the sub-RPE space.
- **Type 2**: CNVM originates from the choriocapillaris and extends into the sub-retinal space (ie, just above the RPE).
- **Type 3**: NVM arises from the deep capillary plexus of the retina and grows down toward the RPE.

**Of the three, which occurs most frequently in ARMD?**
Type 1

**Type 2 CNVM is strongly associated with what condition (it’s not ARMD)?**
Ocular histoplasmosis.

**By what other name is Type 3 known?**
Retinal angiomatous proliferation (RAP).
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative ARMD.

By what two other names are each condition commonly known?

Nonexudative: Non-neovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

Of the three, which occurs most frequently in ARMD?

Type 1

Type 2 CNVM is strongly associated with what condition (it’s not ARMD)?

Type 2 CNVM is strongly associated with Ocular histoplasmosis.

By what other name is Type 3 known?

Retinal angiomatous proliferation (RAP)
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and Exudative.

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

What does it mean to say ARMD is ‘exudative’?

It means a neovascular membrane, (almost always choroidal in origin) is present.

What vessels give rise to the neovascular membrane?

The choriocapillaris (with one exception, to be discussed later).

What will a pt c/o if a CNVM develops?

Blurry vision, metamorphopsia and/or a paracentral scotoma.

Of the three, which occurs most frequently in ARMD?

Type 1

Type 2 CNVM is strongly associated with what condition (it’s not ARMD)?

Ocular histoplasmosis (OHS)

By what other name is Type 3 known?

Retinal angiomatous proliferation (RAP)
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative**.

By what two other names are each condition commonly known?

- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

What does it mean to say ARMD is ‘exudative’?

It means a neovascular membrane, (almost always choroidal in origin) is present.

What vessels give rise to the neovascular membrane?

The choriocapillaris (with one exception, to be discussed later).

What will a pt c/o if a CNVM develops?

Blurry vision, metamorphopsia and/or a paracentral scotoma.

Three types of neovascular membranes occur in ARMD—what are they called? What are the defining features of each?

- **Type 1**: CNVM originates from the choriocapillaris and extends into Bruch's membrane and/or the sub-RPE space.
- **Type 2**: CNVM originates from the choriocapillaris and extends into the sub-retinal space (i.e., just above the RPE).
- **Type 3**: NVM arises from the deep capillary plexus of the retina and grows down toward the RPE.

Of the three, which occurs most frequently in ARMD?

**Type 1**

Type 2 CNVM is strongly associated with what condition (it’s not ARMD)?

Ocular histoplasmosis (OHS)

By what other name is Type 3 known?

Retinal angiomatous proliferation (RAP)
Age-related macular degeneration (ARMD) is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative**

By what two other names are each condition commonly known?

- **Nonexudative**: Nonneovascular ARMD; ‘dry’ ARMD
- **Exudative**: Neovascular ARMD; ‘wet’ ARMD

What does it mean to say ARMD is ‘exudative’?

It means a neovascular membrane, (almost always choroidal in origin) is present.

What vessels give rise to the neovascular membrane?

- Choriocapillaris

What will a pt c/o if a CNVM develops?

Blurry vision, metamorphopsia and/or a paracentral scotoma.

Of the three, which occurs most frequently in ARMD?

- **Type 1**
- **Type 2 CNVM is strongly associated with what condition (it’s not ARMD)?**
  - Ocular histoplasmosis (OHS)

By what other name is Type 3 known?

- **Retinal angiomatous proliferation (RAP)**
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

What does it mean to say ARMD is ‘exudative’?

It means a neovascular membrane, (almost always choroidal in origin) is present.

What vessels give rise to the neovascular membrane?

The choriocapillaris (with one exception, to be discussed later).

What will a pt c/o if a CNVM develops?

Blurry vision, metamorphopsia and/or a paracentral scotoma.

Three types of neovascular membranes develop in ARMD:

---Type 1: CNVM originates from the choriocapillaris and extends into Bruch's membrane and/or the sub-RPE space
---Type 2: CNVM originates from the choriocapillaris and extends into the sub-retinal space (ie, just above the RPE)
---Type 3: NVM arises from the deep capillary plexus of the retina and grows toward the RPE

Of the three, which occurs most frequently in ARMD?

Type 1

Type 2 CNVM is strongly associated with what condition (it’s not ARMD)?

Ocular histoplasmosis

By what other name is Type 3 known?

Ocular histoplasmosis

Retinal angiomatous proliferation (RAP)

Ocular histo is high on the DDx for CNVM. What other non-ARMD conditions are important causes of CNVM?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

By what two other names are each condition commonly known?

Nonexudative: Nonneovascular ARMD; ‘dry’ ARMD
Exudative: Neovascular ARMD; ‘wet’ ARMD

What does it mean to say ARMD is ‘exudative’?

It means a neovascular membrane, (almost always choroidal in origin) is present.

What vessels give rise to the neovascular membrane?

The choriocapillaris (with one exception, to be discussed later).

What will a pt c/o if a CNVM develops?

Blurry vision, metamorphopsia and/or a paracentral scotoma.

Three types of neovascular membranes occur in ARMD—what are they called? What are the defining features of each?

--Type 1: CNVM originates from the choriocapillaris and extends into Bruch’s membrane and/or the sub-RPE space.
--Type 2: CNVM originates from the choriocapillaris and extends into the sub-retinal space (ie, just above the RPE).
--Type 3: NVM arises from the deep capillary plexus of the retina and grows downward toward the RPE.

Of the three, which occurs most frequently in ARMD?

Type 1

Type 2 CNVM is strongly associated with what condition (it’s not ARMD)?

Ocular histoplasmosis

By what other name is Type 3 known?

Retinal angiomatous proliferation (RAP)

Ocular histo is high on the DDx for CNVM. What other non-ARMD conditions are important causes of CNVM?

Coming in hot…
CNVM DDx:

- ARMD
- OHS

Other than these two, what is the DDx for causes of CNVM?
CNVM DDx:
- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

Other than these two, what is the DDx for causes of CNVM?
**CNVM DDx:**

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

Let me stress, these are **all** important clinical alternatives that must come to mind when contemplating CNVM.
Let me stress, these are all important clinical alternatives that must come to mind when contemplating CNVM. That being said, three are discussed in detail in the ARMD chapter of the Retina book, and thus are probably deserving of special attention. Which three?
Let me stress, these are all important clinical alternatives that must come to mind when contemplating CNVM. That being said, three are discussed in detail in the ARMD chapter of the Retina book, and thus are probably deserving of special attention. Which three?
**CNVM DDx:**

- ARMD
- OHS

* Is there a racial predilection in OHS? Yes, OHS occurs almost exclusively among whites of Northern European heritage.

* Is there a geographic predilection? Yes, the majority of cases are found in people who reside in the Mississippi/Ohio River valleys of the US.

* Does OHS manifest unilaterally, or bilaterally? Bilaterally (although it can be somewhat asymmetric).

* Is OHS associated with vitritis? Never. If vitritis is present, it’s not OHS.

* What about AC cell? Never. If AC cell is present, it’s not OHS.
Is there a racial predilection in OHS?
Yes, OHS occurs almost exclusively among whites of Northern European heritage.

Is there a geographic predilection?
Yes, the majority of cases are found in people who reside in the Mississippi/Ohio River valleys of the US.

Does OHS manifest unilaterally, or bilaterally?
Bilaterally (although it can be somewhat asymmetric).

Is OHS associated with vitritis?
Never. If vitritis is present, it's not OHS.

What about AC cell?
Never. If AC cell is present, it's not OHS.

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy
**CNVM DDx:**

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

**Is there a racial predilection in OHS?**
Yes, OHS occurs almost exclusively among whites of Northern European heritage.

**Is there a geographic predilection?**
Yes, the majority of cases are found in people who reside in the Mississippi/Ohio River valleys of the US.

**Does OHS manifest unilaterally, or bilaterally?**
Bilaterally (although it can be somewhat asymmetric).

**Is OHS associated with vitritis?**
Never. If vitritis is present, it's not OHS.

**What about AC cell?**
Never. If AC cell is present, it's not OHS.
CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

Is there a racial predilection in OHS?
Yes, OHS occurs almost exclusively among whites of Northern European heritage

Is there a geographic predilection?

CNVM DDx:
- ARMD
- OHS
- Angiod streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

Is there a racial predilection in OHS?
Yes, OHS occurs almost exclusively among whites of Northern European heritage.

Is there a geographic predilection?
Yes, the majority of cases are found in people who reside in the two rivers valleys of the US.
Is there a racial predilection in OHS?
Yes, OHS occurs almost exclusively among whites of Northern European heritage

Is there a geographic predilection?
Yes, the majority of cases are found in people who reside in the Mississippi/Ohio River valleys of the US
**CNVM DDx:**
- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

**ARMD**

Is there a racial predilection in OHS? 
Yes, OHS occurs almost exclusively among whites of Northern European heritage

Is there a geographic predilection? 
Yes, the majority of cases are found in people who reside in the Mississippi/Ohio River valleys of the US

Does OHS manifest unilaterally, or bilaterally? 
Never. If AC cell is present, it's not OHS.
**CNVM DDx:**

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

**ARMD**

**Is there a racial predilection in OHS?**
Yes, OHS occurs almost exclusively among whites of Northern European heritage

**Is there a geographic predilection?**
Yes, the majority of cases are found in people who reside in the Mississippi/Ohio River valleys of the US

**Does OHS manifest unilaterally, or bilaterally?**
Bilaterally (although it can be somewhat asymmetric)

**Never. If vitritis is present, it's not OHS.**

**Never. If AC cell is present, it's not OHS.**
CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

**ARMD**

**Is there a racial predilection in OHS?**
Yes, OHS occurs almost exclusively among whites of Northern European heritage.

**Is there a geographic predilection?**
Yes, the majority of cases are found in people who reside in the Mississippi/Ohio River valleys of the US.

**Does OHS manifest unilaterally, or bilaterally?**
Bilaterally (although it can be somewhat asymmetric).

**Is OHS associated with vitritis?**
Never. If vitritis is present, it’s not OHS.
Is there a racial predilection in OHS? 
Yes, OHS occurs almost exclusively among whites of Northern European heritage.

Is there a geographic predilection? 
Yes, the majority of cases are found in people who reside in the Mississippi/Ohio River valleys of the US.

Does OHS manifest unilaterally, or bilaterally? 
Bilaterally (although it can be somewhat asymmetric).

Is OHS associated with vitritis? 
Never. If vitritis is present, it’s not OHS.
Is there a racial predilection in OHS?
Yes, OHS occurs almost exclusively among whites of Northern European heritage.

Is there a geographic predilection?
Yes, the majority of cases are found in people who reside in the Mississippi/Ohio River valleys of the US.

Does OHS manifest unilaterally, or bilaterally?
Bilaterally (although it can be somewhat asymmetric).

Is OHS associated with vitritis?
Never. If vitritis is present, it’s not OHS.

What about AC cell?
Never. If AC cell is present, it’s not OHS.
Is there a racial predilection in OHS?
Yes, OHS occurs almost exclusively among whites of Northern European heritage

Is there a geographic predilection?
Yes, the majority of cases are found in people who reside in the Mississippi/Ohio River valleys of the US

Does OHS manifest unilaterally, or bilaterally?
Bilaterally (although it can be somewhat asymmetric)

Is OHS associated with vitritis?
Never. If vitritis is present, it’s not OHS.

What about AC cell?
Never. If AC cell is present, it’s not OHS.
CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

How is the diagnosis of OHS made?

- It is a clinical diagnosis based on DFE findings

What are you looking for on DFE?

- The so-called 'classic triad' of OHS:
  - Histo spots
  - Peripapillary atrophy
  - Disciform macular lesion(s)

Is there a racial predilection in OHS?

- Yes, OHS occurs almost exclusively among whites of Northern European heritage

Is there a geographic predilection?

- Yes, the majority of cases are found in people who reside in the Mississippi/Ohio River valleys of the US

Does OHS manifest unilaterally, or bilaterally?

- Bilaterally (although it can be somewhat asymmetric)

Is OHS associated with vitritis?

- **Never.** If vitritis is present, it’s not OHS.

What about AC cell?

- **Never.** If AC cell is present, it’s not OHS.
CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

How is the diagnosis of OHS made?
It is a clinical diagnosis based on DFE findings.

Does OHS manifest unilaterally, or bilaterally?
Bilaterally (although it can be somewhat asymmetric).

Is OHS associated with vitritis?
Never. If vitritis is present, it's not OHS.

What about AC cell?
Never. If AC cell is present, it's not OHS.
CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

How is the diagnosis of OHS made?
It is a clinical diagnosis based on DFE findings.

What are you looking for on DFE?

Does OHS manifest unilaterally, or bilaterally?
Bilaterally (although it can be somewhat asymmetric)

Is OHS associated with vitritis?
Never. If vitritis is present, it’s not OHS.

What about AC cell?
Never. If AC cell is present, it’s not OHS.
CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

**ARMD**

*How is the diagnosis of OHS made?*

It is a clinical diagnosis based on DFE findings.

*What are you looking for on DFE?*

The so-called ‘classic triad’ of OHS:
- ?
- ?
- ?

*Does OHS manifest unilaterally, or bilaterally?*

Bilaterally (although it can be somewhat asymmetric)

*Is OHS associated with vitritis?*

Never. If vitritis is present, it’s not OHS.

*What about AC cell?*

Never. If AC cell is present, it’s not OHS.

**OHS**

Is there a racial predilection in OHS?

Yes, OHS occurs almost exclusively among whites of Northern European heritage.

Is there a geographic predilection?

Yes, the majority of cases are found in people who reside in the Mississippi/Ohio River valleys of the US.

Does OHS manifest unilaterally, or bilaterally?

Bilaterally (although it can be somewhat asymmetric)

Is OHS associated with vitritis?

Never. If vitritis is present, it’s not OHS.

What about AC cell?

Never. If AC cell is present, it’s not OHS.
CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

ARMD

How is the diagnosis of OHS made?
It is a clinical diagnosis based on DFE findings

What are you looking for on DFE?
The so-called ‘classic triad’ of OHS:
- Histo spots
- Peripapillary atrophy
- Disciform macular lesion(s)

Does OHS manifest unilaterally, or bilaterally?
Bilaterally (although it can be somewhat asymmetric)

Is OHS associated with vitritis?
Never. If vitritis is present, it’s not OHS.

What about AC cell?
Never. If AC cell is present, it’s not OHS.
OHS: The classic triad
For more on OHS, see slide-set U21

OHS: The classic triad
What is the classic DFE appearance of angioid streaks?

Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch's membrane.

What proportion of angioid streaks are associated with systemic abnormalities?

About half

What is the well-known mnemonic for angioid streak's associations? What are these associations?

Pseudoxanthoma elasticum (PXE)

Ehlers-Danlos syndrome

Paget's disease of bone

Sickle-cell disease

Idiopathic (ie, no association)
What is the classic DFE appearance of angioid streaks? Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in retinal structure.

About half of angioid streaks are associated with systemic abnormalities. The well-known mnemonic for angioid streak's associations is the PSEID acronym:

- Pseudoxanthoma elasticum (PXE)
- Ehlers-Danlos syndrome
- Paget's disease of bone
- Sickle-cell disease
- Idiopathic (ie, no association)
**CNVM DDx:**

- ARMD
- OHS
- **Angioid streaks**

*What is the classic DFE appearance of angioid streaks?*

**Reddish-brown** lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane

- Adult-onset vitelliform dystrophy
Angioid streaks (arrowheads). Note that only a few of the many present have been marked.
CNVM DDx:

- ARMD
- OHS
- **Angioid streaks**

*What is the classic DFE appearance of angioid streaks?*

Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane

*What proportion of angioid streaks are associated with systemic abnormalities?*

- About half

*Well-known mnemonic for angioid streak’s associations:*

- Pseudoxanthoma elasticum (PXE)
- Ehlers-Danlos syndrome
- Paget’s disease of bone
- Sickle-cell disease
- Idiopathic (ie, no association)

- Adult-onset vitelliform dystrophy
What is the classic DFE appearance of angioid streaks? 
Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane

What proportion of angioid streaks are associated with systemic abnormalities? 
About half

- **Angioid streaks**
- Adult-onset vitelliform dystrophy
CNVM DDx:
- ARMD
- OHS
- Angioid streaks

What is the classic DFE appearance of angioid streaks?
Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane

What proportion of angioid streaks are associated with systemic abnormalities?
About half

What is the well-known mnemonic for angioid streak’s associations?
What is the classic DFE appearance of angioid streaks?

Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane

What proportion of angioid streaks are associated with systemic abnormalities?

About half

What is the well-known mnemonic for angioid streak’s associations?

P E P S I

Adult-onset vitelliform dystrophy
What is the classic DFE appearance of angioid streaks? Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane.

What proportion of angioid streaks are associated with systemic abnormalities? About half.

What is the well-known mnemonic for angioid streak’s associations? What are these associations? PEPIS (Pattern Dystrophy, Eales Disease, Pathologic Myopia, Sorsby Macular Dystrophy, Industrial Injury).
What is the classic DFE appearance of angioid streaks?
Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane.

What proportion of angioid streaks are associated with systemic abnormalities?
About half.

What is the well-known mnemonic for angioid streak’s associations? What are these associations?
Psuedoxanthoma elasticum (PXE)
Ehlers-Danlos syndrome
Paget’s disease of bone
Sickle-cell disease
Idiopathic (ie, no association)

Adult-onset vitelliform dystrophy
What is the classic DFE appearance of angioid streaks? 
Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane

What proportion of angioid streaks are associated with systemic abnormalities? About half

What is the well-known mnemonic for angioid streak's associations? What are these associations?

- Pseudoxanthoma elasticum (PXE)
- Ehlers-Danlos syndrome
- Paget’s disease of bone
- Sickle-cell disease
- Idiopathic (ie, no association)

~ # of cases are associated with one of these
~ # of cases have no known systemic association

- Adult-onset vitelliform dystrophy
CNVM DDx:

- ARMD
- OHS
- Angioid streaks

What is the classic DFE appearance of angioid streaks?
Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane.

What proportion of angioid streaks are associated with systemic abnormalities?
About half.

What is the well-known mnemonic for angioid streak's associations? What are these associations?

- Pseudoxanthoma elasticum (PXE)
- Ehlers-Danlos syndrome
- Paget’s disease of bone
- Sickle-cell disease
- Idiopathic (i.e., no association)

~50% of cases are associated with one of these
~50% of cases have no known systemic association.
What is the classic DFE appearance of angioid streaks?
Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane

What proportion of angioid streaks are associated with systemic abnormalities?
About half

What is the well-known mnemonic for angioid streak’s associations? What are these associations?
Pseudoxanthoma elasticum (PXE)?
Ehlers-Danlos syndrome?
Paget’s disease of bone?
Sickle-cell disease?
Idiopathic (ie, no association)

Which condition has the strongest association with angioid streaks?

Adult-onset vitelliform dystrophy
What is the classic DFE appearance of angioid streaks? Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane.

What proportion of angioid streaks are associated with systemic abnormalities? About half.

What is the well-known mnemonic for angioid streak’s associations? What are these associations? 

**Pseudoxanthoma elasticum (PXE)**

What condition has the strongest association with angioid streaks?
PXE, by a mile.

**Ehlers-Danlos syndrome**

**Paget’s disease of bone**

**Sickle-cell disease**

**Idiopathic** (ie, no association)

**Adult-onset vitelliform dystrophy**
What is the classic DFE appearance of angioid streaks? Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane.

What proportion of angioid streaks are associated with systemic abnormalities? About half.

What is the well-known mnemonic for angioid streak’s associations? What are these associations? Pseudoxanthoma elasticum (PXE), Ehlers-Danlos syndrome, Paget’s disease of bone, Sickle-cell disease, Idiopathic (ie, no association).

Which condition has the strongest association with angioid streaks? PXE, by a mile.
**CNVM DDx:**

- ARMD
- OHS

**Angioid streaks**

What is the classic DFE appearance of angioid streaks? Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane.

What proportion of angioid streaks are associated with systemic abnormalities? About half.

What is the well-known mnemonic for angioid streak’s associations? What are these associations?

- Pseudoxanthoma elasticum (PXE)
- Ehlers-Danlos syndrome
- Paget’s disease of bone
- Sickle-cell disease
- Idiopathic (ie, no association)

Which condition has the strongest association with angioid streaks? PXE, by a mile.

**Adult-onset vitelliform dystrophy**
CNVM DDx:
- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

What is the classic DFE appearance of angioid streaks? Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane.

What proportion of angioid streaks are associated with systemic abnormalities? About half.

What is the well-known mnemonic for angioid streak’s associations? What are these associations? Pseudoxanthoma elasticum (PXE), Ehlers-Danlos syndrome, Paget’s disease of bone, Sickle-cell disease, Idiopathic (ie, no association).

Which condition has the strongest association with angioid streaks? PXE, by a mile.

What is the appearance of affected skin? An area of waxy-yellow, papule-like lesions. The classic informal descriptor for this appearance is 'Chicken skin'.
**CNVM DDx:**

- ARMD

**Angioid streaks**

- What is the classic DFE appearance of angioid streaks?
  - Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane.

- What proportion of angioid streaks are associated with systemic abnormalities?
  - About half.

- What is the well-known mnemonic for angioid streak's associations? What are these associations?
  - Pseudoxanthoma elasticum (PXE)
  - Ehlers-Danlos syndrome
  - Paget's disease of bone
  - Sickle-cell disease
  - Idiopathic (ie, no association)

- Which condition has the strongest association with angioid streaks? PXE, by a mile.

- What is the appearance of affected skin?
  - An area of waxy-yellow, papule-like lesions.

- What other organ-systems are affected in PXE?
  - Skin
  - Vascular
  - GI tract
  - Eye
CNVM DDx:

- ARMD
- OHS

Angioid streaks

What is the classic DFE appearance of angioid streaks? Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane.

What proportion of angioid streaks are associated with systemic abnormalities? About half.

What is the well-known mnemonic for angioid streak’s associations? What are these associations?

- Pseudoxanthoma elasticum (PXE)
- Ehlers-Danlos syndrome
- Paget’s disease of bone
- Sickle-cell disease
- Idiopathic (ie, no association)

Which condition has the strongest association with angioid streaks? PXE, by a mile.

What is the appearance of affected skin? An area of waxy-yellow, papule-like lesions.

What is the classic informal descriptor for this appearance? 'Chicken skin'.
**CNVM DDx:**

- ARMD
- OHS

**Angioid streaks**

What is the classic DFE appearance of angioid streaks? Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane.

What proportion of angioid streaks are associated with systemic abnormalities? About half.

What is the well-known mnemonic for angioid streak’s associations? What are these associations? Pseudoxanthoma elasticum (PXE), Ehlers-Danlos syndrome, Paget’s disease of bone, Sickle-cell disease, Idiopathic (ie, no association).

Which condition has the strongest association with angioid streaks? PXE, by a mile.

What is the appearance of affected skin? An area of waxy-yellow, papule-like lesions.

What is the classic informal descriptor for this appearance? ‘Chicken skin’.

What other organ-systems are affected in PXE? Skin, Vascular system, GI tract, Eye.

Adult-onset vitelliform dystrophy
PXE skin
CNVM DDx:

- ARMD
- OHS

Angioid streaks

What is the classic DFE appearance of angioid streaks?
Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane.

What proportion of angioid streaks are associated with systemic abnormalities?
About half.

What is the well-known mnemonic for angioid streak’s associations? What are these associations?
Pseudoxanthoma elasticum (PXE), Ehlers-Danlos syndrome, Paget’s disease of bone, Sickle-cell disease, Idiopathic (ie, no association).

Which condition has the strongest association with angioid streaks? PXE, by a mile.

What other organ-systems are affected in PXE?
- Skin
- Vascular system
- GI tract
- Eye

There are three classic eye findings in PXE, one of which is angioid streaks. What are the other two?
--Angioid streaks
--?
--?

Adult-onset vitelliform dystrophy
**CNVM DDx:**
- ARMD
- OHS

**Angioid streaks**

What is the classic DFE appearance of angioid streaks?
Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch's membrane.

What proportion of angioid streaks are associated with systemic abnormalities?
About half.

What is the well-known mnemonic for angioid streak's associations? What are these associations?
- **P**seudoxanthoma elasticum (PXE)
- **E**hlers-Danlos syndrome
- **P**aget's disease of bone
- **S**ickle-cell disease
- **I**diopathic (ie, no association)

Which condition has the strongest association with angioid streaks? PXE, by a mile.

There are three classic eye findings in PXE, one of which is angioid streaks. What are the other two?
- Angioid streaks
- RPE mottling
- Optic disc drusen

**Pseudoxanthoma elasticum (PXE)**

- Skin
- Vascular system
- GI tract
- Eye

There are three classic eye findings in PXE, one of which is angioid streaks. What are the other two?
- Angioid streaks
- RPE mottling
- Optic disc drusen

Which condition has the strongest association with angioid streaks? PXE, by a mile.
CNVM DDx:

- ARMD

OHS

Angioid streaks

What is the classic DFE appearance of angioid streaks?
Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane.

What proportion of angioid streaks are associated with systemic abnormalities?
About half.

What is the well-known mnemonic for angioid streak’s associations? What are these associations?
Pseudoxanthoma elasticum (PXE), Ehlers-Danlos syndrome, Paget’s disease of bone, Sickle-cell disease, Idiopathic (ie, no association).

Which condition has the strongest association with angioid streaks?
PXE, by a mile.

There are three classic eye findings in PXE, one of which is angioid streaks. What are the other two?
RPE mottling, optic disc drusen.

What mellifluous name is used to describe the RPE mottling?
Peau d’orange.
CNVM DDx:

- ARMD
- OHS

**Angioid streaks**

*What is the classic DFE appearance of angioid streaks?*

Reddish-brown lines radiating out from the peripapillary region; these lines represent breaks in Bruch’s membrane.

*What proportion of angioid streaks are associated with systemic abnormalities?*

About half.

*What is the well-known mnemonic for angioid streak’s associations? What are these associations?*

Pseudoxanthoma elasticum (PXE), Ehlers-Danlos syndrome, Paget’s disease of bone, Sickle-cell disease, Idiopathic (ie, no association), Central serous chorioretinopathy, Pattern dystrophy.

*Which condition has the strongest association with angioid streaks?*

PXE, by a mile.

*What other organ-systems are affected in PXE?*

- Skin
- Vascular system
- GI tract
- Eye

*There are three classic eye findings in PXE, one of which is angioid streaks. What are the other two?*

- Angioid streaks
- RPE mottling
- Optic disc drusen

*What mellifluous name is used to describe the RPE mottling?*

Peau d’orange.
PXE: Peau d’orange fundus
PXE: Peau d’orange fundus

For more on angioid streaks, see slide-set R61
CNVM DDx:

- ARMD
- OHS
- Angioid streaks

**Pathologic myopia**
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

*Per the Retina book, what axial length serves as a useful cutoff for defining pathologic myopia?*
CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
  - Idiopathic
  - Sorsby macular dystrophy
  - Traumatic choroidal rupture
  - Iatrogenic
  - Central serous chorioretinopathy
  - Pattern dystrophy
  - Adult-onset vitelliform dystrophy

Per the Retina book, what axial length serves as a useful cutoff for defining pathologic myopia?
26.5 mm
CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- **Pathologic myopia**
  - Idiopathic
  - Sorsby macular dystrophy
  - Traumatic choroidal rupture
  - Iatrogenic
  - Central serous chorioretinopathy
  - Pattern dystrophy
  - Adult-onset vitelliform dystrophy

**Per the Retina book, what axial length serves as a useful cutoff for defining pathologic myopia?**

- 26.5 mm

**What is the classic finding on DFE that puts high myopes at risk for CNVM?**

- Lacquer cracks

Breaks in Bruch’s membrane, yellowish in color, usually found in the macula. These breaks are the nidus for CNVM ingress in pathologic myopia.
**CNVM DDx:**

- ARMD
- OHS
- Angioid streaks
- **Pathologic myopia**
  - Idiopathic
  - Sorsby macular dystrophy
  - Traumatic choroidal rupture
  - Iatrogenic
  - Central serous chorioretinopathy
  - Pattern dystrophy
  - Adult-onset vitelliform dystrophy

---

*Per the Retina book, what axial length serves as a useful cutoff for defining pathologic myopia?*

26.5 mm

*What is the classic finding on DFE that puts high myopes at risk for CNVM?*

Lacquer cracks
CNVM DDx:
- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioidopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

Per the Retina book, what axial length serves as a useful cutoff for defining pathologic myopia? 26.5 mm

What is the classic finding on DFE that puts high myopes at risk for CNVM? Lacquer cracks

What are lacquer cracks?
CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

Per the Retina book, what axial length serves as a useful cutoff for defining pathologic myopia? 26.5 mm

What is the classic finding on DFE that puts high myopes at risk for CNVM? Lacquer cracks

What are lacquer cracks? Breaks in Bruch’s membrane, in color, usually found in the retinal area.
**CNVM DDx:**
- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

*Per the Retina book, what axial length serves as a useful cutoff for defining pathologic myopia?*

26.5 mm

What is the classic finding on DFE that puts high myopes at risk for CNVM?

Lacquer cracks

What are lacquer cracks?

Breaks in Bruch’s membrane, yellowish in color, usually found in the macula.
Lacquer cracks
CNVM DDx:
- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous choritis
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

Per the Retina book, what axial length serves as a useful cutoff for defining pathologic myopia?
26.5 mm

What is the classic finding on DFE that puts high myopes at risk for CNVM?
Lacquer cracks

What are lacquer cracks?
Breaks in Bruch’s membrane, yellowish in color, usually found in the macula. These breaks are the nidus for CNVM ingress in pathologic myopia.
CNVM DDx:

- ARMD
- OHS?
- Angioid streaks?
- Pathologic myopia?
- Idiopathic?
- Sorsby macular dystrophy?
- Traumatic choroidal rupture?
- Iatrogenic?
- Central serous chorioretinopathy?
- Pattern dystrophy?
- Adult-onset vitelliform dystrophy?

The ARMD chapter of the Retina book mentions one of these as being particularly likely to be misdiagnosed as CNVM, ie, to produce the impression that a CNVM is present when it isn’t—which one?
CNVM DDx:
- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

**Central serous chorioretinopathy**
- Pattern dystrophy
- Adult-onset vitelliform dystrophy

The ARMD chapter of the Retina book mentions one of these as being particularly likely to be **misdiagnosed** as CNVM, ie, to produce the impression that a CNVM is present when it isn’t—which one?
In two words, what is the underlying cause of CSC?

Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy
In two words, what is the underlying cause of CSC?
Choroidal hyperpermeability

Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy
In two words, what is the underlying cause of CSC?

- Choroidal hyperpermeability (*choriocapillaris hyperpermeability* is correct as well, and may even be preferred)

Central serous chorioretinopathy

- Pattern dystrophy
- Adult-onset vitelliform dystrophy
In two words, what is the underlying cause of CSC?

Choroidal hyperpermeability (*choriocapillaris hyperpermeability* is correct as well, and may even be preferred)

*To be clear: Is CNVM associated with CSC?*

**Central serous chorioretinopathy**

- Pattern dystrophy
- Adult-onset vitelliform dystrophy
**Central serous chorioretinopathy**

- Pattern dystrophy
- Adult-onset vitelliform dystrophy

---

*In two words, what is the underlying cause of CSC?*

- Choroidal hyperpermeability (*choriocapillaris hyperpermeability* is correct as well, and may even be preferred)

*To be clear: Is CNVM associated with CSC?*

- **Yes**—2ndry CNVM can and does occur in CSC, albeit uncommonly.
In two words, what is the underlying cause of CSC?

Choroidal hyperpermeability (choriocapillaris hyperpermeability is correct as well, and may even be preferred)

To be clear: Is CNVM associated with CSC?

Yes—2ndry CNVM can and does occur in CSC, albeit uncommonly.

The takeaway point: CSC can both cause CNVM and masquerade as it.

Central serous chorioretinopathy

- Pattern dystrophy
- Adult-onset vitelliform dystrophy
In two words, what is the underlying cause of CSC?
Choroidal hyperpermeability (*choriocapillaris hyperpermeability* is correct as well, and may even be preferred)

*To be clear: Is CNVM associated with CSC?*
Yes—2ndry CNVM can and does occur in CSC, albeit uncommonly.
The takeaway point: CSC can both cause CNVM *and* masquerade as it.

For the CSC cases in which no CNVM is present: What clinical finding, common to both wet ARMD and CSC, is responsible for the misdiagnosis?

**Central serous chorioretinopathy**
- Pattern dystrophy
- Adult-onset vitelliform dystrophy
In two words, what is the underlying cause of CSC?

Choroidal hyperpermeability *(choriocapillaris hyperpermeability is correct as well, and may even be preferred)*

To be clear: Is CNVM associated with CSC?

Yes—2ndry CNVM can and does occur in CSC, albeit uncommonly. The takeaway point: CSC can both cause CNVM and masquerade as it.

For the CSC cases in which no CNVM is present: What clinical finding, common to both wet ARMD and CSC, is responsible for the misdiagnosis?

The presence of SRF on OCT

Central serous chorioretinopathy

- Pattern dystrophy
- Adult-onset vitelliform dystrophy
In two words, what is the underlying cause of CSC? Choroidal hyperpermeability (choriocapillaris hyperpermeability is correct as well, and may even be preferred)

To be clear: Is CNVM associated with CSC? Yes—2ndry CNVM can and does occur in CSC, albeit uncommonly. The takeaway point: CSC can both cause CNVM and masquerade as it.

For the CSC cases in which no CNVM is present: What clinical finding, common to both wet ARMD and CSC, is responsible for the misdiagnosis? The presence of SRF on OCT

What distinguishes SRF seen on OCT in CNVM from that seen in CSC?

Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy
In two words, what is the underlying cause of CSC?
Choroidal hyperpermeability (choriocapillaris hyperpermeability is correct as well, and may even be preferred)

To be clear: Is CNVM associated with CSC?
Yes—2ndry CNVM can and does occur in CSC, albeit uncommonly.
The takeaway point: CSC can both cause CNVM and masquerade as it.

For the CSC cases in which no CNVM is present: What clinical finding, common to both wet ARMD and CSC, is responsible for the misdiagnosis?
The presence of SRF on OCT

What distinguishes SRF seen on OCT in CNVM from that seen in CSC?
In CNVM there is usually a concomitant , whereas this will not be present in CSC (absent a 2ndry CNVM)

★ Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy
In two words, what is the underlying cause of CSC?
Choroidal hyperpermeability (choriocapillaris hyperpermeability is correct as well, and may even be preferred)

To be clear: Is CNVM associated with CSC?
Yes—2ndry CNVM can and does occur in CSC, albeit uncommonly.
The takeaway point: CSC can both cause CNVM and masquerade as it.

For the CSC cases in which no CNVM is present: What clinical finding, common to both wet ARMD and CSC, is responsible for the misdiagnosis?
The presence of SRF on OCT

What distinguishes SRF seen on OCT in CNVM from that seen in CSC?
In CNVM there is usually a concomitant subretinal hemorrhage, whereas this will not be present in CSC (absent a 2ndry CNVM)

Central serous chorioretinopathy

Pattern dystrophy
Adult-onset vitelliform dystrophy
**ARMD**: PED (△) and SRF (↓), along with subretinal hemorrhage (*)

**CSC**: PED and SRF, but no hemorrhage
In two words, what is the underlying cause of CSC?
Choroidal hyperpermeability (*choriocapillaris hyperpermeability* is correct as well, and may even be preferred)

To be clear: Is CNVM associated with CSC?
Yes—2ndry CNVM can and does occur in CSC, albeit uncommonly. The takeaway point: CSC can both cause CNVM *and* masquerade as it.

For the CSC cases in which no CNVM is present: What clinical finding.
There is another important OCT finding that distinguishes CSC from ARMD—what is it?

**Central serous chorioretinopathy**

- Pattern dystrophy
- Adult-onset vitelliform dystrophy
In two words, what is the underlying cause of CSC?
Choroidal hyperpermeability (choriocapillaris hyperpermeability is correct as well, and may even be preferred)

To be clear: Is CNVM associated with CSC?
Yes—2ndry CNVM can and does occur in CSC, albeit uncommonly.
The takeaway point: CSC can both cause CNVM and masquerade as it.

For the CSC cases in which no CNVM is present: What clinical finding, common to both wet ARMD and CSC, is responsible for the misdiagnosis?
The presence of SRF on OCT

What distinguishes SRF seen on OCT in CNVM from that seen in CSC?
In CNVM there is usually a concomitant subretinal hemorrhage, whereas this will not be present in CSC (absent a 2ndry CNVM)

There is another important OCT finding that distinguishes CSC from ARMD—what is it?
The thickness of the choroid

Central serous chorioretinopathy

Pattern dystrophy

Adult-onset vitelliform dystrophy
In two words, what is the underlying cause of CSC?

- Choroidal hyperpermeability (*choriocapillaris hyperpermeability* is correct as well, and may even be preferred)

To be clear: Is CNVM associated with CSC?

- Yes—2ndry CNVM can and does occur in CSC, albeit uncommonly.

The takeaway point: CSC can both cause CNVM and masquerade as it.

For the CSC cases in which no CNVM is present: What clinical finding, common to both wet ARMD and CSC, is responsible for the misdiagnosis?

- The presence of SRF on OCT

What distinguishes SRF seen on OCT in CNVM from that seen in CSC?

- In CNVM there is usually a concomitant subretinal hemorrhage, whereas this will not be present in CSC (absent a 2ndry CNVM)

There is another important OCT finding that distinguishes CSC from ARMD—what is it?

- The thickness of the choroid. It tends to be normal or thinned in ARMD, but thickened in CSC.

Central serous chorioretinopathy

- Pattern dystrophy
- Adult-onset vitelliform dystrophy
In two words, what is the underlying cause of CSC?
Choroidal hyperpermeability (*choriocapillaris hyperpermeability* is correct as well, and may even be preferred)

*To be clear: Is CNVM associated with CSC?*
**Yes**—2ndry CNVM can and does occur in CSC, albeit uncommonly. The takeaway point: CSC can both cause CNVM and masquerade as it.

*For the CSC cases in which no CNVM is present: What clinical finding, common to both wet ARMD and CSC, is responsible for the misdiagnosis?*
The presence of SRF on OCT

What distinguishes SRF seen on OCT in CNVM from that seen in CSC?
In CNVM there is usually a concomitant subretinal hemorrhage, whereas this will not be present in CSC (absent a 2ndry CNVM)

There is another important OCT finding that distinguishes CSC from ARMD—what is it?
The thickness of the choroid. It tends to be normal or thinned in ARMD, but thickened in CSC.

**Central serous chorioretinopathy**
- Pattern dystrophy
- Adult-onset vitelliform dystrophy
The choroid is seen in cross section. Subfoveal choroidal thickness was measured vertically from the outer border of the RPE to the inner border of the sclera (brackets) in a healthy eye in a 55-year-old man (A) and in 3 representative eyes with CSC: in a 44-year-old man (B), a 57-year-old man (C), and a 63-year-old man (D).
In two words, what is the underlying cause of CSC? Choroidal hyperpermeability (*choriocapillaris hyperpermeability* is correct as well, and may even be preferred)

*To be clear: Is CNVM associated with CSC?*

**Yes**—2ndry CNVM can and does occur in CSC, albeit uncommonly. The takeaway point: CSC can both cause CNVM and masquerade as it.

For the CSC cases in which no CNVM is present: What clinical finding, common to both wet ARMD and CSC, is responsible for the misdiagnosis?

The presence of SRF on OCT

What distinguishes SRF seen on OCT in CNVM from that seen in CSC?

In CNVM there is usually a concomitant subretinal hemorrhage, whereas this will not be present in CSC (absent a 2ndry CNVM).

There is another important OCT finding that distinguishes CSC from ARMD—what is it? The thickness of the choroid. It tends to be normal or thinned in ARMD, but thickened in CSC.

**Choroidal thickness may not be readily interpretable on spectral-domain OCT (SD-OCT). What OCT modality is preferred for assessing the choroid?** Enhanced-depth imaging OCT (EDI-OCT)

★ Central serous chorioretinopathy

- Pattern dystrophy
- Adult-onset vitelliform dystrophy
In two words, what is the underlying cause of CSC? Choroidal hyperpermeability (*choriocapillaris* hyperpermeability is correct as well, and may even be preferred)

*To be clear: Is CNVM associated with CSC?*

Yes—2ndry CNVM can and does occur in CSC, albeit uncommonly. The takeaway point: CSC can both cause CNVM and masquerade as it.

*For the CSC cases in which no CNVM is present: What clinical finding is common to both wet ARMD and CSC, responsible for the misdiagnosis?*

The presence of SRF on OCT

*What distinguishes SRF seen on OCT in CNVM from that seen in CSC?*

In CNVM there is usually a concomitant subretinal hemorrhage, whereas this will not be present in CSC (absent a 2ndry CNVM)

*There is another important OCT finding that distinguishes CSC from ARMD—what is it?*

The thickness of the choroid. It tends to be normal or thinned in ARMD, but thickened in CSC.

*Choroidal thickness may not be readily interpretable on spectral-domain OCT (SD-OCT). What OCT modality is preferred for assessing the choroid?*

Enhanced-depth imaging OCT (EDI-OCT)

★ **Central serous chorioretinopathy**

- Pattern dystrophy
- Adult-onset vitelliform dystrophy
Dry ARMD

Regarding conditions that can be misdiagnosed as dry ARMD—what feature do they have in common?

- ARMD
- OHS
- Angiod streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy
Dry ARMD

Regarding conditions that can be misdiagnosed as dry ARMD—what feature do they have in common? Abnormalities of the RPE

CNVM

DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic
- Central serous chorioretinopathy
- Pattern dystrophy
- Adult-onset vitelliform dystrophy
Dry ARMD

CNVM DDx:

- ARMD
- OHS?
- Angioid streaks?
- Pathologic myopia?
- Idiopathic?
- Sorsby macular dystrophy?
- Traumatic choroidal rupture?
- Iatrogenic?
- Central serous chorioretinopathy?
- Pattern dystrophy?
- Adult-onset vitelliform dystrophy?

The ARMD chapter of the Retina book mentions three of these as being particularly likely to produce a misdiagnosis of dry ARMD—which three?
Dry ARMD

CNVM DDx:
- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

★ Central serous chorioretinopathy
★ Pattern dystrophy
★ Adult-onset vitelliform dystrophy

The ARMD chapter of the Retina book mentions three of these as being particularly likely to produce a misdiagnosis of dry ARMD—which three?

(Yes, CSC is a prominent member of the DDx for both wet and dry ARMD!)
Dry ARMD

CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

How does CSC—a choroidal condition that produces serous detachments—acquire the RPE abnormalities that characterize dry ARMD masqueraders?

Central serous chorioretinopathy

Pattern dystrophy

Adult-onset vitelliform dystrophy
Dry ARMD

How does CSC—a choroidal condition that produces serous detachments—acquire the RPE abnormalities that characterize dry ARMD masqueraders?

If the SRF is chronic, it can produce RPE mottling

Central serous chorioretinopathy

Pattern dystrophy

Adult-onset vitelliform dystrophy
CSC: RPE mottling
Dry ARMD

How does CSC—a choroidal condition that produces serous detachments—acquire the RPE abnormalities that characterize dry ARMD masqueraders?

If the SRF is chronic, it can produce RPE mottling.

Because SRF is subject to gravity-induced downward migration, the RPE changes often demonstrate a particular pattern. What are the formal and informal names for this pattern?

Central serous chorioretinopathy

Pattern dystrophy

Adult-onset vitelliform dystrophy
Dry ARMD

CNVM

DDx:

• ARMD
• OHS
• Angioid streaks
• Pathologic myopia
• Idiopathic
• Sorsby macular dystrophy
• Traumatic choroidal rupture
• Iatrogenic
• Central serous chorioretinopathy
• Pattern dystrophy
• Adult-onset vitelliform dystrophy

How does CSC—a choroidal condition that produces serous detachments—acquire the RPE abnormalities that characterize dry ARMD masqueraders?

If the SRF is chronic, it can produce RPE mottling

Because SRF is subject to gravity-induced downward migration, the RPE changes often demonstrate a particular pattern. What are the formal and informal names for this pattern?

Descending tracts, aka ‘guttering’
CSC: Descending tracts. These are best seen via fundus autofluorescence imaging.
CSC: Descending tracts. These are best seen via fundus autofluorescence imaging.

For more on CSC, see slide-set R47
Briefly, what is a pattern dystrophy?

Pattern dystrophy

Adult-onset vitelliform dystrophy
**Pattern dystrophy**

★ Adult-onset vitelliform dystrophy
Briefly, what is a pattern dystrophy?
An inherited macular dystrophy that has a characteristic appearance (ie, a particular ‘pattern’)

What is the inheritance pattern?

Pattern dystrophy
Adult-onset vitelliform dystrophy
Briefly, what is a pattern dystrophy?
An inherited macular dystrophy that has a characteristic appearance (ie, a particular ‘pattern’)

What is the inheritance pattern?
AD

★ Pattern dystrophy
★★ Adult-onset vitelliform dystrophy
**Dry ARMD**

**CNVM DDx:**

**Briefly, what is a pattern dystrophy?**
An inherited macular dystrophy that has a characteristic appearance (i.e., a particular ‘pattern’)

**What is the inheritance pattern?**
AD

**Are pattern dystrophies associated with severe vision loss?**

**Pattern dystrophy**

**Adult-onset vitelliform dystrophy**
Briefly, what is a pattern dystrophy?
An inherited macular dystrophy that has a characteristic appearance (ie, a particular ‘pattern’)

What is the inheritance pattern?
AD

Are pattern dystrophies associated with severe vision loss?
Generally no--vision is only slightly affected

Pattern dystrophy
Adult-onset vitelliform dystrophy
**Pattern dystrophy**

★ Adult-onset vitelliform dystrophy
Briefly, what is a pattern dystrophy?
An inherited macular dystrophy that has a characteristic appearance (ie, a particular ‘pattern’)

What is the inheritance pattern?
AD

Are pattern dystrophies associated with severe vision loss?
Generally no--vision is only slightly affected

Do the macular ‘patterns’ appear early in life?
Generally no--they usually show up in middle adulthood

★ Pattern dystrophy
★ Adult-onset vitelliform dystrophy
Briefly, what is a pattern dystrophy?
An inherited macular dystrophy that has a characteristic appearance (ie, a particular ‘pattern’)

What is the inheritance pattern?
AD

Are pattern dystrophies associated with severe vision loss?
Generally no--vision is only slightly affected

Do the macular ‘patterns’ appear early in life?
Generally no--they usually show up in middle adulthood

The BCSC Retina book identifies four pattern dystrophies by name--what are they?
--
--
--

★ Pattern dystrophy
★ Adult-onset vitelliform dystrophy
**Pattern dystrophy**

Adult-onset vitelliform dystrophy
Briefly, what is a pattern dystrophy?
An inherited macular dystrophy that has a characteristic appearance (ie, a particular ‘pattern’)

What is the inheritance pattern?
AD

Are pattern dystrophies associated with severe vision loss?
Generally no--vision is only slightly affected

Do the macular ‘patterns’ appear early in life?
Generally no--they usually show up in middle adulthood

The BCSC Retina book identifies four pattern dystrophies by name--what are they?
--B
--A
--R
--F

The mnemonic is…BARF?

★ Pattern dystrophy
★ Adult-onset vitelliform dystrophy
Dry ARMD

Briefly, what is a pattern dystrophy?
An inherited macular dystrophy that has a characteristic appearance (ie, a particular ‘pattern’)

What is the inheritance pattern?
AD

Are pattern dystrophies associated with severe vision loss?
Generally no--vision is only slightly affected

Do the macular ‘patterns’ appear early in life?
Generally no--they usually show up in middle adulthood

The BCSC Retina book identifies four pattern dystrophies by name--what are they?  
--Butterfly dystrophy  
--Adult-onset foveomacular vitelliform dystrophy  
--Reticular dystrophy  
--Fundus pulverulentus

Pattern dystrophy

Adult-onset vitelliform dystrophy
Butterfly dystrophy

Adult-onset foveomacular vitelliform dystrophy

Reticular dystrophy

Fundus pulverulentus
Briefly, what is a pattern dystrophy?
An inherited macular dystrophy that has a characteristic appearance (ie, a particular ‘pattern’)

What is the inheritance pattern?
AD

Are pattern dystrophies associated with severe vision loss?
Generally no--vision is only slightly affected

Do the macular ‘patterns’ appear early in life?
Generally no--they usually show up in middle adulthood

The BCSC Retina book identifies four pattern dystrophies by name--what are they?
--Butterfly dystrophy
--Adult-onset foveomacular vitelliform dystrophy
--Reticular dystrophy
--Fundus pulverulentus

These terms are awfully similar…Do they refer to the same, or different conditions?

★ Pattern dystrophy
★ Adult-onset vitelliform dystrophy
**Pattern dystrophy**

**Adult-onset vitelliform dystrophy**

*Briefly, what is a pattern dystrophy?*
An inherited macular dystrophy that has a characteristic appearance (ie, a particular ‘pattern’)

*What is the inheritance pattern?*
AD

*Are pattern dystrophies associated with severe vision loss?*
Generally no--vision is only slightly affected

*Do the macular ‘patterns’ appear early in life?*
Generally no--they usually show up in middle adulthood

*The BCSC Retina book identifies four pattern dystrophies by name--what are they?*
--Butterfly dystrophy
--Adult-onset foveomacular vitelliform dystrophy
--Reticular dystrophy
--Fundus pulverulentus

*These terms are awfully similar…Do they refer to the same, or different conditions?*
The same (the *Retina* book uses both)
Dry ARMD

At what age do AOVD lesions appear?

30s to 50s

What do pts c/o initially?

Not much—maybe a little blurring or metamorphopsia

What does DFE reveal?

Bilateral vitelliform (which means egg-yolk like) lesions

How might such a lesion lead to a misdiagnosis of dry ARMD?

Its DFE and OCT appearance could be misinterpreted as representative of a drusenoid PED
Dry ARMD

**CNVM DDx:**
- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

★ Central serous chorioretinopathy
★ Pattern dystrophy
★ **Adult-onset vitelliform dystrophy**

At what age do AOVD lesions appear?
30s to 50s
**Dry ARMD**

**CNVM DDx:**
- ARM
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

**Central serous chorioretinopathy**

**Pattern dystrophy**

**Adult-onset vitelliform dystrophy**

---

At what age do AOVD lesions appear?
30s to 50s

What do pts c/o initially?

What do pts c/o initially?
**Dry ARMD**

- At what age do AOVD lesions appear?
  30s to 50s

- What do pts c/o initially?
  Not much—maybe a little blurring or metamorphopsia

- What does DFE reveal?
  Bilateral vitelliform (which means egg-yolk like) lesions

- How might such a lesion lead to a misdiagnosis of dry ARMD?
  Its DFE and OCT appearance could be misinterpreted as representative of a drusenoid PED

- Adult-onset vitelliform dystrophy
Dry ARMD

At what age do AOVD lesions appear?
30s to 50s

What do pts c/o initially?
Not much—maybe a little blurring or metamorphopsia

What does DFE reveal?
Bilateral vitelliform (which means egg-yolk like) lesions

How might such a lesion lead to a misdiagnosis of dry ARMD?
Its DFE and OCT appearance could be misinterpreted as representative of a drusenoid PED

Adult-onset vitelliform dystrophy
Dry ARMD

CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

Adult-onset vitelliform dystrophy

At what age do AOVD lesions appear?
30s to 50s

What do pts c/o initially?
Not much—maybe a little blurring or metamorphopsia

What does DFE reveal?
Bilateral vitelliform (which means like) lesions

Central serous chorioretinopathy
Pattern dystrophy
Dry ARMD

CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

Central serous chorioretinopathy
Pattern dystrophy

★ Adult-onset vitelliform dystrophy

At what age do AOVD lesions appear?
30s to 50s

What do pts c/o initially?
Not much—maybe a little blurring or metamorphopsia

What does DFE reveal?
Bilateral vitelliform (which means egg-yolk like) lesions
Dry ARMD

CNVM _DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

★ Central serous chorioretinopathy
★ Pattern dystrophy
★ Adult-onset vitelliform dystrophy

At what age do AOVD lesions appear?
30s to 50s

What do pts c/o initially?
Not much—maybe a little blurring or metamorphopsia

What does DFE reveal?
Bilateral vitelliform (which means egg-yolk-like) lesions

Because they’re egg-yolk-like, what can you infer about the vitelliform lesion’s:
--Color?
Yellow(ish)
--Shape?
Round
--Contour?
Domed
Dry ARMD

CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

At what age do AOVD lesions appear?
30s to 50s

What do pts c/o initially?
Not much—maybe a little blurring or metamorphopsia

What does DFE reveal?
Bilateral vitelliform (which means egg-yolk like) lesions

Because they’re egg-yolk-like, what can you infer about the vitelliform lesion’s:
-- Color? Yellow(ish)

-- Shape? Round

-- Contour? Domed

★ Central serous chorioretinopathy
★ Pattern dystrophy
★ Adult-onset vitelliform dystrophy
Dry ARMD

CNVM DDx:

- ARMD
- OHS
- Angiomatous
growth
- Pathologic
myopia
- Sorsby
macular
dystrophy
- Traumatic
central serous
chorioretinopathy
- Pattern
dystrophy
- Adult-onset
telliform dystrophy

At what age do AOVD lesions appear?
30s to 50s

What do pts c/o initially?
Not much—maybe a little blurring or metamorphopsia

What does DFE reveal?
Bilateral vitelliform (which means egg-yolk-like) lesions

Because they’re egg-yolk-like, what can you infer about the vitelliform lesion’s:
--Color? Yellow(ish)
--Shape?

What does DFE reveal?
Bilateral vitelliform (which means egg-yolk-like) lesions
Dry ARMD

At what age do AOVD lesions appear?
30s to 50s

What do pts c/o initially?
Not much—maybe a little blurring or metamorphopsia

What does DFE reveal?
Bilateral vitelliform (which means egg-yolk-like) lesions

Because they’re egg-yolk-like, what can you infer about the vitelliform lesion’s:
--Color? Yellow(ish)
--Shape? Round

--Contour? Domed
Typical round, yellow lesion of AOVD
**Dry ARMD**

- CNVM^\_DDx:
  - ARMD
  - OHS
  - Angioid streaks
  - Pathologic myopia
  - Idiopathic
  - Sorsby macular dystrophy
  - Traumatic choroidal rupture
  - Iatrogenic

★ Central serous chorioretinopathy
★ Pattern dystrophy
★ **Adult-onset vitelliform dystrophy**

**At what age do AOVD lesions appear?**
30s to 50s

**What do pts c/o initially?**
Not much—maybe a little blurring or metamorphopsia

**What does DFE reveal?**
Bilateral vitelliform (which means egg-yolk-like) lesions

Because they’re egg-yolk-like, what can you infer about the vitelliform lesion’s:
--Color? Yellow(ish)
--Shape? Round
--Contour? 

**egg-yolk like**
Dry ARMD

At what age do AOVD lesions appear?
30s to 50s

What do pts c/o initially?
Not much—maybe a little blurring or metamorphopsia

What does DFE reveal?
Bilateral vitelliform (which means egg-yolk-like) lesions

Because they’re egg-yolk-like, what can you infer about the vitelliform lesion’s:
---Color? Yellow(ish)
---Shape? Round
---Contour? Domed

Adult-onset vitelliform dystrophy
OCT showing dome-like lesion in AOVD
Dry ARMD

CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

At what age do AOVD lesions appear?
30s to 50s

What do pts c/o initially?
Not much—maybe a little blurring or metamorphopsia

What does DFE reveal?
Bilateral vitelliform (which means egg-yolk like) lesions

How might such a lesion lead to a misdiagnosis of dry ARMD?

★ Central serous chorioretinopathy
★ Pattern dystrophy
★ Adult-onset vitelliform dystrophy
**Dry ARMD**

**CNVM DDx:**
- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

★ Central serous chorioretinopathy
★ Pattern dystrophy
★ **Adult-onset vitelliform dystrophy**

---

At what age do AOVD lesions appear?
30s to 50s

What do pts c/o initially?
Not much—maybe a little blurring or metamorphopsia

What does DFE reveal?
Bilateral vitelliform (which means *egg-yolk like*) lesions

How might such a lesion lead to a misdiagnosis of dry ARMD?
Its DFE and OCT appearance could be misinterpreted as representative of a drusenoid PED
Here’s a clinical challenge: AOVD in a patient with extensive drusen. Fundus photo demonstrates drusen, and an ill-defined vitelliform lesion. OCT shows the material over the soft drusen (yellow arrow) that could be misinterpreted as a CNVM related to wet ARMD.
Here’s a clinical challenge: AOVD in a patient with extensive drusen. Fundus photo demonstrates drusen, and an ill-defined vitelliform lesion. OCT shows the material over the soft drusen (yellow arrow) that could be misinterpreted as a CNVM related to wet ARMD.

For more on the pattern dystrophies, see slide-set R11
Dry ARMD

CNVM DDx:
- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

★ Central serous chorioretinopathy
★ Pattern dystrophy
★ Vitelliform dystrophy
★?

Finally: The book emphasizes another condition (not on this list—yet) as being high on the DDx for dry ARMD—what is it?
Dry ARMD

CNVM DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

★ Central serous chorioretinopathy
★ Pattern dystrophy
★ Vitelliform dystrophy
★ Drug toxicity

Finally: The book emphasizes another condition (not on this list—yet) as being high on the DDx for dry ARMD—what is it?
Dry ARMD

CNVM DDx:
- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

★ Central serous chorioretinopathy
★ Pattern dystrophy
★ Vitelliform dystrophy
★ Drug toxicity, especially...
Dry ARMD

CNVM^DDx:

- ARMD
- OHS
- Angioid streaks
- Pathologic myopia
- Idiopathic
- Sorsby macular dystrophy
- Traumatic choroidal rupture
- Iatrogenic

★ Central serous chorioretinopathy
★ Pattern dystrophy
★ Vitelliform dystrophy
★ **Drug toxicity**, especially... hydroxychloroquine

Finally: The book emphasizes another condition (not on this list—yet) as being high on the DDx for dry ARMD—what is it?
Dry ARMD

CNVM DDx:
- ARMD
- OHS
- Angioid streaks
- Pathologic myopia

Finally: The book emphasizes another condition (not on this list—yet) as being high on the DDx for dry ARMD—what is it?

*Plaquenil maculopathy is covered in slide-set R25*
Age-related macular degeneration (ARMD) is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: Nonexudative and exudative. Abnormalities in ARMD are typical.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

**Age** is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

The two RPE changes most typical of ARMD are:
-- Atrophy (we knew this one already because of GA)
-- Focal
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: Nonexudative and exudative. RPE abnormalities in ARMD are typical.

*The two RPE changes most typical of ARMD are:*
--Atrophy (we knew this one already because of GA)
--Focal hyperpigmentation
ARMD: RPE hyperpigmentation
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

**Age** is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of **drusen** in the macula.

There are two types: **Nonexudative** and **exudative**.

**RPE** abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

What’s abnormal about the photoreceptors (PRs) in ARMD?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

What’s abnormal about the photoreceptors (PRs) in ARMD?

They are reduced in density (ie, they die off)
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations

Age is the strongest risk factor for ARMD

The clinical hallmark of ARMD is the presence of drusen in the macula

There are two types: Nonexudative and exudative

RPE abnormalities in ARMD are typical

Photoreceptors in ARMD are abnormal as well

What’s abnormal about the photoreceptors (PRs) in ARMD? They are reduced in density (ie, they die off)

Do the RPE abnormalities cause the PR abnormalities?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

What’s abnormal about the photoreceptors (PRs) in ARMD?
They are reduced in density (ie, they die off)

Do the RPE abnormalities cause the PR abnormalities?
I’s not clear how changes in the RPE and PR are causally linked to one another.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

What’s abnormal about the photoreceptors (PRs) in ARMD?
They are reduced in density (ie, they die off).

Do the RPE abnormalities cause the PR abnormalities?
It’s not clear how changes in the RPE and PR are causally linked to one another. That is, we don’t know for certain whether RPE damage leads to PR damage, or PR to RPE, or whether both result from some other cause.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

What’s abnormal about the photoreceptors (PRs) in ARMD? They are reduced in density (ie, they die off).

Do the RPE abnormalities cause the PR abnormalities? It’s not clear how changes in the RPE and PR are causally linked to one another. That is, we don’t know for certain whether RPE damage leads to PR damage, or PR to RPE, or whether both result from some other cause.

Speaking of being unsure about causality in ARMD…
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

So, changes in ARMD include:

--Basal laminar/linear deposits accumulate.

No question—advance when ready.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

So, changes in ARMD include:

--Basal laminar/linear deposits accumulate

--Ultrastructural changes in the pigment epithelium include loss of melanin granules, formation of lipofuscin granules, and accumulation of residual bodies.

No question—advance when ready.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

So, changes in ARMD include:
--Basal laminar/linear deposits accumulate
--Ultrastructural changes in the pigment epithelium include loss of melanin granules, formation of lipofuscin granules, and accumulation of residual bodies
--Photoreceptors are reduced in density and distribution.

No question—advance when ready.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

So, changes in ARMD include:
--Basal laminar/linear deposits accumulate
--Ultrastructural changes in the pigment epithelium include loss of melanin granules, formation of lipofuscin granules, and accumulation of residual bodies
--Photoreceptors are reduced in density and distribution

Which if any of these can occur as part of the normal aging process?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

So, changes in ARMD include:
--Basal laminar/linear deposits accumulate
--Ultrastructural changes in the pigment epithelium include loss of melanin granules, formation of lipofuscin granules, and accumulation of residual bodies
--Photoreceptors are reduced in density and distribution.

Which if any of these can occur as part of the normal aging process? All of them. This is one of the challenges of ARMD—finding a bright line between its pathologic changes and those associated with normal aging.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

So, changes in ARMD include:

--Basal laminar/linear deposits accumulate
--Ultrastructural changes in the pigment epithelium include loss of melanin granules, formation of lipofuscin granules, and accumulation of residual bodies
--Photoreceptors are reduced in density and distribution.

Which if any of these can occur as part of the normal aging process? All of them. This is one of the challenges of ARMD—finding a bright line between its pathologic changes and those associated with normal aging. Normal aging changes can be observed in the outer retina, RPE, Bruch’s membrane, and choriocapillaris, and many of these changes are difficult to separate from those seen in ARMD.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: **Nonexudative** and **exudative**. RPE abnormalities in ARMD are typical. Photoreceptors in ARMD are abnormal as well. The pathogenesis of ARMD is not well understood; that said, the complement system is strongly implicated in it.
Age-related macular degeneration (ARMD) is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: Nonexudative and exudative. RPE abnormalities in ARMD are typical. Photoreceptors in ARMD are abnormal as well. The pathogenesis of ARMD is not well understood; that said, the complement system is strongly implicated in it.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: nonexudative and exudative. RPE abnormalities in ARMD are typical. Photoreceptors in ARMD are abnormal as well. The pathogenesis of ARMD is not well understood; that said, the complement system is strongly implicated in it.

What is the complement system?
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

The pathogenesis of ARMD is not well understood; that said, the complement system is strongly implicated in it.

What is the complement system? To answer this, we need to unpack the notion of the immune response...
Immune response

What are the two fundamental immune responses?
What are the two fundamental immune responses?
Immune response

Innate
aka.. immunity

Adaptive
aka... immunity

What word is used to capture the essence of each?
Immune response

Innate
aka...natural immunity

Adaptive
aka...acquired immunity

What word is used to capture the essence of each?
Immune response

**Innate**
aka... *natural* immunity

*does not provide immediate protection*

**Adaptive**
aka... *acquired* immunity

*does not provide immediate protection*

*Which provides immediate protection against antigens deemed threatening?*
Immune response

<table>
<thead>
<tr>
<th>Innate</th>
<th>Adaptive</th>
</tr>
</thead>
<tbody>
<tr>
<td>aka...natural immunity</td>
<td>aka...acquired immunity</td>
</tr>
<tr>
<td>Does provide immediate protection</td>
<td>Does not provide immediate protection</td>
</tr>
</tbody>
</table>

Which provides immediate protection against antigens deemed threatening?
Immune response

**Innate**
- aka... **natural** immunity
- Does **not** provide immediate protection
- require previous contact with the threat

**Adaptive**
- aka... **acquired** immunity
- Does **not** provide immediate protection
- require previous contact with the threat

*Which must have previous experience with an antigen to gain the capacity to neutralize it?*
**Immune response**

<table>
<thead>
<tr>
<th>Innate</th>
<th>Adaptive</th>
</tr>
</thead>
<tbody>
<tr>
<td>aka…<strong>natural</strong> immunity</td>
<td>aka…<strong>acquired</strong> immunity</td>
</tr>
<tr>
<td><strong>Does</strong> provide immediate protection</td>
<td><strong>Does not</strong> provide immediate protection</td>
</tr>
<tr>
<td><strong>Does not</strong> require previous contact with the threat</td>
<td><strong>Does</strong> require previous contact with the threat</td>
</tr>
</tbody>
</table>

Which must have previous experience with an antigen to gain the capacity to neutralize it?
Immune response

**Innate**
aka…natural immunity
Does provide immediate protection
Does not require previous contact with the threat
Primary effector cells: --?
--?

**Adaptive**
aka…acquired immunity
Does not provide immediate protection
Does require previous contact with the threat
Primary effector cells: --?
--?

What are the primary effector cells for each?
Immune response

Innate
aka…natural immunity

Does not provide immediate protection

Does not require previous contact with the threat

Primary effector cells:
--PMNs
--Monocytes/macrophages

Adaptive
aka…acquired immunity

Does not provide immediate protection

Does require previous contact with the threat

Primary effector cells:
--T cells
--B cells

What are the primary effector cells for each?
The *innate* (or *natural*) immune response relies on ‘preprogrammed’ immune cells to recognize foreign material encountered in tissue or blood, whereas the *adaptive* (or *acquired*) immune response involves ‘education,’ with surveillance cells learning to recognize and remember foreign material.

Primary effector cells:
- PMNs
- Monocytes/macrophages

Primary effector cells:
- T cells
- B cells
The *innate* (or *natural*) immune response relies on ‘preprogrammed’ immune cells to recognize foreign material encountered in tissue or blood, whereas the *adaptive* (or *acquired*) immune response involves ‘education,’ with surveillance cells learning to recognize and remember foreign material. All that said, neither response type is adequate in and of itself to produce an effective immune response. Instead, both rely on inflammatory mediators—host-generated substances that act as force-multipliers for innate and/or adaptive immune responses.

**Primary effector cells:**
- PMNs
- Monocytes/macrophages

**Primary effector cells:**
- T cells
- B cells
The *innate* (or *natural*) immune response relies on ‘preprogrammed’ immune cells to recognize foreign material encountered in tissue or blood, whereas the *adaptive* (or *acquired*) immune response involves ‘education,’ with surveillance cells learning to recognize and remember foreign material. All that said, neither response type is adequate in and of itself to produce an effective immune response. Instead, both rely on *inflammatory mediators*—host-generated substances that act as force-multipliers for innate and/or adaptive immune responses.

Primary effector cells:
- PMNs
- Monocytes/macrophages

Primary effector cells:
- T cells
- B cells
Immune response

**Innate**

aka...natural immunity

Primary effector cells:
--PMNs
--Monocytes/macrophages

**Adaptive**

aka...acquired immunity

Primary effector cells:
--T cells
--B cells

The *innate* (or natural) immune response relies on ‘preprogrammed’ immune cells to recognize foreign material encountered in tissue or blood, whereas the *adaptive* (or acquired) immune response involves ‘education,’ with surveillance cells learning to recognize and remember foreign material. All that said, neither response type is adequate in and of itself to produce an effective immune response. Instead, both rely on **inflammatory mediators**—host-generated substances that act as force-multipliers for innate and/or adaptive immune responses. Inflammatory mediators can be a single molecule, or a complex enzymatic cascade.
The *innate* (or *natural*) immune response relies on ‘preprogrammed’ immune cells to recognize foreign material encountered in tissue or blood, whereas the *adaptive* (or *acquired*) immune response involves ‘education,’ with surveillance cells learning to recognize and remember foreign material. All that said, *neither* response type is adequate in and of itself to produce an effective immune response. Instead, both rely on *inflammatory mediators*—host-generated substances that act as force-multipliers for innate and/or adaptive immune responses. *Inflammatory mediators can be a single molecule*.

**Primary effector cells:**
- PMNs
- Monocytes/macrophages

**What would be an example of a single-molecule inflammatory mediator?**
- ?
- ?
- ?

(list not exhaustive obv)
The *innate* (or *natural*) immune response relies on ‘preprogrammed’ immune cells to recognize foreign material encountered in tissue or blood, whereas the *adaptive* (or *acquired*) immune response involves ‘education,’ with surveillance cells learning to recognize and remember foreign material. All that said, neither response type is adequate in and of itself to produce an effective immune response. Instead, both rely on *inflammatory mediators*—host-generated substances that act as force-multipliers for innate and/or adaptive immune responses.

**Inflammatory mediators can be a single molecule**

What would be an example of a single-molecule inflammatory mediator?

- Histamine
- Cytokines
- PMN degranulation products

(list not exhaustive obv)
The innate (or natural) immune response relies on ‘preprogrammed’ immune cells to recognize foreign material encountered in tissue or blood, whereas the adaptive (or acquired) immune response involves ‘education,’ with surveillance cells learning to recognize and remember foreign material. All that said, neither response type is adequate in and of itself to produce an effective immune response. Instead, both rely on inflammatory mediators—host-generated substances that act as force-multipliers for innate and/or adaptive immune responses. Inflammatory mediators can be a single molecule, or a complex enzymatic cascade.

What would be an example of a single-molecule inflammatory mediator?

What is the classic example of a complex, enzymatic-cascade inflammatory mediator (and the reason for this long detour on our ARMD journey)?
The innate (or natural) immune response relies on ‘preprogrammed’ immune cells to recognize foreign material encountered in tissue or blood, whereas the adaptive (or acquired) immune response involves ‘education,’ with surveillance cells learning to recognize and remember foreign material. All that said, neither response type is adequate in and of itself to produce an effective immune response. Instead, both rely on inflammatory mediators—host-generated substances that act as force-multipliers for innate and/or adaptive immune responses. Inflammatory mediators can be a single molecule, or a complex enzymatic cascade.

**What would be an example of a single-molecule inflammatory mediator?**

--Histamine
--Cytokines
--PMN degranulation products
(list not exhaustive obv)

**What is the classic example of a complex, enzymatic-cascade inflammatory mediator (and the reason for this long detour on our ARMD journey)?**

The complement cascade
The innate (or natural) immune response relies on ‘preprogrammed’ immune cells to recognize foreign material encountered in tissue or blood, whereas the adaptive (or acquired) immune response involves ‘education,’ with surveillance cells learning to recognize and remember foreign material. All that said, neither response type is adequate in and of itself to produce an effective immune response. Instead, both rely on inflammatory mediators—host-generated substances that act as force-multipliers for innate and/or adaptive immune responses. Inflammatory mediators can be a single molecule, or a complex enzymatic cascade.

**What would be an example of a single-molecule inflammatory mediator?**

--Histamine
--Cytokines
--PMN degranulation products
(list not exhaustive obv)

**What is the classic example of a complex, enzymatic-cascade inflammatory mediator (and the reason for this long detour on our ARMD journey)?**

The complement cascade. Activation of the complement cascade results in cellular damage that is central in the pathogenesis of both dry and wet forms of ARMD.
The innate (or natural) immune response relies on ‘preprogrammed’ immune cells to recognize foreign material encountered in tissue or blood, whereas the adaptive (or acquired) immune response involves ‘education,’ with surveillance cells learning to recognize and remember foreign material. All that said, neither response type is adequate in and of itself to produce an effective immune response. Instead, both rely on inflammatory mediators—host-generated substances that act as force-multipliers for innate and/or adaptive immune responses. Inflammatory mediators can be a single molecule, or a complex enzymatic cascade.

What would be an example of a single-molecule inflammatory mediator?

- Histamine
- Cytokines
- PMN degranulation products

What is the classic example of a complex, enzymatic-cascade inflammatory mediator (and the reason for this long detour on our ARMD journey)? The complement cascade. Activation of the complement cascade results in cellular damage that is central in the pathogenesis of both dry and wet forms of ARMD.

The complement cascade is indeed complex, with ~ components comprising different pathways.
The innate (or natural) immune response relies on ‘preprogrammed’ immune cells to recognize foreign material encountered in tissue or blood, whereas the adaptive (or acquired) immune response involves ‘education,’ with surveillance cells learning to recognize and remember foreign material. All that said, neither response type is adequate in and of itself to produce an effective immune response. Instead, both rely on inflammatory mediators—host-generated substances that act as force-multipliers for innate and/or adaptive immune responses. Inflammatory mediators can be a single molecule, or a complex enzymatic cascade.

What would be an example of a single-molecule inflammatory mediator?

---

What is the classic example of a complex, enzymatic-cascade inflammatory mediator (and the reason for this long detour on our ARMD journey)?

The complement cascade. Activation of the complement cascade results in cellular damage that is central in the pathogenesis of both dry and wet forms of ARMD.

The complement cascade is indeed complex, with 30+ components comprising three different pathways.
The *innate* (or natural) immune response relies on ‘preprogrammed’ immune cells to recognize foreign material encountered in tissue or blood, whereas the *adaptive* (or acquired) immune response involves ‘education,’ with surveillance cells learning to recognize and remember foreign material. All that said, *neither* response type is adequate in and of itself to produce an effective immune response. Instead, both rely on *inflammatory mediators*—host-generated substances that act as force-multipliers for innate and/or adaptive immune responses. *Inflammatory mediators can be a single molecule, or a complex enzymatic cascade*.

**What would be an example of a single-molecule inflammatory mediator?**

--Histamine
--Cytokines
--PMN degranulation products
(list not exhaustive obv)

**What is the classic example of a complex, enzymatic-cascade inflammatory mediator (and the reason for this long detour on our ARMD journey)?**

**The complement cascade.** Activation of the complement cascade results in cellular damage that is central in the pathogenesis of both dry and wet forms of ARMD.

**The complement cascade is indeed complex, with 30+ components comprising three different pathways.** But of all these, there is one specific factor particularly important in ARMD pathogenesis. The point being, if you remember nothing else from this sidebar, remember this factor. Which one?
The innate (or natural) immune response relies on ‘preprogrammed’ immune cells to recognize foreign material encountered in tissue or blood, whereas the adaptive (or acquired) immune response involves ‘education,’ with surveillance cells learning to recognize and remember foreign material. All that said, neither response type is adequate in and of itself to produce an effective immune response. Instead, both rely on inflammatory mediators—host-generated substances that act as force-multipliers for innate and/or adaptive immune responses. Inflammatory mediators can be a single molecule, or a complex enzymatic cascade.

**What would be an example of a single-molecule inflammatory mediator?**

- Histamine
- Cytokines
- PMN degranulation products

**What is the classic example of a complex, enzymatic-cascade inflammatory mediator (and the reason for this long detour on our ARMD journey)?**

The complement cascade. Activation of the complement cascade results in cellular damage that is central in the pathogenesis of both dry and wet forms of ARMD.

The complement cascade is indeed complex, with 30+ components comprising three different pathways. But of all these, there is one specific factor particularly important in ARMD pathogenesis. The point being, if you remember nothing else from this sidebar, remember this factor. Which one? Complement factor H (CFH)
(This is a good point in the set to take a break)
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

- **Age** is the strongest risk factor for ARMD.
- The clinical hallmark of ARMD is the presence of drusen in the macula.
- There are two types: Nonexudative and exudative.
- RPE abnormalities in ARMD are typical.
- Photoreceptors in ARMD are abnormal as well.
- The pathogenesis of ARMD is not well understood; that said, the complement system is strongly implicated in it.
- VEGF plays a key role in exudative ARMD.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations

Age is the strongest risk factor for ARMD

The clinical hallmark of ARMD is the presence of drusen in the macula

There are two types: Nonexudative and exudative

RPE abnormalities in ARMD are typical

Photoreceptors in ARMD are abnormal as well

The pathogenesis of ARMD is not well understood; that said, the complement system is strongly implicated in it

VEGF plays a key role in exudative ARMD
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

The pathogenesis of ARMD is not well understood; that said, the complement system is strongly implicated in it.

Let’s drill down on VEGF for a bit…

VEGF plays a key role in exudative ARMD.
What does VEGF stand for?

VEGF-A$_{165}$
What does VEGF stand for?
Vascular endothelial growth factor
What does VEGF stand for?
Vascular endothelial growth factor

What is a growth factor?
One of a diverse group of proteins that affect cell function, including cell proliferation and tissue differentiation.

What are some other growth factors of note regarding ocular development and health?
-- Epidermal growth factor
-- Fibroblast growth factor(s)
-- Transforming growth factor β(s)
-- Insulin-like growth factor(s)
What does VEGF stand for?
Vascular endothelial growth factor

What is a growth factor?
One of a diverse group of proteins that affect cell function, including cell proliferation and tissue differentiation

VEGF-A165

ARMD
What does VEGF stand for?
Vascular endothelial growth factor

What is a growth factor?
One of a diverse group of proteins that affect cell function, including cell proliferation and tissue differentiation

What are some other growth factors of note regarding ocular development and health?
--?
--?
--?
--?
What does VEGF stand for?
Vascular endothelial growth factor

What is a growth factor?
One of a diverse group of proteins that affect cell function, including cell proliferation and tissue differentiation

What are some other growth factors of note regarding ocular development and health?
-- Epidermal growth factor
-- Fibroblast growth factor(s)
-- Transforming growth factor β(s)
-- Insulin-like growth factor(s)
What does VEGF stand for?
Vascular endothelial growth factor

What is a growth factor?
One of a diverse group of proteins that affect cell function, including cell proliferation and tissue differentiation.

What are some other growth factors of note regarding ocular development and health?
-- Epidermal growth factor
-- Fibroblast growth factor(s)
-- Transforming growth factor β(s)
-- Insulin-like growth factor(s)

When you hear ‘transforming growth factor β,’ a particular type of condition should spring to mind.

hint
What does VEGF stand for?
Vascular endothelial growth factor

What is a growth factor?
One of a diverse group of proteins that affect cell function, including cell proliferation and tissue differentiation.

What are some other growth factors of note regarding ocular development and health?
- Epidermal growth factor
- Fibroblast growth factor(s)
- Transforming growth factor $\beta(s)$
- Insulin-like growth factor(s)

When you hear ‘transforming growth factor $\beta$,’ a particular type of corneal condition should spring to mind.
What does VEGF stand for? Vascular endothelial growth factor

What is a growth factor? One of a diverse group of proteins that affect cell function, including cell proliferation and tissue differentiation.

What are some other growth factors of note regarding ocular development and health?
--Epidermal growth factor
--Fibroblast growth factor(s)
--Transforming growth factor β(s)
--Insulin-like growth factor(s)

When you hear ‘transforming growth factor β,’ a particular type of corneal condition should spring to mind. Which one?
What does VEGF stand for?
Vascular endothelial growth factor

What is a growth factor?
One of a diverse group of proteins that affect cell function, including cell proliferation and tissue differentiation.

What are some other growth factors of note regarding ocular development and health?
--Epidermal growth factor
--Fibroblast growth factor(s)
--Transforming growth factor β(s)
--Insulin-like growth factor(s)

When you hear ‘transforming growth factor β,’ a particular type of corneal condition should spring to mind. Which one? Corneal dystrophy, specifically, the so-called transforming growth factor β–induced (TGFBI) dystrophies.

There are 6 TGFBI dystrophies:
1) ?
2) ?
3) ?
4) ?
5) ?
6) ?
What does VEGF stand for?
Vascular endothelial growth factor

What is a growth factor?
One of a diverse group of proteins that affect cell function, including cell proliferation and tissue differentiation.

What are some other growth factors of note regarding ocular development and health?
--Epidermal growth factor
--Fibroblast growth factor(s)
--Transforming growth factor β(s)
--Insulin-like growth factor(s)

When you hear ‘transforming growth factor β,’ a particular type of corneal condition should spring to mind. Which one?
Corneal dystrophy, specifically, the so-called transforming growth factor β-induced (TGFBI) dystrophies

There are six TGFBI dystrophies.
What does VEGF stand for?
Vascular endothelial growth factor

What is a growth factor?
One of a diverse group of proteins that affect cell function, including cell proliferation and tissue differentiation

What are some other growth factors of note regarding ocular development and health?
--Epidermal growth factor
--Fibroblast growth factor(s)
--Transforming growth factor β(s)
--Insulin-like growth factor(s)

When you hear ‘transforming growth factor β,’ a particular type of corneal condition should spring to mind. Which one?
Corneal dystrophy, specifically, the so-called transforming growth factor β–induced (TGFBI) dystrophies

There are six TGFBI dystrophies—what are they? (Note: The Cornea book treats four subtypes as a single dystrophy, and they are treated the same way in the list below.)
1) ?
2) ?
3) ?
4) ?
5) ?
6) ?
What does VEGF stand for?
Vascular endothelial growth factor

What is a growth factor?
One of a diverse group of proteins that affect cell function, including cell proliferation and tissue differentiation

What are some other growth factors of note regarding ocular development and health?
--Epidermal growth factor
--Fibroblast growth factor(s)
--Transforming growth factor β(s)
--Insulin-like growth factor(s)

When you hear ‘transforming growth factor β,’ a particular type of corneal condition should spring to mind. Which one?
Corneal dystrophy, specifically, the so-called transforming growth factor β−induced (TGFBI) dystrophies

There are six TGFBI dystrophies—what are they? (Note: The Cornea book treats four subtypes as a single dystrophy, and they are treated the same way in the list below.)
1) Reis-Bücklers
2) Thiel-Behnke
3) Lattice, type 1
4) Lattice, variant types (III, IIIA, I/IIIA, IV)
5) Granular type 1
6) Granular type 2
What does **VEGF** stand for?
Vascular endothelial growth factor

_Broadly speaking, what is VEGF?_
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

VEGF-A₁₆₅
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

Does VEGF do anything besides grow new blood vessels?

ARMD
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

Does VEGF do anything besides grow new blood vessels?
Yes, it also is a potent vasodilator (it was known originally as vascular permeability factor).
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

Does VEGF do anything besides grow new blood vessels?
Yes, it also is a potent vasodilator (it was known originally as vascular permeability factor). This property is important in the development of diabetic macular edema, which explains the effectiveness of anti-VEGF therapies in the treatment of this condition.
**What does VEGF stand for?**
Vascular endothelial growth factor

**Broadly speaking, what is VEGF?**
An extracellular signaling protein involved in vascular development

**How does VEGF work?**

**VEGF-A**
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells.

In a nutshell, what sort of structure is the VEGFR?
It is a so-called 'transmembrane receptor tyrosine kinase' structure (if nothing else, make sure you hold onto the term tyrosine kinase in connection to the VEGFRs).

Are there multiple subtypes of VEGFRs?
Yes. VEGF-A binds to two: VEGFR-1 and VEGFR-2.

Is one of these more important in the pathogenesis of ARMD?
Yes, VEGFR-2 seems to be responsible for all of the findings in ARMD.
The function of VEGFR-1 is unclear at this time.
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

In a nutshell, what sort of structure is the VEGFR?
It is a so-called ‘transmembrane receptor tyrosine kinase structures’ (if nothing else, make sure you hold onto the term tyrosine kinase in connection to the VEGFRs)

Are there multiple subtypes of VEGFRs?
Yes. VEGF-A binds to two: VEGFR-1 and VEGFR-2.

Is one of these more important in the pathogenesis of ARMD?
Yes, VEGFR-2 seems to be responsible for all of the findings in ARMD.

The function of VEGFR-1 is unclear at this time.
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

In a nutshell, what sort of structure is the VEGFR?
It is a so-called ‘transmembrane receptor tyrosine kinase structures’
(if nothing else, make sure you hold onto the term tyrosine kinase in connection to the VEGFRs)

Are there multiple subtypes of VEGFRs?

Yes. VEGF-A binds to two: VEGFR-1 and VEGFR-2.

Is one of these more important in the pathogenesis of ARMD?
Yes, VEGFR-2 seems to be responsible for all of the findings in ARMD.
The function of VEGFR-1 is unclear at this time.
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR)

In a nutshell, what sort of structure is the VEGFR?
It is a so-called 'transmembrane receptor tyrosine kinase structures' (if nothing else, make sure you hold onto the term tyrosine kinase in connection to the VEGFRs)

Are there multiple subtypes of VEGFRs?
Yes. VEGF-A binds to two: VEGFR-1 and VEGFR-2.
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR)

In a nutshell, what sort of structure is the VEGFR?
It is a so-called ‘transmembrane receptor tyrosine kinase structures’ (if nothing else, make sure you hold onto the term tyrosine kinase in connection to the VEGFRs)

Are there multiple subtypes of VEGFRs?
Yes. VEGF-A binds to two: VEGFR-1 and VEGFR-2.

Is one of these more important in the pathogenesis of ARMD?

Yes, VEGFR-2 seems to be responsible for all of the findings in ARMD.
The function of VEGFR-1 is unclear at this time.
What does VEGF stand for?  
Vascular endothelial growth factor

Broadly speaking, what is VEGF?  
An extracellular signaling protein involved in vascular development

How does VEGF work?  
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

In a nutshell, what sort of structure is the VEGFR?  
It is a so-called ‘transmembrane receptor tyrosine kinase structures’ (if nothing else, make sure you hold onto the term tyrosine kinase in connection to the VEGFRs)

Are there multiple subtypes of VEGFRs?  
Yes. VEGF-A binds to two: VEGFR-1 and VEGFR-2.

Is one of these more important in the pathogenesis of ARMD?  
Yes, VEGFR-2 seems to be responsible for all of the findings in ARMD.
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR)

In a nutshell, what sort of structure is the VEGFR?
It is a so-called ‘transmembrane receptor tyrosine kinase structures’ (if nothing else, make sure you hold onto the term tyrosine kinase in connection to the VEGFRs)

Are there multiple subtypes of VEGFRs?
Yes. VEGF-A binds to two: VEGFR-1 and VEGFR-2.

Is one of these more important in the pathogenesis of ARMD?
Yes, VEGFR-2 seems to be responsible for all of the findings in ARMD.
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR)

In a nutshell, what sort of structure is the VEGFR?
It is a so-called ‘transmembrane receptor tyrosine kinase structures’ (if nothing else, make sure you hold onto the term tyrosine kinase in connection to the VEGFRs)

Are there multiple subtypes of VEGFRs?
Yes. VEGF-A binds to two: VEGFR-1 and VEGFR-2.

Is one of these more important in the pathogenesis of ARMD?
Yes, VEGFR-2 seems to be responsible for all of the findings in ARMD. The function of VEGFR-1 is unclear at this time.
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

What does the A signify?
VEGF-A

ARMD
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

What does the A signify?
VEGF is not a single entity—a number of similar-but-different proteins comprise the ‘VEGF family.’ These are differentiated as VEGF-A through

VEGF-A

165
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

What does the A signify?
VEGF is not a single entity—a number of similar-but-different proteins comprise the ‘VEGF family.’ These are differentiated as VEGF-A through VEGF-F.
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

What does the A signify?
VEGF is not a single entity—a number of similar-but-different proteins comprise the ‘VEGF family.’ These are differentiated as VEGF-A through VEGF-F. (One family member, placental growth factor [PlGF], is the exception to the naming rule.)
What does VEGF stand for? Vascular endothelial growth factor

Broadly speaking, what is VEGF? An extracellular signaling protein involved in vascular development

How does VEGF work? Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

What does the A signify? VEGF is not a single entity—a number of similar-but-different proteins comprise the ‘VEGF family.’ These are differentiated as VEGF-A through VEGF-F. (One family member, placental growth factor [PlGF], is the exception to the naming rule.)
**What does VEGF stand for?**
Vascular endothelial growth factor

**Broadly speaking, what is VEGF?**
An extracellular signaling protein involved in vascular development

**How does VEGF work?**
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

---

**What does the A signify?**
VEGF is not a single entity—a number of similar-but-different proteins comprise the ‘VEGF family.’ These are differentiated as VEGF-A through VEGF-F. (One family member, *placental growth factor* [PlGF], is the exception to the naming rule.) When the term VEGF is used in the ophthalmology literature without a sub-family designation, it is understood to mean VEGF-A.

---

**VEGF-A**

---

**ARMD**
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

What does the A signify?
VEGF is not a single entity—a number of similar-but-different proteins comprise the ‘VEGF family.’ These are differentiated as VEGF-A through VEGF-F. (One family member, placental growth factor [PlGF], is the exception to the naming rule.) When the term VEGF is used in the ophthalmology literature without a sub-family designation, it is understood to mean VEGF-A.

What does 165 signify?

VEGF-A

ARMD
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

What does the A signify?
VEGF is not a single entity—a number of similar-but-different proteins comprise the ‘VEGF family.’ These are differentiated as VEGF-A through VEGF-F. (One family member, placental growth factor [PlGF], is the exception to the naming rule.) When the term VEGF is used in the ophthalmology literature without a sub-family designation, it is understood to mean VEGF-A.

What does VEGF-A\textsubscript{165} signify?
VEGF-A is not a single entity either. At least \# isoforms exist; these differ in the number of peptides they contain, and that number is used as a subscript to identify specific isoforms.
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

What does the A signify?
VEGF is not a single entity—a number of similar-but-different proteins comprise the ‘VEGF family.’ These are differentiated as VEGF-A through VEGF-F. (One family member, placental growth factor [PIGF], is the exception to the naming rule.) When the term VEGF is used in the ophthalmology literature without a sub-family designation, it is understood to mean VEGF-A.

What does 165 signify?
VEGF-A is not a single entity either. At least 4 isoforms exist; these differ in the number of peptides they contain, and that number is used as a subscript to identify specific isoforms.
**What does VEGF stand for?**
Vascular endothelial growth factor

**Broadly speaking, what is VEGF?**
An extracellular signaling protein involved in vascular development

**How does VEGF work?**
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

**What does the A signify?**
VEGF is not a single entity—a number of similar-but-different proteins comprise the ‘VEGF family.’ These are differentiated as VEGF-A through VEGF-F. (One family member, *placental growth factor* [PlGF], is the exception to the naming rule.) When the term *VEGF* is used in the ophthalmology literature without a sub-family designation, it is understood to mean VEGF-A.

**What does 165 signify?**
VEGF-A is not a single entity either. At least 4 isoforms exist; these differ in the number of peptides they contain, and that number is used as a subscript to identify specific isoforms.

**Why focus on isoform 165?**
**What does VEGF stand for?**
Vascular endothelial growth factor

**Broadly speaking, what is VEGF?**
An extracellular signaling protein involved in vascular development

**How does VEGF work?**
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

---

**What does the A signify?**
VEGF is not a single entity—a number of similar-but-different proteins comprise the ‘VEGF family.’ These are differentiated as VEGF-A through VEGF-F. (One family member, placental growth factor [PlGF], is the exception to the naming rule.) When the term VEGF is used in the ophthalmology literature without a sub-family designation, it is understood to mean VEGF-A.

**VEGF-A**

---

**What does 165 signify?**
VEGF-A is not a single entity either. At least 4 isoforms exist; these differ in the number of peptides they contain, and that number is used as a subscript to identify specific isoforms.

**Why focus on isoform 165?**
It seems to be the most important with respect to pathologic angiogenesis in the human eye
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

What does the A signify?
VEGF is not a single entity—a number of similar-but-different proteins comprise the ‘VEGF family.’ These are differentiated as VEGF-A through VEGF-F. (One family member, placental growth factor [PlGF], is the exception to the naming rule.) When the term VEGF is used in the ophthalmology literature without a sub-family designation, it is understood to mean VEGF-A.

What does 165 signify?
VEGF-A is not a single entity either. At least 4 isoforms exist; these differ in the number of peptides they contain, and that number is used as a subscript to identify specific isoforms.

Why focus on isoform 165?
It seems to be the most important with respect to pathologic angiogenesis in the human eye

How strong is the evidence implicating VEGF in ARMD?
Very. Elevated VEGF levels are found within the RPE and vitreous of eyes with early ARMD, and within excised choroidal neovascular membranes. The Retina book goes so far as to say the evidence suggests “a causal role for VEGF in the initiation of neovascularization” in ARMD.
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How strong is the evidence implicating VEGF in ARMD?
Very. Elevated VEGF levels are found within the RPE and vitreous of eyes with early ARMD, and within excised choroidal neovascular membranes.

What does the A signify?
VEGF is not a single entity—a number of similar-but-different proteins comprise the ‘VEGF family.’ These are differentiated as VEGF-A through VEGF-F. (One family member, placental growth factor [PlGF], is the exception to the naming rule.) When the term VEGF is used in the ophthalmology literature without a sub-family designation, it is understood to mean VEGF-A.

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

What does 165 signify?
VEGF-A is not a single entity either. At least 4 isoforms exist; these differ in the number of peptides they contain, and that number is used as a subscript to identify specific isoforms.

Why focus on isoform 165?
It seems to be the most important with respect to pathologic angiogenesis in the human eye
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is VEGF?
An extracellular signaling protein involved in vascular development

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR) on target cells

How strong is the evidence implicating VEGF in ARMD?
Very. Elevated VEGF levels are found within the RPE and vitreous of eyes with early ARMD, and within excised choroidal neovascular membranes. The Retina book goes so far as to say the evidence suggests “a causal role for VEGF in the initiation of neovascularization” in ARMD.

What does the A signify?
VEGF is not a single entity—a number of similar-but-different proteins comprise the ‘VEGF family.’ These are differentiated as VEGF-A through VEGF-F. (One family member, placental growth factor [PlGF], is the exception to the naming rule.) When the term VEGF is used in the ophthalmology literature without a sub-family designation, it is understood to mean VEGF-A.

What does 165 signify?
VEGF-A is not a single entity either. At least 4 isoforms exist; these differ in the number of peptides they contain, and that number is used as a subscript to identify specific isoforms.

Why focus on isoform 165?
It seems to be the most important with respect to pathologic angiogenesis in the human eye.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

The pathogenesis of ARMD is not well understood; that said, the complement system is strongly implicated in it.

VEGF plays a key role in exudative ARMD; likewise, interdicting is key in managing it.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations. **Age** is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: **Nonexudative** and **exudative**. RPE abnormalities in ARMD are typical. **Photoreceptors** in ARMD are abnormal as well. The pathogenesis of ARMD is not well understood; that said, the **complement** system is strongly implicated in it. **VEGF** plays a key role in exudative ARMD; likewise, interdicting **VEGF** is key in managing it.
Age-related macular degeneration (ARMD) is the #1 cause of blindness in adults age 50+ in resource-rich nations. Age is the strongest risk factor for ARMD. The clinical hallmark of ARMD is the presence of drusen in the macula. There are two types: Nonexudative and exudative. RPE abnormalities in ARMD are typical. Photoreceptors in ARMD are abnormal as well. The pathogenesis of ARMD is not well understood; that said, the complement system is strongly implicated in it. VEGF plays a key role in exudative ARMD; likewise, interdicting VEGF is key in managing it.

Next let’s drill down on anti-VEGF therapy…
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment for the treatment of ARMD.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment
Ranibizumab is the generic, nonproprietary name. What is the brand name for this drug?

Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.
Ranibizumab is the generic, nonproprietary name. What is the brand name for this drug? Lucentis.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

What does recombinant mean?

Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

*What does recombinant mean?* That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

**What does recombinant mean?**
That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

**What does humanized mean?**
Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign by the human immune system and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

**ARMD**

Ranibizumab is a *recombinant, humanized, affinity-matured, monoclonal antibody fragment*. 

*ARMD*
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

**What does recombinant mean?**
That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

**What does humanized mean?**
Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign by the human immune system and attacked as such.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

What does recombinant mean? That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

What does humanized mean? Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign by the human immune system and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

ARMD
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

What does recombinant mean? That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

What does humanized mean? Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign by the human immune system and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

What does affinity-matured mean? Affinity maturation is a process in which antibody-producing cells are repeatedly exposed to the antigen of interest, resulting in antibody crops with progressively greater affinity for the antigen.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

**What does recombinant mean?**
That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

**What does humanized mean?**
Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign by the human immune system and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

**What does affinity-matured mean?**
Affinity maturation is a process in which antibody-producing cells are repeatedly exposed to the antigen of interest, resulting in antibody crops with progressively greater affinity for the antigen.

ARMD
**Ranibizumab** is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

**What does recombinant mean?**
That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

**What does humanized mean?**
Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign by the human immune system and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

**What does affinity-matured mean?**
Affinity maturation is a process in which antibody-producing cells are repeatedly exposed to the antigen of interest, resulting in antibody crops with progressively greater affinity for the antigen.

**What is a monoclonal antibody?**
Antibodies produced by a set of immune cells that all derived from (i.e., clones of) the same parent cell.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment

What does recombinant mean? That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

What does humanized mean? Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign by the human immune system and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

What does affinity-matured mean? Affinity maturation is a process in which antibody-producing cells are repeatedly exposed to the antigen of interest, resulting in antibody crops with progressively greater affinity for the antigen.

What is a monoclonal antibody? Antibodies produced by a set of immune cells that all derived from (i.e., clones of) the same parent cell.

ARMD
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

What does recombinant mean? That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

What does humanized mean? Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign by the human immune system and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

What does affinity-matured mean? Affinity maturation is a process in which antibody-producing cells are repeatedly exposed to the antigen of interest, resulting in antibody crops with progressively greater affinity for the antigen.

What is a monoclonal antibody? Antibodies produced by a set of immune cells that all derived from (i.e., clones of) the same parent cell.

What does fragment mean in this context? Ranibizumab is not a complete antibody; rather, it consists of a portion—or fragment—of an antibody.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

**What does recombinant mean?**
That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

**What does humanized mean?**
Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign by the human immune system and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

**What does affinity-matured mean?**
Affinity maturation is a process in which antibody-producing cells are repeatedly exposed to the antigen of interest, resulting in antibody crops with progressively greater affinity for the antigen.

**What is a monoclonal antibody?**
Antibodies produced by a set of immune cells that all derived from (i.e., clones of) the same parent cell.

**What does fragment mean in this context?**
Ranibizumab is not a complete antibody; rather, it consists of a portion—or fragment—of an antibody.
**What does recombinant mean?**

That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

**What does humanized mean?**

Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

**What does the suffix –mab indicate?**

That the drug is a monoclonal antibody.

**What does affinity-matured mean?**

Affinity maturation is a process in which antibody-producing cells are repeatedly exposed to the antigen of interest, resulting in antibody crops with progressively greater affinity for the antigen.

**What is a monoclonal antibody?**

Antibodies produced by a set of immune cells that all derived from (i.e., clones of) the same parent cell.

**What does fragment mean in this context?**

Ranibizumab is not a complete antibody; rather, it consists of a portion—or fragment—of an antibody.

Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

**What does recombinant mean?**
That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

**What does humanized mean?**
Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign by the human immune system and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

**What does the suffix –mab indicate?**
That the drug is a monoclonal antibody.

**What does affinity-matured mean?**
Affinity maturation is a process in which antibody-producing cells are repeatedly exposed to the antigen of interest, resulting in antibody crops with progressively greater affinity for the antigen.

**What is a monoclonal antibody?**
Antibodies produced by a set of immune cells that all derived from (i.e., clones of) the same parent cell.

**What does fragment mean in this context?**
Ranibizumab is not a complete antibody; rather, it consists of a portion—or fragment—of an antibody.
**Ranibizumab** is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

**What does recombinant mean?**
That the substance was produced via recombinant DNA; i.e., DNA created by recombining portions of 2+ different DNA molecules.

**What does humanized mean?**
Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign by the human immune system and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

**What does affinity-matured mean?**
Affinity maturation is a process in which antibody-producing cells are repeatedly exposed to the antigen of interest, resulting in antibody crops with progressively greater affinity for the antigen.

**What does the suffix –mab indicate?**
That the drug is a monoclonal antibody.

**What does the infix (yes, infix) –zu- indicate?**
That the monoclonal antibody has been humanized.

**What does fragment mean in this context?**
Ranibizumab is not a complete antibody; rather, it consists of a portion—or fragment—of an antibody.

**What is a monoclonal antibody?**
Antibodies produced by a set of immune cells that all derived from (i.e., clones of) the same parent cell.

**What does the suffix –mab indicate?**
That the drug is a monoclonal antibody.

**What does fragment mean in this context?**
Ranibizumab is not a complete antibody; rather, it consists of a portion—or fragment—of an antibody.
**Ranibizumab** is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

**What does recombinant mean?**
That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

**What does humanized mean?**
Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

**What does the suffix –mab indicate?**
That the drug is a monoclonal antibody.

**What does the infix (yes, infix) –zu- indicate?**
That the monoclonal antibody has been humanized.

**What is a monoclonal antibody?**
Antibodies produced by a set of immune cells that all derived from (i.e., clones of) the same parent cell.

**What does fragment mean in this context?**
Ranibizumab is not a complete antibody; rather, it consists of a portion—or fragment—of an antibody.

**What does affinity-matured mean?**
Affinity maturation is a process in which antibody-producing cells are repeatedly exposed to the antigen of interest, resulting in antibody crops with progressively greater affinity for the antigen.

**What does the suffix –mab indicate?**
That the drug is a monoclonal antibody.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

**What does recombinant mean?**
That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

**What does humanized mean?**
Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

**What does affinity-matured mean?**
Affinity maturation is a process in which antibody-producing cells are repeatedly exposed to the antigen of interest, resulting in antibody crops with progressively greater affinity for the antigen.

**What does the suffix –mab indicate?**
That the drug is a monoclonal antibody.

**What does the infix –zu- indicate?**
That the monoclonal antibody has been humanized.

**What does fragment mean in this context?**
Ranibizumab is not a complete antibody; rather, it consists of a portion—or fragment—of an antibody.

Next we will take a deep dive into the key clinical trials that established the safety and effectiveness of ranibizumab in the tx of wet ARMD.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

What does recombinant mean?
That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

What does humanized mean?
Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign by the human immune system and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

What does affinity-matured mean?
Affinity maturation is a process in which antibody-producing cells are repeatedly exposed to the antigen of interest, resulting in antibody crops with progressively greater affinity for the antigen.

What does the suffix –mab indicate?
That the drug is a monoclonal antibody.

What does the infix –zu- indicate?
That the monoclonal antibody has been humanized.

What does fragment mean in this context?
Ranibizumab is not a complete antibody; rather, it consists of a portion—or fragment—of an antibody.

Next we will take a deep dive into the key clinical trials that established the safety and effectiveness of ranibizumab in the tx of wet ARMD. Dr Flynn, are we expected (by the authors of the OKAP, WQE and Boards) to know these trial by name? Yes you are. Are we expected to be familiar with their outcomes, as well as the implications of those outcomes? Yes you are.
What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?
What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?
MARINA

What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

What does MARINA stand for?

ANCHOR

What does ANCHOR stand for?

ARMD
What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

**MARINA**

*What does MARINA stand for?*
- Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab In the Treatment of Neovascular Age-Related Macular Degeneration

**ANCHOR**

*What does ANCHOR stand for?*
- ANti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularization in Age-Related Macular Degeneration
What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

What does MARINA stand for? Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab In the Treatment of Neovascular Age-Related Macular Degeneration

What does ANCHOR stand for? ANti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularization in Age-Related Macular Degeneration

What was the dosing schedule?
What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

What does MARINA stand for? Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab In the Treatment of Neovascular Age-Related Macular Degeneration

One injection every month for 24 months

What was the dosing schedule?

What does ANCHOR stand for? ANti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularization in Age-Related Macular Degeneration

One injection every month for 24 months
MARINA: What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

What does MARINA stand for?
Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab In the Treatment of Neovascular Age-Related Macular Degeneration

One injection every month for 24 months

ANCHOR: What does ANCHOR stand for?
ANti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularization in Age-Related Macular Degeneration

What was the dosing schedule?

One injection every month for 24 months

Was another intervention involved?

Was another intervention involved?
What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

**MARINA**

*What does MARINA stand for?*
Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab In the Treatment of Neovascular Age-Related Macular Degeneration

What was the dosing schedule?
One injection every month for 24 months

Was another intervention involved?
No (other than a sham inj group)

**ANCHOR**

*What does ANCHOR stand for?*
ANti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularization in Age-Related Macular Degeneration

One injection every month for 24 months

Yes—PDT. Participants received either sham injections + real PDT or sham PDT + real injections
What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

**MARINA**
- What does MARINA stand for?
  - Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab In the Treatment of Neovascular Age-Related Macular Degeneration

**ANCHOR**
- What does ANCHOR stand for?
  - ANti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularization in Age-Related Macular Degeneration

**What was the dosing schedule?**
- One injection every month for 24 months

**What was the primary outcome measure?**

?  

**Was another intervention involved?**
- Yes—PDT. Participants received either sham injections + real PDT or sham PDT + real injections

?  

No (other than a sham inj group)
What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

**MARINA**

What does MARINA stand for?
Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab In the Treatment of Neovascular Age-Related Macular Degeneration

One injection every month for 24 months

No (other than a sham inj group)

Proportion of patients losing <15 ETDRS letters

**ANCHOR**

What does ANCHOR stand for?
ANti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularization in Age-Related Macular Degeneration

One injection every month for 24 months

Yes—PDT. Participants received either sham injections + real PDT or sham PDT + real injections

**ARMD**

What was the primary outcome measure?

Proportion of patients losing <15 ETDRS letters
What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

**MARINA**

- **What does MARINA stand for?**
  - Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab In the Treatment of Neovascular Age-Related Macular Degeneration

- **One injection every month for 24 months**

- **No (other than a sham inj group)**

- **Proportion of patients losing <15 ETDRS letters**

**ANCHOR**

- **What does ANCHOR stand for?**
  - ANti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularization in Age-Related Macular Degeneration

- **One injection every month for 24 months**

- **Yes—PDT. Participants received either sham injections + real PDT or sham PDT + real injections**

- **Proportion of patients losing <15 ETDRS letters**

<table>
<thead>
<tr>
<th>What was the dosing schedule?</th>
<th>What was the primary outcome measure?</th>
</tr>
</thead>
<tbody>
<tr>
<td>One injection every month for 24 months</td>
<td>Proportion of patients losing &lt;15 ETDRS letters</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Was another intervention involved?</th>
<th>What was the secondary outcome measure?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No (other than a sham inj group)</td>
<td>?</td>
</tr>
</tbody>
</table>

?
**MARINA**

What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

What does MARINA stand for?
Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab In the Treatment of Neovascular Age-Related Macular Degeneration

One injection every month for 24 months

No (other than a sham inj group)

Proportion of patients losing <15 ETDRS letters

[**What was the primary outcome measure?**](#)

Proportion of patients gaining >15 ETDRS letters

[**What was the secondary outcome measure?**](#)

**ANCHOR**

What does ANCHOR stand for?
ANti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularization in Age-Related Macular Degeneration

One injection every month for 24 months

Yes—PDT. Participants received either sham injections + real PDT or sham PDT + real injections

Proportion of patients losing <15 ETDRS letters

[**What was the primary outcome measure?**](#)

Proportion of patients gaining >15 ETDRS letters

[**What was the secondary outcome measure?**](#)
### MARINA

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Loss &lt;15 letters</strong></td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td><strong>Gained &gt;15 letters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### ANCHOR

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Loss &lt;15 letters</strong></td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td><strong>Gained &gt;15 letters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### RESULTS

- Evaluated ranibizumab for the treatment of minimally classic/occult CNVM
- Either 0.3 and 0.5 mg by intravitreal injection (or sham injections)
- One injection every month for 24 months
- **YEAR ONE**

0.3 mg 0.5 mg Sham

0.3 mg 0.5 mg PDT

**ARMD**

**MARINA**

**RESULTS**

**ANCHOR**
MARINA Evaluated ranibizumab for the treatment of minimally classic/occult CNVM. Either 0.3 and 0.5 mg by intravitreal injection (or sham injections). One injection every month for 24 months. 0.3 mg 0.5 mg Sham Loss <15 letters 95% 95% 62% Gained >15 letters

RESULTS

ANCHOR

YEARD ONE

<table>
<thead>
<tr>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>94%</td>
<td>96%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MARINA

ANCHOR

MARINA

ANCHOR

MARINA

ANCHOR
**ARMD**

**MARINA**

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>95%</td>
<td>95%</td>
<td>62%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**RESULTS**

**YEAR ONE**

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>94%</td>
<td>96%</td>
<td>64%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**ANCHOR**

Note: Only 1 in 20 tx’d pts lost >15 letters of VA
Evaluated ranibizumab for the treatment of predominantly classic CNVM (or sham injections). One injection every month for 24 months.

- **Loss <15 letters:**
  - 0.3 mg: 95%
  - 0.5 mg: 95%
  - Sham: 62%

- **Gained >15 letters:**
  - 0.3 mg: ?
  - 0.5 mg: ?
  - Sham: ?

---

Evaluated ranibizumab for the treatment of minimally classic/occult CNVM (or sham injections). One injection every month for 24 months.

- **Loss <15 letters:**
  - 0.3 mg: 95%
  - 0.5 mg: 95%
  - Sham: 62%

- **Gained >15 letters:**
  - 0.3 mg: ?
  - 0.5 mg: ?
  - Sham: ?

---

**ARMD**

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>95%</td>
<td>95%</td>
<td>62%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>94%</td>
<td>96%</td>
<td>64%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>
Evaluated ranibizumab for the treatment of predominantly classic CNVM. Either 0.3 and 0.5 mg by intravitreal injection (or sham injections). One injection every month for 24 months.

- **Loss <15 letters**:
  - 0.3 mg: 95%
  - 0.5 mg: 95%
  - Sham: 62%

- **Gained >15 letters**:
  - 0.3 mg: 25%
  - 0.5 mg: 34%
  - Sham: 5%

---

Evaluated ranibizumab for the treatment of minimally classic/occult CNVM. Either 0.3 and 0.5 mg by intravitreal injection (or sham injections). One injection every month for 24 months.

- **Loss <15 letters**:
  - 0.3 mg: 95%
  - 0.5 mg: 95%
  - Sham: 62%

- **Gained >15 letters**:
  - 0.3 mg: 25%
  - 0.5 mg: 34%
  - Sham: 5%
Evaluated ranibizumab for the treatment of predominantly classic CNVM. Either 0.3 and 0.5 mg by intravitreal injection (or sham injections) One injection every month for 24 months.

- **0.3 mg**:
  - Loss <15 letters: 95%
  - Gained >15 letters: 25%

- **0.5 mg**:
  - Loss <15 letters: 95%
  - Gained >15 letters: 34%

- **Sham**:
  - Loss <15 letters: 62%
  - Gained >15 letters: 5%

Note: --30 to 40% of (0.5) pts gained 15+ letters of VA, compared to only ~5% of sham/PDT pts.

Evaluated ranibizumab for the treatment of minimally classic/occult CNVM. Either 0.3 and 0.5 mg by intravitreal injection (or sham injections) One injection every month for 24 months.

- **0.3 mg**:
  - Loss <15 letters: 94%
  - Gained >15 letters: 36%

- **0.5 mg**:
  - Loss <15 letters: 96%
  - Gained >15 letters: 40%

- **Sham**:
  - Loss <15 letters: 64%
  - Gained >15 letters: 5%

- **PDT**:
  - Loss <15 letters: 64%
  - Gained >15 letters: 6%
Marina evaluated ranibizumab for the treatment of minimally classic/occult CNVM

- Either 0.3 and 0.5 mg by intravitreal injection (or sham injections)
- One injection every month for 24 months

Proportion of patients losing <15 ETDRS letters

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>95%</td>
<td>95%</td>
<td>62%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>25%</td>
<td>34%</td>
<td>5%</td>
</tr>
</tbody>
</table>

Proportion of patients gaining >15 ETDRS letters

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>94%</td>
<td>96%</td>
<td>64%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>36%</td>
<td>40%</td>
<td>6%</td>
</tr>
</tbody>
</table>

Anchor evaluated ranibizumab for the treatment of predominantly classic CNVM

- Either 0.3 and 0.5 mg by intravitreal injection (or sham injections)
- One injection every month for 24 months

Proportion of patients losing <15 ETDRS letters

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

Proportion of patients gaining >15 ETDRS letters

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>34%</td>
<td>41%</td>
<td>6%</td>
</tr>
</tbody>
</table>
**MARINA**

**RESULTS**

**ANCHOR**

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Loss &lt;15 letters</strong></td>
<td>95%</td>
<td>95%</td>
<td>62%</td>
</tr>
<tr>
<td><strong>Gained &gt;15 letters</strong></td>
<td>25%</td>
<td>34%</td>
<td>5%</td>
</tr>
</tbody>
</table>

**YEAR ONE**

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Loss &lt;15 letters</strong></td>
<td>94%</td>
<td>96%</td>
<td>64%</td>
</tr>
<tr>
<td><strong>Gained &gt;15 letters</strong></td>
<td>36%</td>
<td>40%</td>
<td>6%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Loss &lt;15 letters</strong></td>
<td>90%</td>
<td>90%</td>
<td>66%</td>
</tr>
<tr>
<td><strong>Gained &gt;15 letters</strong></td>
<td>34%</td>
<td>41%</td>
<td>5%</td>
</tr>
</tbody>
</table>
MARINA ANCHOR

**RESULTS**

<table>
<thead>
<tr>
<th></th>
<th>MARINA 0.3 mg</th>
<th>MARINA 0.5 mg</th>
<th>MARINA Sham</th>
<th>ANCHOR 0.3 mg</th>
<th>ANCHOR 0.5 mg</th>
<th>ANCHOR PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>YEAR ONE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss &lt;15 letters</td>
<td>95%</td>
<td>95%</td>
<td>62%</td>
<td>94%</td>
<td>96%</td>
<td>64%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>25%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**YEAR TWO**

<table>
<thead>
<tr>
<th></th>
<th>MARINA 0.3 mg</th>
<th>MARINA 0.5 mg</th>
<th>MARINA Sham</th>
<th>ANCHOR 0.3 mg</th>
<th>ANCHOR 0.5 mg</th>
<th>ANCHOR PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>92%</td>
<td>90%</td>
<td>53%</td>
<td>90%</td>
<td>90%</td>
<td>66%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:**
--The vast majority of ranibizumab-tx’d pts still hadn’t last >15 letters at the 24-month mark
**MARINA**

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>95%</td>
<td>95%</td>
<td>62%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>25%</td>
<td>34%</td>
<td>5%</td>
</tr>
</tbody>
</table>

**RESULTS**

<table>
<thead>
<tr>
<th></th>
<th>Year One</th>
<th>Year Two</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>94%</td>
<td>90%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>36%</td>
<td>36%</td>
</tr>
</tbody>
</table>

**ANCHOR**

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>96%</td>
<td>90%</td>
<td>66%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

**ARMD**
# MARINA

Evaluated ranibizumab for the treatment of minimally classic/occult CNVM. Evaluated ranibizumab for the treatment of predominantly classic CNVM. Either 0.3 and 0.5 mg by intravitreal injection (or sham injections).

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>95%</td>
<td>95%</td>
<td>62%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>25%</td>
<td>34%</td>
<td>5%</td>
</tr>
</tbody>
</table>

One injection every month for 24 months.

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>92%</td>
<td>90%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>26%</td>
<td>33%</td>
</tr>
</tbody>
</table>

# ANCHOR

YEAR ONE

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>94%</td>
<td>96%</td>
<td>64%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>36%</td>
<td>40%</td>
<td>6%</td>
</tr>
</tbody>
</table>

YEAR TWO

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>90%</td>
<td>90%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>34%</td>
<td>41%</td>
</tr>
</tbody>
</table>

Proportion of patients losing <15 ETDRS letters. Proportion of patients gaining >15 ETDRS letters.

- **MARINA**
  - **Results**: See table.

- **ANCHOR**
  - **Results**: See table.

**ARMD**
**MARINA**

**RESULTS**

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>95%</td>
<td>95%</td>
<td>62%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>25%</td>
<td>34%</td>
<td>5%</td>
</tr>
</tbody>
</table>

**YEAR ONE**

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>94%</td>
<td>96%</td>
<td>64%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>36%</td>
<td>40%</td>
<td>6%</td>
</tr>
</tbody>
</table>

**ANCHOR**

<table>
<thead>
<tr>
<th></th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>92%</td>
<td>90%</td>
<td>53%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>26%</td>
<td>33%</td>
<td>4%</td>
</tr>
</tbody>
</table>

**YEAR TWO**

<table>
<thead>
<tr>
<th></th>
<th>0.5 mg</th>
<th>PDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss &lt;15 letters</td>
<td>90%</td>
<td>66%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>34%</td>
<td>41%</td>
</tr>
</tbody>
</table>

*Note:* --And the (0.5) pts maintained their VA gains

**ARMD**
MARINA and ANCHOR tl;dr:
1) Both were strong Phase III clinical trials
2) Both evaluated monthly injections of ranibizumab for 2 years
3) The studies found that only 1 in 20 (5%) of treated pts lost more than 15 letters of VA at 1 yr, and 1 in 10 (10%) at 2 yrs
4) 30-40% of treated pts gained 15+ letters

Was another intervention involved? No

Proportion of patients losing <15 ETDRS letters

Proportion of patients gaining >15 ETDRS letters

What was the primary outcome measure? Proportion of patients losing <15 ETDRS letters

What was the secondary outcome measure? Proportion of patients gaining >15 ETDRS letters

Yes—PDT. Participants received either sham injections + real PDT or sham PDT + real injections

What does MARINA stand for? Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular Age-Related Macular Degeneration

What does ANCHOR stand for? ANti-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in Age-Related Macular Degeneration

MARINA What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

What does MARINA stand for?

What does ANCHOR stand for?

ARMD What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

What does MARINA stand for?

What does ANCHOR stand for?

ARMD What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

What does MARINA stand for?

What does ANCHOR stand for?

ARMD What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

What does MARINA stand for?

What does ANCHOR stand for?
MARINA

What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

**MARINA**

What does MARINA stand for?
Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab In the Treatment of Neovascular Age-Related Macular Degeneration

**ANCHOR**

What does ANCHOR stand for?
ANti-VEGF Antibody for the Treatment of Predominantly Classic ChORoidal Neovascularization in Age-Related Macular Degeneration

What significant ocular and/or systemic safety issues manifested in the MARINA and/or ANCHOR trials?

Nothing too concerning. The rates of endophthalmitis, RD, uveitis, etc., were comparable between the ranibizumab and sham groups, although there was a trend toward higher rates with ranibizumab. The same was true of possible systemic side effects: There was a trend toward higher rates of HTN, CVA and MI, but these differences were not significant either.

What was the primary outcome measure?
Proportion of patients losing <15 ETDRS letters

What was the secondary outcome measure?
Proportion of patients gaining >15 ETDRS letters

Proportion of patients losing <15 ETDRS letters

What was the follow-up schedule? One injection every month for 24 months

Was another intervention involved? Yes—PDT. Participants received either sham injections + real PDT or sham PDT + real injections

Proportion of patients gaining >15 ETDRS letters
What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

MARINA

What does MARINA stand for?
Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab In the Treatment of Neovascular Age-Related Macular Degeneration

ANCHOR

What does ANCHOR stand for?
ANTI-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in Age-Related Macular Degeneration

What significant ocular and/or systemic safety issues manifested in the MARINA and/or ANCHOR trials?
Nothing too concerning. The rates of endophthalmitis, RD, uveitis, etc., were comparable between the ranibizumab and sham groups, although there was a trend toward higher rates with ranibizumab. The same was true of possible systemic side effects: There was a trend toward higher rates of HTN, CVA and MI, but these differences were not significant either.

What was the primary outcome measure?
Proportion of patients losing <15 ETDRS letters

What was the secondary outcome measure?
Proportion of patients gaining >15 ETDRS letters

One injection every month for 24 months

Was another intervention involved?
Yes—PDT. Participants received either sham injections + real PDT or sham PDT + real injections.

Proportion of patients losing <15 ETDRS letters

Proportion of patients gaining >15 ETDRS letters
What were the 2 key clinical trials demonstrating the safety and efficacy of ranibizumab in the treatment of ARMD?

What does MARINA stand for? Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab In the Treatment of Neovascular Age-Related Macular Degeneration

One injection every month for 24 months

What does ANCHOR stand for? ANti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularization in Age-Related Macular Degeneration

One injection every month for 24 months

The MARINA and ANCHOR trials left little doubt re the safety and efficacy of ranibizumab therapy for wet ARMD. But what was in doubt was the treatment schedule, ie, was it really necessary to inject every month?

Proportion of patients losing <15 ETDRS letters

What was the primary outcome measure?

Proportion of patients gaining >15 ETDRS letters

What was the secondary outcome measure?

No

Was another intervention involved?

Yes—PDT. Participants received either sham injections + real PDT or sham PDT + real injections.
The MARINA and ANCHOR trials left little doubt re the safety and efficacy of ranibizumab therapy for wet ARMD. But what was in doubt was the treatment schedule, ie, was it really necessary to inject every month? Clearly, a monthly continuous schedule such as this was not sustainable indefinitely—the burden imposed (both in cost and labor) would overwhelm the resources of any healthcare system. To address this very important issue, several clinical trials were initiated, including…
What are 2 key studies addressing the **dosing schedule** of ranibizumab in the treatment of ARMD?
What are 2 key studies addressing the dosing schedule of ranibizumab in the treatment of ARMD?

(Other acceptable answers: SAILOR; SUSTAIN; HORIZON; HARBOR)
What are 2 key studies addressing the **dosing schedule** of ranibizumab in the treatment of ARMD?

What does PIER stand for?

What does PrONTO stand for?

ARMD
What are 2 key studies addressing the dosing schedule of ranibizumab in the treatment of ARMD?

**PIER**

What does PIER stand for?

*Phase IIIb, Multicenter, Randomized, Double-Masked, Sham-Injection-Controlled Study of the Efficacy and Safety of Ranibizumab in Subjects with Subfoveal Choroidal Neovascularization with or without Classic CNV Secondary to Age-Related Macular Degeneration*

**PrONTO**

What does PrONTO stand for?

*Prospective Optical Coherence Tomography Imaging of Patients with Neovascular AMD Treated with Intra-Ocular Ranibizumab*
What are 2 key studies addressing the dosing schedule of ranibizumab in the treatment of ARMD?

PIER

What does PIER stand for?
Phase IIIb, Multicenter, Randomized, Double-Masked, Sham-Injection-Controlled Study of the Efficacy and Safety of Ranibizumab in Subjects with Subfoveal Choroidal Neovascularization with or without Classic CNV Secondary to Age-Related Macular Degeneration

PrONTO

What does PrONTO stand for?
Prospective Optical Coherence Tomography Imaging of Patients with Neovascular AMD Treated with Intra-Ocular Ranibizumab

What were the dosing schedules?
What are 2 key studies addressing the dosing schedule of ranibizumab in the treatment of ARMD?

What does PIER stand for?
Phase IIIb, Multicenter, Randomized, Double-Masked, Sham-Injection-Controlled Study of the Efficacy and Safety of Ranibizumab in Subjects with Subfoveal Choroidal Neovascularization with or without Classic CNV Secondary to Age-Related Macular Degeneration

What does PrONTO stand for?
Prospective Optical Coherence Tomography Imaging of Patients with Neovascular AMD Treated with Intra-Ocular Ranibizumab

The dosing schedules were:
- One injection every month for 3 months, then every 3 months to 12 months
- One injection every month for 3 months, then PRN as indicated by OCT, VA and DFE findings at monthly exams
One injection every month for 3 months, then every 3 months to 12 months

What were the dosing schedules?

<table>
<thead>
<tr>
<th>Three Months</th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average VA change (ETDRS letters)</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

(Note the different outcome variable)

What were the three-month results?

Focus your attention on the 0.5 outcome

ARMD
What were the three-month results? Consistent with MARINA and ANCHOR, monthly ranibizumab injections led to improved visual acuity.

One injection every month for 3 months, then every 3 months to 12 months.

<table>
<thead>
<tr>
<th>Three Months</th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average VA change (ETDRS letters)</td>
<td>↑2.9</td>
<td>↑4.3</td>
<td>↓8.7</td>
</tr>
</tbody>
</table>
One injection every month for 3 months, then every 3 months to 12 months

What were the three-month results?
Consistent with MARINA and ANCHOR, monthly ranibizumab injections led to improved visual acuity. Which makes sense, because the first three months of PIER were identical to the first three months of MARINA and ANCHOR (ie, a shot every month).
PIER: Results at 3 months
One injection every month for 3 months, then every 3 months to 12 months.

What were the dosing schedules?

What about the one-year results?

<table>
<thead>
<tr>
<th>One Year</th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average VA change (ETDRS letters)</td>
<td>↓1.6</td>
<td>?</td>
<td>↓16.3</td>
</tr>
</tbody>
</table>
One injection every month for 3 months, then every 3 months to 12 months.

What were the dosing schedules?

What about the one-year results?
These are much less encouraging—after dropping to q3-month injections, VA had returned to baseline levels.
PIER: Results at 12 months
What were the dosing schedules?

One injection every month for 3 months, then every 3 months to 12 months.

What about the one-year results?

These are much less encouraging—after dropping to q3-month injections, VA had returned to baseline levels. So while better than no treatment (ie, the sham arm), this was a dramatically worse outcome than what was achieved via monthly injections in MARINA and ANCHOR.
One injection every month for 3 months, then every 3 months to 12 months.

What were the dosing schedules?

What about the one-year results?
These are much less encouraging—after dropping to q3-month injections, VA had returned to baseline levels. So while better than no treatment (ie, the sham arm), this was a dramatically worse outcome than what was achieved via monthly injections in MARINA and ANCHOR. Clearly, a q3 month schedule was not going to be acceptable.

No question—advance when ready.

<table>
<thead>
<tr>
<th>One Year</th>
<th>0.3 mg</th>
<th>0.5 mg</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average VA change (ETDRS letters)</td>
<td>↓1.6</td>
<td>↓0.2</td>
<td>↓16.3</td>
</tr>
</tbody>
</table>
So if the PIER schedule isn’t effective, what about the PRN PrONTO schedule? Recall these pts received a monthly injection x 3, after which they were examined (not injected!) monthly, receiving an injection only if evidence of worsening was found.
For comparison purposes, here are the year-one results from the MARINA and ANCHOR trials.

<table>
<thead>
<tr>
<th></th>
<th>Year One</th>
<th>MARINA</th>
<th>ANCHOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost &lt;15 letters</td>
<td>?</td>
<td>95%</td>
<td>96%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>?</td>
<td>34%</td>
<td>40%</td>
</tr>
<tr>
<td>Mean ↑ in letters</td>
<td>?</td>
<td>7.2</td>
<td>11.3</td>
</tr>
</tbody>
</table>

For comparison purposes, here are the year-one results from the MARINA and ANCHOR trials.
What doses of ranibizumab were used?

What is the dosing schedule?

Is another intervention involved?

MARINA ANCHOR

<table>
<thead>
<tr>
<th>Lost &lt;15 letters</th>
<th>95%</th>
<th>95%</th>
<th>96%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gained &gt;15 letters</td>
<td>35%</td>
<td>34%</td>
<td>40%</td>
</tr>
<tr>
<td>Mean ↑ in letters</td>
<td>9.3</td>
<td>7.2</td>
<td>11.3</td>
</tr>
</tbody>
</table>

For comparison purposes, here are the year-one results from the MARINA and ANCHOR trials. Note that the PrONTO protocol (3 monthly injections, then PRN) produced results essentially identical to those of MARINA and ANCHOR (monthly injections)…
For comparison purposes, here are the year-one results from the MARINA and ANCHOR trials. Note that the PrONTO protocol (3 monthly injections, then PRN) produced results essentially identical to those of MARINA and ANCHOR (monthly injections)… but with fewer than half the number of injections!

<table>
<thead>
<tr>
<th></th>
<th>Year One</th>
<th>MARINA</th>
<th>ANCHOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost &lt;15 letters</td>
<td>95%</td>
<td>95%</td>
<td>96%</td>
</tr>
<tr>
<td>Gained &gt;15 letters</td>
<td>35%</td>
<td>34%</td>
<td>40%</td>
</tr>
<tr>
<td>Mean ↑ in letters</td>
<td>9.3</td>
<td>7.2</td>
<td>11.3</td>
</tr>
<tr>
<td>Mean # of injections</td>
<td>5.6</td>
<td>13</td>
<td>13</td>
</tr>
</tbody>
</table>

MARINA/ANCHOR RESULTS

PrONTO RESULTS

ARMD

PrONTO
The PIER and PrONTO studies (and others) were undertaken to explore alternative tx schedules to the effective-but-impractical ‘continuous monthly’ schedule employed in MARINA and ANCHOR.
The PIER and PrONTO studies (and others) were undertaken to explore alternative tx schedules to the effective-but-impractical ‘continuous monthly’ schedule employed in MARINA and ANCHOR. The indicated that a ‘continuous q3-month’ schedule was not an effective alternative.
The PIER and PrONTO studies (and others) were undertaken to explore alternative tx schedules to the effective-but-impractical ‘continuous monthly’ schedule employed in MARINA and ANCHOR. **The PIER indicated that a ‘continuous q3-month’ schedule was not an effective alternative.**
The PIER and PrONTO studies (and others) were undertaken to explore alternative tx schedules to the effective-but-impractical ‘continuous monthly’ schedule employed in MARINA and ANCHOR. The PIER indicated that a ‘continuous q3-month’ schedule was not an effective alternative. However, the PrONTO demonstrated that a PRN tx schedule—in which the pt was examined every month, but injected only if evidence of dz progression was found—could be as effective as monthly injections, with far fewer injections needed.
The PIER and PrONTO studies (and others) were undertaken to explore alternative tx schedules to the effective-but-impractical ‘continuous monthly’ schedule employed in MARINA and ANCHOR. The PIER indicated that a ‘continuous q3-month’ schedule was not an effective alternative. However, the PrONTO demonstrated that a PRN tx schedule—in which the pt was examined every month, but injected only if evidence of dz progression was found—could be as effective as monthly injections, with far fewer injections needed.
The PIER and PrONTO studies (and others) were undertaken to explore alternative tx schedules to the effective-but-impractical ‘continuous monthly’ schedule employed in MARINA and ANCHOR. The PIER indicated that a ‘continuous q3-month’ schedule was not an effective alternative. However, the PrONTO demonstrated that a PRN tx schedule—in which the pt was examined every month, but injected only if evidence of dz progression was found—could be as effective as monthly injections, with far fewer injections needed. Unfortunately, PRN scheduling still required monthly visits, which is very burdensome even if no injection is administered. Thus, an alternative to PRN scheduling was sought.
The PIER and PrONTO studies (and others) were undertaken to explore alternative tx schedules to the effective-but-impractical ‘continuous monthly’ schedule employed in MARINA and ANCHOR. The PIER indicated that a ‘continuous q3-month’ schedule was not an effective alternative. However, the PrONTO demonstrated that a PRN tx schedule—in which the pt was examined every month, but injected only if evidence of dz progression was found—could be as effective as monthly injections, with far fewer injections needed. Unfortunately, PRN scheduling still required monthly visits, which is very burdensome even if no injection is administered. Thus, an alternative to PRN scheduling was sought.

Enter the treat-and-extend approach.
The PIER and PrONTO studies (and others) were undertaken to explore alternative tx schedules to the effective-but-impractical ‘continuous monthly’ schedule employed in MARINA and ANCHOR. The PIER indicated that a ‘continuous q3-month’ schedule was not an effective alternative. However, the PrONTO demonstrated that a PRN tx schedule—in which the pt was examined every month, but injected only if evidence of dz progression was found—could be as effective as monthly injections, with far fewer injections needed. Unfortunately, PRN scheduling still required monthly visits, which is very burdensome even if no injection is administered. Thus, an alternative to PRN scheduling was sought.

Enter the treat-and-extend approach.
The PIER and PrONTO studies (and others) were undertaken to explore alternative tx schedules to the effective-but-impractical ‘continuous monthly’ schedule employed in MARINA and ANCHOR. The PIER indicated that a ‘continuous q3-month’ schedule was not an effective alternative. However, the PrONTO demonstrated that a PRN tx schedule—in which the pt was examined every month, but injected only if evidence of dz progression was found—could be as effective as monthly injections, with far fewer injections needed. Unfortunately, PRN scheduling still required monthly visits, which is very burdensome even if no injection is administered. Thus, an alternative to PRN scheduling was sought.

Enter the treat-and-extend approach. While specifics vary among clinicians, most do something along these lines: First, the pt is treated monthly until the macula is ‘dry.’ Once dryness has been achieved, the time until the next visit is extended to 6 weeks. At the 6-week visit the pt is both evaluated and injected. If the 6-week evaluation revealed that the macula remained dry, the interval until the next visit is extended to 8 weeks. Again, at the 8-week visit the pt is both evaluated and injected, and if the eval indicates she remained dry, the interval until the next visit is extended by another 2 weeks to 10.
The PIER and PrONTO studies (and others) were undertaken to explore alternative tx schedules to the effective-but-impractical ‘continuous monthly’ schedule employed in MARINA and ANCHOR. The PIER indicated that a ‘continuous q3-month’ schedule was not an effective alternative. However, the PrONTO demonstrated that a PRN tx schedule—in which the pt was examined every month, but injected only if evidence of dz progression was found—could be as effective as monthly injections, with far fewer injections needed. Unfortunately, PRN scheduling still required monthly visits, which is very burdensome even if no injection is administered. Thus, an alternative to PRN scheduling was sought.

Enter the treat-and-extend approach. While specifics vary among clinicians, most do something along these lines: First, the pt is treated monthly until the macula is ‘dry.’ Once dryness has been achieved, the time until the next visit is extended to 6 weeks. At the 6-week visit the pt is both evaluated and injected. If the 6-week evaluation revealed that the macula remained dry, the interval until the next visit is extended to 8 weeks. Again, at the 8-week visit the pt is both evaluated and injected, and if the eval indicates she remained dry, the interval until the next visit is extended by another 2 weeks to 10. If at any point the evaluation revealed the return of edema/heme, the pt’s inter-tx interval is rolled back to whatever was the longest progression-free interval they had achieved. (Many clinicians use an inter-tx interval of 12 weeks as a cap, ie, they don’t try to extend beyond it.)
The PIER and PrONTO studies (and others) were undertaken to explore alternative tx schedules to the effective-but-impractical ‘continuous monthly’ schedule employed in MARINA and ANCHOR. The PIER indicated that a ‘continuous q3-month’ schedule was not an effective alternative. However, the PrONTO demonstrated that a PRN tx schedule—in which the pt was examined every month, but injected only if evidence of dz progression was found—could be as effective as monthly injections, with far fewer injections needed. Unfortunately, PRN scheduling still required monthly visits, which is very burdensome even if no injection is administered. Thus, an alternative to PRN scheduling was sought.

Enter the treat-and-extend approach. While specifics vary among clinicians, most do something along these lines: First, the pt is treated monthly until the macula is ‘dry.’ Once dryness has been achieved, the time until the next visit is extended to 6 weeks. At the 6-week visit the pt is both evaluated and injected. If the 6-week evaluation revealed that the macula remained dry, the interval until the next visit is extended to 8 weeks. Again, at the 8-week visit the pt is both evaluated and injected, and if the eval indicates she remained dry, the interval until the next visit is extended by another 2 weeks to 10. If at any point the evaluation revealed the return of edema/heme, the pt’s inter-tx interval is rolled back to whatever was the longest progression-free interval they had achieved. (Many clinicians use an inter-tx interval of 12 weeks as a cap, ie, they don’t try to extend beyond it.)

At present, most clinicians employ some version of treat-and-extend with most of their pts.
The PIER and PrONTO studies (and others) were undertaken to explore alternative tx schedules to the effective-but-impractical ‘continuous monthly’ schedule employed in MARINA and ANCHOR. The PIER indicated that a ‘continuous q3-month’ schedule was not an effective alternative. However, the PrONTO demonstrated that a PRN tx schedule—in which the pt was examined every month, but injected only if evidence of dz progression was found—could be as effective as monthly injections, with far fewer injections needed. Unfortunately, PRN scheduling still required monthly visits, which is very burdensome even if no injection is administered. Thus, an alternative to PRN scheduling was sought.

Enter the treat-and-extend approach. While specifics vary among clinicians, most do something along these lines: First, the pt is treated monthly until the macula is ‘dry.’ Once dryness has been achieved, the time until the next visit is extended to 6 weeks. At the 6-week visit the pt is both evaluated and injected. If the 6-week evaluation revealed that the macula remained dry, the interval until the next visit is extended to 8 weeks. Again, at the 8-week visit the pt is both evaluated and injected, and if the eval indicates she remained dry, the interval until the next visit is extended by another 2 weeks to 10. If at any point the evaluation revealed the return of edema/heme, the pt’s inter-tx interval is rolled back to whatever was the longest progression-free interval they had achieved. (Many clinicians use an inter-tx interval of 12 weeks as a cap, ie, they don’t try to extend beyond it.)

At present, most clinicians employ some version of treat-and-extend with most of their pts.
The PIER and PrONTO studies (and others) were undertaken to explore alternative tx schedules to the effective-but-impractical ‘continuous monthly’ schedule employed in MARINA and ANCHOR. The PIER indicated that a ‘continuous q3-month’ schedule was not an effective alternative. However, the PrONTO demonstrated that a PRN tx schedule—in which the pt was examined every month, but injected only if evidence of dz progression was found—produced results essentially identical to those of MARINA and ANCHOR (monthly injections)… but with fewer than half the number of injections!

What doses of ranibizumab were used? What is the dosing schedule? Is another intervention involved? What is the primary outcome measure? What is the secondary outcome measure?

MARINA ANCHOR

<table>
<thead>
<tr>
<th></th>
<th>Lost &lt;15 letters</th>
<th>Gained &gt;15 letters</th>
<th>Mean ↑ in letters</th>
<th>Mean # of injections</th>
</tr>
</thead>
<tbody>
<tr>
<td>PrONTO</td>
<td>95%</td>
<td>34%</td>
<td>9.3</td>
<td>5.6</td>
</tr>
<tr>
<td>MARINA/ANCHOR</td>
<td>95%</td>
<td>40%</td>
<td>11.3</td>
<td>13</td>
</tr>
</tbody>
</table>

**Anti-VEGF injection scheduling tl;dr**

**Continuous**: Pt evaluated and treated monthly

**PRN**: Pt evaluated monthly; treated if evidence of active dz

**Treat and extend**: After dz resolution achieved, interval between eval/tx visits gradually increased to the max the pt can sustain w/o recurrence (or 12 weeks, whichever comes first)

At present, most clinicians employ some version of treat-and-extend with most of their pts.

*But that’s a topic for another slide-set*
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

What does recombinant mean? That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

What does humanized mean? Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign by the human immune system and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

What is a monoclonal antibody? Antibodies produced by a set of immune cells that all derived from (i.e., clones of) the same parent cell.

What is the ‘parent’ antibody from which the ranibizumab fragment is derived? Bevacizumab.

What does fragment mean in this context? Ranibizumab is not a complete antibody; rather, it consists of a portion—or fragment—of an antibody.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

What does recombinant mean? That the substance was produced via recombinant DNA; i.e., DNA created by re-combining portions of 2+ different DNA molecules.

What does humanized mean? Like many monoclonal antibodies, the parent molecule of ranibizumab was derived from mouse cells. Such murine antibodies would be recognized as foreign by the human immune system and attacked as such. To preclude this, a portion of the mouse antibody is replaced with its human counterpart via recombinant DNA techniques.

What is a monoclonal antibody? Antibodies produced by a set of antibody-producing cells that all derived from (i.e., clones of) the same parent cell.

What is the ‘parent’ antibody from which the ranibizumab fragment is derived? Bevacizumab.

What does fragment mean in this context? Ranibizumab is not a complete antibody; rather, it consists of a portion—or fragment—of an antibody.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

Bevacizumab

Note: Different drug!
Bevacizumab is the generic, nonproprietary name. What is the brand name for this drug?

Bevacizumab
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

Bevacizumab is the generic, nonproprietary name. What is the brand name for this drug? Avastin.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

You know bevacizumab is **humanized** because of the infix **Bevacizumab**.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment. You know it is a monoclonal antibody because of the suffix.

You know bevacizumab is humanized because of the infix.

ARMD
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

Why did we lose the term affinity matured?

Bevacizumab

Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

Why did we lose the term affinity matured?
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

Why did we lose the term affinity matured?
Unlike ranibizumab, bevacizumab was not affinity-matured for VEGF-A.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

Unlike ranibizumab, which consists of an antibody fragment, bevacizumab is a full-length antibody.

Why did we lose the term affinity matured? Unlike ranibizumab, bevacizumab was not affinity-matured for VEGF-A.

Why did we lose the word fragment?
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

Why did we lose the word fragment? Unlike ranibizumab, which consists of an antibody fragment, bevacizumab is a full-length antibody.

Why did we lose the term affinity matured? Unlike ranibizumab, bevacizumab was not affinity-matured for VEGF-A.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

Unlike ranibizumab, which consists of an antibody fragment, bevacizumab is a full-length antibody.

Bevacizumab

Why did we lose the term affinity matured? Unlike ranibizumab, bevacizumab was not affinity-matured for VEGF-A.

Why did we lose the word fragment? Unlike ranibizumab, which consists of an antibody fragment, bevacizumab is a full-length antibody.

Because it is smaller, ranibizumab clears faster than bevacizumab. What are their systemic half-lives?
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment. Unlike ranibizumab, which consists of an antibody fragment, bevacizumab is a full-length antibody. Bevacizumab's systemic half-life is about 21 days, whereas ranibizumab's is only 2.1 hours.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

Why go to the trouble of engineering an antibody fragment in the first place?

Unlike ranibizumab, which consists of an antibody fragment, bevacizumab is a full-length antibody.

Why did we lose the term affinity matured? Unlike ranibizumab, bevacizumab was not affinity-matured for VEGF-A.

Why did we lose the word fragment? Unlike ranibizumab, which consists of an antibody fragment, bevacizumab is a full-length antibody.

Because it is smaller, ranibizumab clears faster than bevacizumab. What are their systemic half-lives? Bevacizumab’s is about 21 days, whereas ranibizumab’s is only 2.1 hours.
Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment. Why did we lose the word fragment? Unlike ranibizumab, which consists of an antibody fragment, bevacizumab is a full-length antibody.

Researchers initially believed that the full-length bevacizumab molecule was too large to pass through the ILM and enter the sub-retinal space. Why go to the trouble of engineering an antibody fragment in the first place?

Bevacizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.

Why did we lose the term affinity matured? Unlike ranibizumab, bevacizumab was not affinity-matured for VEGF-A.

Because it is smaller, ranibizumab clears faster than bevacizumab. What are their systemic half-lives? Bevacizumab’s is about 21 days, whereas ranibizumab’s is only 2.1 hours.
Which drug was created first—ranibizumab, or bevacizumab?

- **Bevacizumab**
- **Ranibizumab** is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.
Which drug was created first—ranibizumab, or bevacizumab?

Bevacizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.
Which drug was created first—ranibizumab, or bevacizumab?
Bevacizumab

Was bevacizumab developed to treat ARMD?

Bevacizumab

Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.
Which drug was created first—ranibizumab, or bevacizumab?

Bevacizumab

Was bevacizumab developed to treat ARMD?

No, it was developed and FDA-approved to treat cancer.

Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment.
Which drug was created first—ranibizumab, or bevacizumab?
Bevacizumab

Was bevacizumab developed to treat ARMD?
No, it was developed and FDA-approved to treat cancer

Ranibizumab is a recombinant, humanized, affinity-matured, monoclonal antibody fragment

Bevacizumab
| What were the key clinical trials demonstrating the safety and efficacy of bevacizumab in the treatment of ARMD? | ARMD |
What were the key clinical trials demonstrating the safety and efficacy of bevacizumab in the treatment of ARMD?

To date there have been NO randomized, prospective clinical trials of intravitreal bevacizumab for the treatment of wet ARMD.
To date there have been NO randomized, prospective clinical trials of intravitreal bevacizumab for the treatment of wet ARMD.

For that matter, there weren’t even any animal trials of intravitreal bevacizumab prior to its use in humans. Clinicians started using it off-label based on what they knew about its ‘next-of-kin’ (ranibizumab).
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?

What does CATT stand for?
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?

What does CATT stand for?
Comparison of Age-related Macular Degeneration Treatments Trial
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?

What doses of each were used?

Ranibizumab: 0.5 mg
Bevacizumab: 1.25 mg
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?

What doses of each were used?

Ranibizumab: 0.5 mg
Bevacizumab: 1.25 mg
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?

What doses of each were used?

Ranibizumab: 0.5 mg
Bevacizumab: 1.25 mg

What were the two dosing schedules?
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?

What doses of each were used?

Ranibizumab: 0.5 mg
Bevacizumab: 1.25 mg

What were the two dosing schedules?

Continuous, and PRN
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?

What doses of each were used?

What were the two dosing schedules?

Was another intervention involved?

Ranibizumab: 0.5 mg
Bevacizumab: 1.25 mg

Continuous, and PRN
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?

What doses of each were used?

Ranibizumab: 0.5 mg
Bevacizumab: 1.25 mg

What were the two dosing schedules?

Continuous, and PRN

Was another intervention involved?

No
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?

What doses of each were used?

Ranibizumab: 0.5 mg
Bevacizumab: 1.25 mg

What were the two dosing schedules?

Continuous, and PRN

Was another intervention involved?

No

What was the primary outcome measure?
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?

What doses of each were used? Ranibizumab: 0.5 mg Bevacizumab: 1.25 mg

What were the two dosing schedules? Continuous, and PRN

Was another intervention involved? No

What was the primary outcome measure? Mean change in VA
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?

What doses of each were used?

Ranibizumab: 0.5 mg
Bevacizumab: 1.25 mg

What were the two dosing schedules?

Continuous, and PRN

Was another intervention involved?

No

What was the primary outcome measure?

Mean change in VA

What was the secondary outcome measure?
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?

What doses of each were used?

Ranibizumab: 0.5 mg
Bevacizumab: 1.25 mg

What were the two dosing schedules?

Continuous, and PRN

Was another intervention involved?

No

What was the primary outcome measure?

Mean change in VA

What was the secondary outcome measure?

Number of treatments
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?

What doses of each were used?

Ranibizumab: 0.5 mg
Bevacizumab: 1.25 mg

What were the two dosing schedules?

Continuous, and PRN

Was another intervention involved?

No

What was the primary outcome measure?

Mean change in VA

What was the secondary outcome measure?

Number of treatments

What was another oft-discussed secondary outcome measure?
What study 1) compared the safety and efficacy of bevacizumab vs ranibizumab, and 2) evaluated dosing schedule of these meds in the treatment of ARMD?

What doses of each were used?

Ranibizumab: 0.5 mg
Bevacizumab: 1.25 mg

What were the two dosing schedules?

Continuous, and PRN

Was another intervention involved?

No

What was the primary outcome measure?

Mean change in VA

What was the secondary outcome measure?

Number of treatments

What was another oft-discussed secondary outcome measure?

Incidence of adverse events
## CATT RESULTS

*Average Number of Letters Gained at One Year*

<table>
<thead>
<tr>
<th></th>
<th>Ranibizumab</th>
<th>Bevacizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Every Month Dosing</strong></td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td><strong>PRN Dosing</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CATT RESULTS

*Average Number of Letters Gained at One Year*

<table>
<thead>
<tr>
<th></th>
<th>Ranibizumab</th>
<th>Bevacizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Every Month Dosing</strong></td>
<td>8.5</td>
<td>8.0</td>
</tr>
<tr>
<td><strong>PRN Dosing</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CATT RESULTS

Average Number of Letters Gained at One Year

<table>
<thead>
<tr>
<th></th>
<th>Ranibizumab</th>
<th>Bevacizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Every Month Dosing</strong></td>
<td>8.5</td>
<td>8.0</td>
</tr>
<tr>
<td><strong>PRN Dosing</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

These are statistically equivalent
# CATT RESULTS

*Average Number of Letters Gained at One Year*

<table>
<thead>
<tr>
<th></th>
<th>Ranibizumab</th>
<th>Bevacizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Every Month Dosing</strong></td>
<td>8.5</td>
<td>8.0</td>
</tr>
<tr>
<td><strong>PRN Dosing</strong></td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>
CATT RESULTS

Average Number of Letters Gained at One Year

<table>
<thead>
<tr>
<th>Dosing</th>
<th>Ranibizumab</th>
<th>Bevacizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every Month Dosing</td>
<td>8.5</td>
<td>8.0</td>
</tr>
<tr>
<td>PRN Dosing</td>
<td>6.8</td>
<td>5.9</td>
</tr>
</tbody>
</table>

ARMD
# CATT RESULTS

*Average Number of Letters Gained at One Year*

<table>
<thead>
<tr>
<th></th>
<th>Ranibizumab</th>
<th>Bevacizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Every Month Dosing</strong></td>
<td>8.5</td>
<td>8.0</td>
</tr>
<tr>
<td><strong>PRN Dosing</strong></td>
<td>6.8</td>
<td>5.9</td>
</tr>
</tbody>
</table>

As are these
# CATT RESULTS

*Average Number of Letters Gained at One Year*

<table>
<thead>
<tr>
<th>Dosing</th>
<th>Ranibizumab</th>
<th>Bevacizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Every Month</strong></td>
<td><img src="image" alt="8.5" /></td>
<td><img src="image" alt="8.0" /></td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td><strong>6.8</strong></td>
<td><strong>5.9</strong></td>
</tr>
</tbody>
</table>

*These are statistically equivalent as well*
**CATT RESULTS**

*Average Number of Letters Gained at One Year*

<table>
<thead>
<tr>
<th></th>
<th>Ranibizumab</th>
<th>Bevacizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Every Month Dosing</strong></td>
<td>8.5</td>
<td>8.0</td>
</tr>
<tr>
<td><strong>PRN Dosing</strong></td>
<td>6.8</td>
<td>5.9</td>
</tr>
</tbody>
</table>

However, PRN bevacizumab yielded a significantly lower average gain when compared to monthly bevacizumab…
## CATT RESULTS

*Average Number of Letters Gained at One Year*

<table>
<thead>
<tr>
<th></th>
<th>Ranibizumab</th>
<th>Bevacizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Every Month Dosing</strong></td>
<td><strong>8.5</strong></td>
<td><strong>8.0</strong></td>
</tr>
<tr>
<td><strong>PRN Dosing</strong></td>
<td><strong>6.8</strong></td>
<td><strong>5.9</strong></td>
</tr>
</tbody>
</table>

However, PRN bevacizumab yielded a significantly lower average gain when compared to monthly bevacizumab… or when compared to monthly ranibizumab.
CATT RESULTS

Average Number of Letters Gained at One Year
(and average number of injections)

<table>
<thead>
<tr>
<th></th>
<th>Ranibizumab</th>
<th>Bevacizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Every Month Dosing</strong></td>
<td><strong>8.5(12)</strong></td>
<td><strong>8.0(12)</strong></td>
</tr>
<tr>
<td><strong>PRN Dosing</strong></td>
<td><strong>6.8(?)</strong></td>
<td><strong>5.9(?)</strong></td>
</tr>
</tbody>
</table>

Another important issue concerns the number of injections needed. The fixed-schedule pts received 12 monthly injections over the first year (obviously), but what about in the PRN-dosing conditions?
CATT RESULTS

Average Number of Letters Gained at One Year
(and average number of injections)

<table>
<thead>
<tr>
<th></th>
<th>Ranibizumab</th>
<th>Bevacizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every Month Dosing</td>
<td>8.5(12)</td>
<td>8.0(12)</td>
</tr>
<tr>
<td>PRN Dosing</td>
<td>6.8(7)</td>
<td>5.9(8)</td>
</tr>
</tbody>
</table>

Another important issue concerns the number of injections needed. The fixed-schedule pts received 12 monthly injections over the first year (obviously), but what about in the PRN-dosing conditions? On average, the PRN ranibizumab and PRN bevacizumab pts received 7 and 8 injections respectively.
What about adverse events?

CATT RESULTS

What about adverse events?
What about adverse events?
Certain events were identified a priori to be tracked; these included MI, CVA and death. In terms of these events, no differences obtained between the bevacizumab and the ranibizumab cohorts.
What about adverse events?
Certain events were identified a priori to be tracked; these included MI, CVA and death. In terms of these events, no differences obtained between the bevacizumab and the ranibizumab cohorts. However, post hoc analysis of the rates of other adverse events (eg, hospitalization) suggested an association between these events and bevacizumab.
What about adverse events?
Certain events were identified a priori to be tracked; these included MI, CVA and death. In terms of these events, no differences obtained between the bevacizumab and the ranibizumab cohorts. However, post hoc analysis of the rates of other adverse events (eg, hospitalization) suggested an association between these events and bevacizumab.

Is this finding concerning enough to warrant using ranibizumab preferentially?
What about adverse events?
Certain events were identified a priori to be tracked; these included MI, CVA and death. In terms of these events, no differences obtained between the bevacizumab and the ranibizumab cohorts. However, post hoc analysis of the rates of other adverse events (eg, hospitalization) suggested an association between these events and bevacizumab.

Is this finding concerning enough to warrant using ranibizumab preferentially?
Probably not. As of this writing, the opinion seems to be that the increased adverse effects were probably happenstance. This opinion is based on two facts:
1)
What about adverse events?
Certain events were identified a priori to be tracked; these included MI, CVA and death. In terms of these events, no differences obtained between the bevacizumab and the ranibizumab cohorts. However, post hoc analysis of the rates of other adverse events (eg, hospitalization) suggested an association between these events and bevacizumab.

Is this finding concerning enough to warrant using ranibizumab preferentially?
Probably not. As of this writing, the opinion seems to be that the increased adverse effects were probably happenstance. This opinion is based on two facts:
1) The reported adverse events have not been found in studies involving the systemic administration of bevacizumab. If these events were triggered by the minute amounts of bevacizumab that might have entered the systemic circulation after intravitreal injection, the thinking goes, surely they would have occurred during systemic bavacizumab trials (in which systemic concentrations were at least 500 times greater).
2)
What about adverse events?
Certain events were identified a priori to be tracked; these included MI, CVA and death. In terms of these events, no differences obtained between the bevacizumab and the ranibizumab cohorts. However, post hoc analysis of the rates of other adverse events (eg, hospitalization) suggested an association between these events and bevacizumab.

Is this finding concerning enough to warrant using ranibizumab preferentially?
Probably not. As of this writing, the opinion seems to be that the increased adverse effects were probably happenstance. This opinion is based on two facts:
1) The reported adverse events have not been found in studies involving the systemic administration of bevacizumab. If these events were triggered by the minute amounts of bevacizumab that might have entered the systemic circulation after intravitreal injection, the thinking goes, surely they would have occurred during systemic bavacizumab trials (in which systemic concentrations were at least 500 times greater).
2) The reported adverse events did not correlate with bevacizumab dosing, as would be expected if a causal relationship held.
What about adverse events?
Certain events were identified a priori to be tracked; these included MI, CVA and death. In terms of these events, no differences obtained between the bevacizumab and the ranibizumab cohorts. However, post hoc analysis of the rates of other adverse events (e.g., hospitalization) suggested an association between these events and bevacizumab.

Is this finding concerning enough to warrant using ranibizumab preferentially? Probably not. As of this writing, the opinion seems to be that the increased adverse effects were probably happenstance. This opinion is based on two facts:
1) The reported adverse events have not been found in studies involving the systemic administration of bevacizumab. If these events were triggered by the minute amounts of bevacizumab that might have entered the systemic circulation after intravitreal injection, the thinking goes, surely they would have occurred during systemic bavacizumab trials (in which systemic concentrations were at least 500 times greater).
2) The reported adverse events did not correlate with bevacizumab dosing, as would be expected if a causal relationship held.

Next we drill down on a third drug that has come to play a vital role in the management of wet ARMD
Aflibercept is a recombinant fusion protein.

ARMD
Aflibercept is a *recombinant fusion protein*
Aflibercept is a *recombinant fusion protein*

What is a fusion protein?
Aflibercept is a recombinant fusion protein

What is a fusion protein?
A novel protein constructed by joining (fusing) the genetic information coding for two other proteins.
Aflibercept is the generic, nonproprietary name. What is the brand name for this drug?

Aflibercept is a recombinant fusion protein.
Aflibercept is the generic, nonproprietary name. What is the brand name for this drug? Eylea

Aflibercept is a recombinant fusion protein.
Aflibercept is a recombinant fusion protein. What does the suffix –cept indicate?
What does the suffix –cept indicate?
That the drug functions by mimicking a receptor molecule

Aflibercept is a recombinant fusion protein
Aflibercept is a recombinant fusion protein

What does the suffix –cept indicate? That the drug functions by mimicking a receptor molecule

What does the infix –ber- indicate?
Afribeccept is a recombinant fusion protein

What does the suffix –cept indicate? That the drug functions by mimicking a receptor molecule

What does the infix –ber- indicate? That the mimicked receptor is the VEGF receptor
Afib\textauthor{ercept} is a recombinant fusion protein

What does the suffix \textit{–cept} indicate? That the drug functions by mimicking a receptor molecule

Afib\textauthor{ercept} is a recombinant fusion protein

What does the infix \textit{–ber-} indicate? That the mimicked receptor is the VEGF receptor

Spell it out for me—what does it mean to say afib\textauthor{ercept} ‘mimics the VEGF receptor’? Put another way: How does afib\textauthor{ercept} work?
Afli\text{ber}cept is a recombinant fusion protein

What does the suffix \textit{–cept} indicate?
That the drug functions by mimicking a receptor molecule

What does the infix \textit{–ber-} indicate?
That the mimicked receptor is the VEGF receptor

Spell it out for me—what does it mean to say afli\text{ber}cept ‘mimics the VEGF receptor’?
Put another way: How does afli\text{ber}cept work?
Afli\text{ber}cept is a decoy receptor that locks up unbound VEGF in the retinal space before it (the VEGF) can find an actual VEGF receptor on a target structure.
Afli**bercept** is a recombinant fusion protein

What does the suffix –**cept** indicate? That the drug functions by mimicking a receptor molecule

What does the infix –**ber**- indicate? That the mimicked receptor is the VEGF receptor

Spell it out for me—what does it mean to say aflibercept ‘mimics the VEGF receptor’? Put another way: How does aflibercept work?

Afli**bercept** is a **decoy receptor** that locks up unbound VEGF in the retinal space before it (the VEGF) can find an actual VEGF receptor on a target structure. **This strategy is referred to as** [VEGF trap].
Afli
bercept is a recombinant fusion protein.

What does the suffix –cept indicate?
That the drug functions by mimicking a receptor molecule.

Afli
bercept is a recombinant fusion protein.

What does the infix –ber- indicate?
That the mimicked receptor is the VEGF receptor.

Spell it out for me—what does it mean to say afli
bercept ‘mimics the VEGF receptor’?
Put another way: How does afli
bercept work?
Afli
bercept is a decoy receptor that locks up unbound VEGF in the retinal space before it (the VEGF) can find an actual VEGF receptor on a target structure. This strategy is referred to as ‘VEGF trap.’
Aflibercept is a recombinant fusion protein.

Which isoforms of VEGF-A does aflibercept bind?

Of bevacizumab, ranibizumab and aflibercept, which binds VEGF-A with the greatest affinity?

Aflibercept

In addition to VEGF-A, aflibercept binds another protein implicated in the pathogenesis of CNVM—what is it?

Placental growth factor (PLGF)
Afiblercept is a recombinant fusion protein.

Which isoforms of VEGF-A does afiblercept bind?
- All of them
Aflibercept is a recombinant fusion protein.

Which isoforms of VEGF-A does aflibercept bind?
All of them

Of bevacizumab, ranibizumab and aflibercept, which binds VEGF-A with the greatest affinity?
Aflibercept is a recombinant fusion protein.

*Which isoforms of VEGF-A does aflibercept bind?*
*All of them*

*Of bevacizumab, ranibizumab and aflibercept, which binds VEGF-A with the greatest affinity?*
*Aflibercept*
Afiblercept is a recombinant fusion protein

**Which isoforms of VEGF-A does afiblercept bind?**
All of them

**Of bevacizumab, ranibizumab and afiblercept, which binds VEGF-A with the greatest affinity?**
Afiblercept

**In addition to VEGF-A, afiblercept binds another protein implicated in the pathogenesis of CNVM—what is it?**
Aflibercept is a recombinant fusion protein

Which isoforms of VEGF-A does aflibercept bind?
All of them

Of bevacizumab, ranibizumab and aflibercept, which binds VEGF-A with the greatest affinity?
Aflibercept

In addition to VEGF-A, aflibercept binds another protein implicated in the pathogenesis of CNVM—what is it?
Placental growth factor (PLGF)
Aflibercept is a recombinant fusion protein

Which isoforms of VEGF-A does aflibercept bind?
All of them

Of bevacizumab, ranibizumab and aflibercept, which binds VEGF-A with the greatest affinity?
Aflibercept

This ability to bind PLGF may account for the fact that aflibercept is effective in some cases of ranibizumab-refractory CNVM—what is it?
Placental growth factor (PLGF)
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

Technically, there were two VIEW trials—**VIEW1** was conducted in the US and Canada, **VIEW2** overseas. However, because the results of the two studies were essentially identical, for simplicity's sake we will treat them as if they were a single study.
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

What does VIEW stand for?

VIEW

ARMD
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

**VIEW**

What does VIEW stand for? The **VEGF Trap-Eye: Investigation of Efficacy and Safety in Wet ARMD**

ARMD
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

What doses of aflibercept were used?
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

What doses of aflibercept were used?

Either 0.5 or 2 mg by intravitreal injection
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

What doses of aflibercept were used?

What was the dosing schedule?

Either 0.5 or 2 mg by intravitreal injection
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

What doses of aflibercept were used?

Either 0.5 or 2 mg by intravitreal injection.

What was the dosing schedule?

There were 3:
- a) 0.5 mg every 4 weeks, or
- b) 2 mg every 4 weeks, or
- c) 2 mg every 8 weeks after three q4 week loading doses
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

What doses of aflibercept were used?

Either 0.5 or 2 mg by intravitreal injection.

What was the dosing schedule?

There were 3:
- a) 0.5 mg every 4 weeks, or
- b) 2 mg every 4 weeks, or
- c) 2 mg every 8 weeks after three q4 week loading doses.

Take note of the q8 week condition. Remember, one of the drawbacks of ranibizumab is its q4 week dosing requirement, which places tremendous financial and structural strain on the healthcare system. (Consider: In 2003, prior to the advent of intravitreal anti-VEGF meds, Medicare was billed for ~3000 intravitreal injections. In 2010, it was billed for over a MILLION.) Thus there was considerable interest in whether a q8 week dosing schedule would work.
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

What doses of aflibercept were used?

Either 0.5 or 2 mg by intravitreal injection

What was the dosing schedule?

There were 3:
   a) 0.5 mg every 4 weeks, or
   b) 2 mg every 4 weeks, or
   c) 2 mg every 8 weeks after three q4 week loading doses

Was another intervention involved?
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

What doses of aflibercept were used?

Either 0.5 or 2 mg by intravitreal injection

What was the dosing schedule?

There were 3:
- a) 0.5 mg every 4 weeks, or
- b) 2 mg every 4 weeks, or
- c) 2 mg every 8 weeks after three q4 week loading doses

Was another intervention involved?

A control group received ranibizumab 0.5 mg every 4 weeks
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

The VIEW was a noninferiority trial, meaning the efficacy/safety of a new treatment was being compared to that of a ‘gold standard’ treatment. In other words, the VIEW had to demonstrate that aflibercept was at least as good and at least as safe as ranibizumab in order to gain approval.

Was another intervention involved?

A control group received ranibizumab 0.5 mg every 4 weeks.
The VIEW was a *noninferiority trial*, meaning the efficacy/safety of a new treatment was being compared to that of a ‘gold standard’ treatment. In other words, the VIEW had to demonstrate that aflibercept was *at least* as good and *at least* as safe as ranibizumab in order to gain approval. To do so required:

1) the presence of a ranibizumab arm in the study, and
2) that patients in the VIEW have lesions similar to those of the participants in the studies used to prove the safety and efficacy of ranibizumab in the first place (ie, the MARINA and ANCHOR studies).

**Was another intervention involved?**

*A control group received ranibizumab 0.5 mg every 4 weeks*
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

What doses of aflibercept were used?

Either 0.5 or 2 mg by intravitreal injection

What was the dosing schedule?

There were 3:
- a) 0.5 mg every 4 weeks, or
- b) 2 mg every 4 weeks, or
- c) 2 mg every 8 weeks after three q4 week loading doses

A control group received ranibizumab 0.5 mg every 4 weeks

Was another intervention involved?

What was the primary outcome measure?
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

What doses of aflibercept were used?

Either 0.5 or 2 mg by intravitreal injection

What was the dosing schedule?

There were 3:
- a) 0.5 mg every 4 weeks, or
- b) 2 mg every 4 weeks, or
- c) 2 mg every 8 weeks after three q4 week loading doses

Was another intervention involved?

A control group received ranibizumab 0.5 mg every 4 weeks

What was the primary outcome measure?

Proportion of patients losing <15 ETDRS letters
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

What doses of aflibercept were used?

Either 0.5 or 2 mg by intravitreal injection

What was the dosing schedule?

There were 3:
- a) 0.5 mg every 4 weeks, or
- b) 2 mg every 4 weeks, or
- c) 2 mg every 8 weeks after three q4 week loading doses

Was another intervention involved?

A control group received ranibizumab 0.5 mg every 4 weeks

What was the primary outcome measure?

Proportion of patients losing <15 ETDRS letters

What was the secondary outcome measure?
What was the key clinical trial demonstrating the safety and efficacy of aflibercept in the treatment of ARMD?

What doses of aflibercept were used?

Either 0.5 or 2 mg by intravitreal injection

There were 3:
- a) 0.5 mg every 4 weeks, or
- b) 2 mg every 4 weeks, or
- c) 2 mg every 8 weeks after three q4 week loading doses

A control group received ranibizumab 0.5 mg every 4 weeks

What was the primary outcome measure?

Proportion of patients losing <15 ETDRS letters

What was the secondary outcome measure?

Proportion of patients maintaining (i.e., losing zero ETDRS letters) or gaining ETDRS letters
**VIEW study:**
Year One Results

<table>
<thead>
<tr>
<th></th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ranbизumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost &lt;15 letters</td>
<td>?%</td>
<td>?%</td>
<td>?%</td>
<td>?%</td>
</tr>
<tr>
<td>Mean gain in ETDRS letters read</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**VIEW study:**  
Year One Results

<table>
<thead>
<tr>
<th>Lost &lt;15 letters</th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ran-bizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>96%</td>
<td>95%</td>
<td>95%</td>
<td>94%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean gain in ETDRS letters read</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

ARMD
**VIEW study:**

*Year One Results*

<table>
<thead>
<tr>
<th></th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ranbizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost &lt;15 letters</td>
<td>96%</td>
<td>95%</td>
<td>95%</td>
<td>94%</td>
</tr>
<tr>
<td>Mean gain in ETDRS letters read</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>
**VIEW study:**
Year One Results

<table>
<thead>
<tr>
<th></th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ranbizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost &lt;15 letters</td>
<td>96%</td>
<td>95%</td>
<td>95%</td>
<td>94%</td>
</tr>
<tr>
<td>Mean gain in ETDRS letters read</td>
<td>8.3</td>
<td>9.2</td>
<td>8.4</td>
<td>8.7</td>
</tr>
</tbody>
</table>
**VIEW study:**

Year One Results

<table>
<thead>
<tr>
<th>Lost &lt;15 letters</th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ranibizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>96%</td>
<td>95%</td>
<td>95%</td>
<td>94%</td>
<td></td>
</tr>
</tbody>
</table>

| Mean gain in ETDRS letters read | 8.3 | 9.2 | 8.4 | 8.7 |

The key finding is that q8 weeks aflibercept worked just as well as monthly ranibizumab.
### VIEW study: Year One Results

<table>
<thead>
<tr>
<th>Lost &lt;15 letters</th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ranbuzumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost &lt;15 letters</td>
<td>96%</td>
<td>95%</td>
<td>95%</td>
<td>94%</td>
</tr>
<tr>
<td>Mean gain in ETDRS letters read</td>
<td>8.3</td>
<td>9.2</td>
<td>8.4</td>
<td>8.7</td>
</tr>
</tbody>
</table>

### VIEW study: Year Two Results

The VIEW was carried into a second year. The basic Year 2 study criteria were:
1) Participants remained in the same treatment condition
2) Participants were evaluated monthly and treated PRN
3) All participants were treated at least every 12 weeks
**VIEW study:**  
**Year One Results**

<table>
<thead>
<tr>
<th>Lost &lt;15 letters</th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ran-bizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>96%</td>
<td>95%</td>
<td>95%</td>
<td>94%</td>
<td></td>
</tr>
</tbody>
</table>

| Mean gain in ETDRS letters read | 8.3 | 9.2 | 8.4 | 8.7 |

**VIEW study:**  
**Year Two Results**

<table>
<thead>
<tr>
<th>Lost &lt;15 letters</th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ran-bizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>?%</td>
<td>?%</td>
<td>?%</td>
<td>?%</td>
<td></td>
</tr>
</tbody>
</table>

| Mean gain in ETDRS letters read | ?% | ?% | ?% | ?% | ?% | ?% |

**ARMD**
**VIEW study:**

**Year One Results**

<table>
<thead>
<tr>
<th>Lost &lt;15 letters</th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ranbizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>96%</td>
<td>95%</td>
<td>95%</td>
<td>94%</td>
<td></td>
</tr>
</tbody>
</table>

| Mean gain in ETDRS letters read | 8.3 | 9.2 | 8.4 | 8.7 |

**VIEW study:**

**Year Two Results**

<table>
<thead>
<tr>
<th>Lost &lt;15 letters</th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ranbizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>91%</td>
<td>92%</td>
<td>92%</td>
<td>92%</td>
<td></td>
</tr>
</tbody>
</table>

| Mean gain in ETDRS letters read | 8.3 | 9.2 | 8.4 | 8.7 |
### VIEW study: Year One Results

<table>
<thead>
<tr>
<th></th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ranbizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost &lt;15 letters</td>
<td>96%</td>
<td>95%</td>
<td>95%</td>
<td>94%</td>
</tr>
<tr>
<td>Mean gain in ETDRS letters read</td>
<td>8.3</td>
<td>9.2</td>
<td>8.4</td>
<td>8.7</td>
</tr>
</tbody>
</table>

### VIEW study: Year Two Results

<table>
<thead>
<tr>
<th></th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ranbizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost &lt;15 letters</td>
<td>91%</td>
<td>92%</td>
<td>92%</td>
<td>92%</td>
</tr>
<tr>
<td>Mean gain in ETDRS letters read</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>
### VIEW study: Year One Results

<table>
<thead>
<tr>
<th></th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ran-bizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost &lt;15 letters</td>
<td>96%</td>
<td>95%</td>
<td>95%</td>
<td>94%</td>
</tr>
<tr>
<td>Mean gain in ETDRS letters read</td>
<td>8.3</td>
<td>9.2</td>
<td>8.4</td>
<td>8.7</td>
</tr>
</tbody>
</table>

### VIEW study: Year Two Results

<table>
<thead>
<tr>
<th></th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ran-bizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost &lt;15 letters</td>
<td>91%</td>
<td>92%</td>
<td>92%</td>
<td>92%</td>
</tr>
<tr>
<td>Mean gain in ETDRS letters read</td>
<td>6.6</td>
<td>7.6</td>
<td>7.6</td>
<td>7.9</td>
</tr>
</tbody>
</table>
As with the Year One data, the key finding is that q8 weeks aflibercept worked **just as well** as monthly ranibizumab.
**VIEW study:**

### Year One Results

<table>
<thead>
<tr>
<th>Lost &lt;15 letters</th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ranbizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>96%</td>
<td>95%</td>
<td>94%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean gain in ETDRS letters read</th>
<th>8.3</th>
<th>9.2</th>
<th>8.4</th>
<th>8.7</th>
</tr>
</thead>
</table>

### Year Two Results

<table>
<thead>
<tr>
<th>Lost &lt;15 letters</th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ranbizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>91%</td>
<td>92%</td>
<td>92%</td>
<td>92%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean gain in ETDRS letters read</th>
<th>6.6</th>
<th>7.6</th>
<th>7.6</th>
<th>7.9</th>
</tr>
</thead>
</table>

Also of note is the fact that the Year Two results are similar to those of Year One.
Another much-anticipated outcome concerned the average number of treatments required in the q8 week aflibercept vs ranibizumab conditions.
**VIEW study: Year One Results**

<table>
<thead>
<tr>
<th>Lost &lt;15 letters</th>
<th>0.5 mg q4 week</th>
<th>2.0 mg q4 week</th>
<th>2.0 mg q8 week</th>
<th>Ranibizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean number of treatments</td>
<td>7</td>
<td>12</td>
<td>8.3</td>
<td>9.2</td>
</tr>
</tbody>
</table>

Another much-anticipated outcome concerned the **average number of treatments** required in the q8 week aflibercept vs ranibizumab conditions.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

The pathogenesis of ARMD is not well understood; that said, the complement system is strongly implicated in it.

VEGF plays a key role in exudative ARMD; likewise, interdicting VEGF is key in managing it.

Nonexudative ARMD is treatable at present.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

**Age** is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: *Nonexudative* and *exudative*.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

The pathogenesis of ARMD is not well understood; that said, the *complement* system is strongly implicated in it.

VEGF plays a key role in exudative ARMD; likewise, interdicting VEGF is key in managing it.

Nonexudative ARMD isn’t treatable at present.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations.

Age is the strongest risk factor for ARMD.

The clinical hallmark of ARMD is the presence of drusen in the macula.

There are two types: Nonexudative and exudative.

RPE abnormalities in ARMD are typical.

Photoreceptors in ARMD are abnormal as well.

The pathogenesis of ARMD is not well understood; that said, the complement system is strongly implicated in it.

VEGF plays a key role in exudative ARMD; likewise, interdicting VEGF is key in managing it.

Nonexudative ARMD isn’t treatable at present.

The clinical trial (abb) found that micronutrient supplementation reduces the likelihood of exudative ARMD in at-risk pts.
Age-related macular degeneration is the #1 cause of blindness in adults age 50+ in resource-rich nations

**Age** is the strongest risk factor for ARMD

The clinical hallmark of ARMD is the presence of drusen in the macula

There are two types: *Nonexudative* and *exudative*

RPE abnormalities in ARMD are typical

Photoreceptors in ARMD are abnormal as well

The pathogenesis of ARMD is not well understood; that said, the **complement** system is strongly implicated in it

**VEGF** plays a key role in exudative ARMD; likewise, interdicting **VEGF** is key in managing it

Nonexudative ARMD isn’t treatable at present

The **AREDS** found that micronutrient supplementation reduces the likelihood of exudative ARMD in at-risk pts
**ARMD: The AREDS**

- AREDS is the...
ARMD: The AREDS

- AREDS is the Age-Related Eye Disease Study
- **ARMD: The AREDS**
  - AREDS is the Age-Related Eye Disease Study
  - Looked at dietary supplements and ARMD:
    - ?
    - Vitamin C 500 mg
    - Vitamin E 400 IU
    - β-carotene 15 mg
    - Zinc 80 mg
    - Cupric oxide 2 mg
  - **Findings:**
    - Patients with intermediate/advanced dry ARMD had a 25% reduced risk of advanced disease and vision loss
    - Patients with no/early ARMD: No benefit
  - Note: Don't give AREDS supplements to smokers (β-carotene increases the risk of lung Ca in these patients)
**ARMD: The AREDS**

- AREDS is the *Age-Related Eye Disease Study*
- Looked at dietary supplements and ARMD:
  - Vitamin C
  - Vitamin E
  - β-carotene
  - Antioxidants
  - Minerals

Findings:
- Patients with intermediate/advanced dry ARMD had a 25% reduced risk of advanced disease and vision loss.
- Patients with no/early ARMD: No benefit.

Note: Don’t give AREDS supplements to smokers (β-carotene increases the risk of lung Ca in these patients).
**ARMD: The AREDS**

- AREDS is the Age-Related Eye Disease Study
- Looked at dietary supplements and ARMD:
  - Vitamin C
  - Vitamin E
  - β-carotene

**Findings:**
- Patients with intermediate/advanced dry ARMD had a 25% reduced risk of advanced disease and vision loss
- Patients with no/early ARMD: No benefit

- Note: Don’t give AREDS supplements to smokers (β-carotene increases the risk of lung Ca in these patients)

**Antioxidants**

**Minerals**
ARMD: The AREDS

- AREDS is the Age-Related Eye Disease Study
- Looked at dietary supplements and ARMD:
  - Vitamin C 500 mg
  - Vitamin E 400 IU
  - β-carotene 15 mg
  - Antioxidants
  - Minerals

Findings:
- Patients with intermediate/advanced dry ARMD had a 25% reduced risk of advanced disease and vision loss
- Patients with no/early ARMD: No benefit

Note: Don’t give AREDS supplements to smokers (β-carotene increases the risk of lung Ca in these patients)
ARMD: The AREDS

- AREDS is the Age-Related Eye Disease Study
- Looked at dietary supplements and ARMD:
  - Vitamin C 500 mg
  - Vitamin E 400 IU
  - β-carotene 15 mg
  - Antioxidants
  - Minerals
  - ?
**ARMD: The AREDS**

- AREDS is the Age-Related Eye Disease Study
- Looked at dietary supplements and ARMD:
  - **Vitamin C** 500 mg
  - **Vitamin E** 400 IU
  - **β-carotene** 15 mg
  - **Zinc**
  - **Cupric oxide**

**Antioxidants**

**Minerals**
**ARMD: The AREDS**

- AREDS is the *Age-Related Eye Disease Study*
- Looked at dietary supplements and ARMD:
  - **Vitamin C** 500 mg
  - **Vitamin E** 400 IU
  - **β-carotene** 15 mg
  - **Zinc** dose?
  - **Cupric oxide** dose?
  
  **antioxidants**
  
  **minerals**
ARMD: The AREDS

AREDS is the Age-Related Eye Disease Study

Looked at dietary supplements and ARMD:

- **Vitamin C**: 500 mg
- **Vitamin E**: 400 IU
- **β-carotene**: 15 mg
- **Zinc**: 80 mg
- **Cupric oxide**: 2 mg

**Antioxidants**

**Minerals**
ARMD: The AREDS

AREDS is the Age-Related Eye Disease Study

Looked at dietary supplements and ARMD:

- **Vitamin C** 500 mg
- **Vitamin E** 400 IU
- **β-carotene** 15 mg
- **Zinc** 80 mg
- **Cupric oxide** 2 mg

**Study findings:**

- Patients with ARMD had a reduced risk of advanced disease and vision loss

Note: Don't give AREDS supplements to smokers (β-carotene increases the risk of lung Ca in these patients)
**ARMD: The AREDS**

- AREDS is the *Age-Related Eye Disease Study*
- Looked at dietary supplements and ARMD:
  - **Vitamin C** 500 mg
  - **Vitamin E** 400 IU
  - **β-carotene** 15 mg
  - **Zinc** 80 mg
  - **Cupric oxide** 2 mg

  **Antioxidants**

  **Minerals**

**Study findings:**

- Patients with *intermediate/advanced dry* ARMD had a **25%** reduced risk of advanced disease and vision loss.

- Note: Don’t give AREDS supplements to smokers (β-carotene increases the risk of lung Ca in these patients).
**ARMD: The AREDS**

- AREDS is the *Age-Related Eye Disease Study*
- Looked at dietary supplements and ARMD:
  - **Vitamin C** 500 mg
  - **Vitamin E** 400 IU
  - **β-carotene** 15 mg
  - **Zinc** 80 mg
  - **Cupric oxide** 2 mg

- Study findings:
  - Patients with *intermediate/advanced dry* ARMD had a **25%** reduced risk of advanced disease and vision loss
  - Patients with *severity* ARMD: No benefit

Note: Don't give AREDS supplements to smokers (β-carotene increases the risk of lung Ca in these patients)
**ARMD: The AREDS**

- AREDS is the *Age-Related Eye Disease Study*
- Looked at dietary supplements and ARMD:
  - **Vitamin C** 500 mg
  - **Vitamin E** 400 IU
  - **β-carotene** 15 mg
  - **Zinc** 80 mg
  - **Cupric oxide** 2 mg

- **Study findings:**
  - Patients with *intermediate/advanced dry* ARMD had a **25%** reduced risk of advanced disease and vision loss
  - Patients with *no/early* ARMD: No benefit

Note: Don’t give AREDS supplements to smokers (*β-carotene increases the risk of lung Ca in these patients*)
**ARMD: The AREDS**

- AREDS is the Age-Related Eye Disease Study
- Looked at dietary supplements and ARMD:
  - Vitamin C 500 mg
  - Vitamin E 400 IU
  - β-carotene 15 mg
  - Zinc 80 mg
  - Cupric oxide 2 mg
- **Study findings:**
  - Patients with *intermediate/advanced dry* ARMD had a **25%** reduced risk of advanced disease and vision loss
  - Patients with *no/early* ARMD: No benefit
- Note: Don’t give AREDS supplements to **pt population**

*Note: Don’t give AREDS supplements to smokers (β-carotene increases the risk of lung Ca in these patients)*
**ARMD: The AREDS**

- AREDS is the **Age-Related Eye Disease Study**
- Looked at dietary supplements and ARMD:
  - **Vitamin C** 500 mg
  - **Vitamin E** 400 IU
  - **β-carotene** 15 mg
  - **Zinc** 80 mg
  - **Cupric oxide** 2 mg

**Study findings:**
- Patients with **intermediate/advanced dry** ARMD had a **25%** reduced risk of advanced disease and vision loss
- Patients with **no/early** ARMD: No benefit
- Note: Don’t give AREDS supplements to **smokers**
**ARMD: The AREDS**

AREDS is the Age-Related Eye Disease Study. Looked at dietary supplements and ARMD:

- **Vitamin C** 500 mg
- **Vitamin E** 400 IU
- **β-carotene** 15 mg
- **Zinc** 80 mg
- **Cupric oxide** 2 mg

### Antioxidants

- **Vitamin C** and **Vitamin E**

### Minerals

- **Zinc**
- **Cupric oxide**

**Study findings:**

- Patients with **intermediate/advanced dry** ARMD had a **25%** reduced risk of advanced disease and vision loss.
- Patients with **no/early** ARMD: No benefit.

**Note:** Don’t give AREDS supplements to **smokers**. An AREDS anti-ox increases the risk of lung Ca in these patients.
ARMD: The AREDS

- AREDS is the Age-Related Eye Disease Study
- Looked at dietary supplements and ARMD:
  - Vitamin C 500 mg
  - Vitamin E 400 IU
  - β-carotene 15 mg
  - Zinc 80 mg
  - Cupric oxide 2 mg

Study findings:
- Patients with intermediate/advanced dry ARMD had a 25% reduced risk of advanced disease and vision loss
- Patients with no/early ARMD: No benefit
- Note: Don’t give AREDS supplements to smokers
  - β-carotene increases the risk of lung Ca in these patients
ARMD: The AREDS

AREDS is the Age-Related Eye Disease Study

Looked at dietary supplements and ARMD:

- Vitamin C  500 mg
- Vitamin E  400 IU
- β-carotene  15 mg
- Zinc            80 mg
- Cupric oxide  2 mg

Study findings:

- Patients with intermediate/advanced dry ARMD had a 25% reduced risk of advanced disease and vision loss
- Patients with no/early ARMD: No benefit

Note: Don’t give AREDS supplements to smokers
- β-carotene increases the risk of lung Ca in these patients

Next, let’s drill down on the AREDS2
**ARMD: The AREDS2**

- Follow-up to the AREDS

- **Vitamin C** 500 mg
- **Vitamin E** 400 IU
- **β-carotene** 15 mg
- **Zinc** 80 mg
- **Cupric oxide** 2 mg
ARMD: The AREDS2

- Follow-up to the AREDS
- Subbed for \( \beta \)-carotene

- Vitamin C 500 mg
- Vitamin E 400 IU
- \( \beta \)-carotene
- Zinc 80 mg
- Cupric oxide 2 mg
ARMD: The AREDS2

- Follow-up to the AREDS
- Subbed xanthophylls for β-carotene
  - Vitamin C 500 mg
  - Vitamin E 400 IU
  - β-carotene Lutein & Zeaxanthin (These are the two xanthophylls employed)
  - Zinc 80 mg
  - Cupric oxide 2 mg
**ARMD: The AREDS2**

- Follow-up to the AREDS
- Subbed **xanthophylls** for β-carotene; added:
  - **Vitamin C** 500 mg
  - **Vitamin E** 400 IU
  - β-carotene
  - **Lutein & Zeaxanthin**
  - **Zinc** 80 mg
  - Cupric oxide 2 mg
  - ?
ARMD: The AREDS2

- Follow-up to the AREDS
- Subbed xanthophylls for β-carotene; added O3FAs:
  - Vitamin C 500 mg
  - Vitamin E 400 IU
  - β-carotene
  - Zinc 80 mg
  - Cupric oxide 2 mg

Lutein & Zeaxanthin

Omega-3 fatty acids
ARMD: The AREDS2

Follow-up to the AREDS

Subbed xanthophylls for β-carotene; added O3FAs:

- Vitamin C 500 mg
- Vitamin E 400 IU
- β-carotene
- Lutein & Zeaxanthin
- Zinc 80 mg
- Cupric oxide 2 mg
- Omega-3 fatty acids

Study findings:

Reaffirmed vs Disputed results of the AREDS
ARMD: The AREDS2

- Follow-up to the AREDS
- Subbed xanthophylls for β-carotene; added O3FAs:
  - Vitamin C 500 mg
  - Vitamin E 400 IU
  - β-carotene
  - Lutein & Zeaxanthin
  - Zinc 80 mg
  - Cupric oxide 2 mg

- Study findings:
  - Reaffirmed results of the AREDS
**ARMD: The AREDS2**

- Follow-up to the AREDS
- Subbed **xanthophylls** for β-carotene; added **O3FAs:**
  - **Vitamin C** 500 mg
  - **Vitamin E** 400 IU
  - **β-carotene** **Lutein & Zeaxanthin**
  - **Zinc** 80 mg
  - **Cupric oxide** 2 mg

**Study findings:**
- **Reaffirmed** results of the AREDS
- Xanthophylls **effective vs ineffective** substitute for β-carotene
**ARMD: The AREDS2**

- Follow-up to the AREDS
- Subbed **xanthophylls** for β-carotene; added **O3FAs**:
  - **Vitamin C**: 500 mg
  - **Vitamin E**: 400 IU
  - **β-carotene**: Lutein & Zeaxanthin
  - **Zinc**: 80 mg
  - **Cupric oxide**: 2 mg

- **Study findings**:
  - **Reaffirmed** results of the AREDS
  - Xanthophylls **suitable** substitute for β-carotene
**ARMD: The AREDS2**
- Follow-up to the AREDS
- Subbed xanthophylls for β-carotene; added **O3FAs**:
  - Vitamin C 500 mg
  - Vitamin E 400 IU
  - β-carotene
  - Zinc 80 mg
  - Cupric oxide 2 mg

**Study findings:**
- Reaffirmed results of the AREDS
- **Xanthophylls suitable** substitute for β-carotene

*Why is this important?*
ARMD: The AREDS2

- Follow-up to the AREDS
- Subbed xanthophylls for β-carotene; added O3FAs:
  - Vitamin C 500 mg
  - Vitamin E 400 IU
  - β-carotene
  - Zinc 80 mg
  - Cupric oxide 2 mg
- Study findings:
  - Reaffirmed results of the AREDS
  - Xanthophylls suitable substitute for β-carotene
  - Why is this important? Because it means β-carotene can be dropped, obviating this concern
- Note: Don’t give AREDS supplements to smokers
  - β-carotene increases the risk of lung Ca in these patients
ARMD: The AREDS2

- Follow-up to the AREDS
- Subbed xanthophylls for β-carotene; added O3FAs:
  - Vitamin C 500 mg
  - Vitamin E 400 IU
  - β-carotene
  - Lutein & Zeaxanthin
  - Zinc 80 mg
  - Cupric oxide 2 mg
- Study findings:
  - Reaffirmed results of the AREDS
  - Xanthophylls suitable substitute for β-carotene
  - O3FAs effective vs ineffective at reducing risk of progression
ARMD: The AREDS$_2$

- Follow-up to the AREDS
- Subbed xanthophylls for β-carotene; added O3FAs:
  - **Vitamin C** 500 mg
  - **Vitamin E** 400 IU
  - **β-carotene** Lutein & Zeaxanthin
  - **Zinc** 80 mg
  - **Cupric oxide** 2 mg

- Study findings:
  - **Reaffirmed** results of the AREDS
  - Xanthophylls **suitable** substitute for β-carotene
  - O3FAs **ineffective** at reducing risk of progression