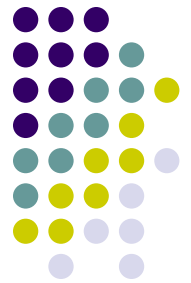
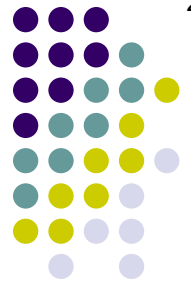


Q

Diabetic Retinopathy: Diabetic Macular Edema

- What are the three histological vascular derangements in DBR?
 - 1)
 - 2)
 - 3)





Q/A

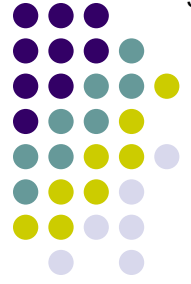
Diabetic Retinopathy: Diabetic Macular Edema

- What are the three histological vascular derangements in DBR?

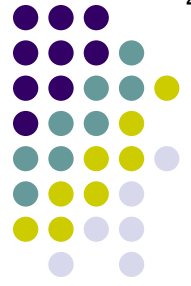
- 1) cell type **loss** *BM = Basement membrane*
- 2) abb. **thickening** → ↓ **lumen diameter**
- 3) **Loss of** diff dell type **barrier function**

A

Diabetic Retinopathy: Diabetic Macular Edema



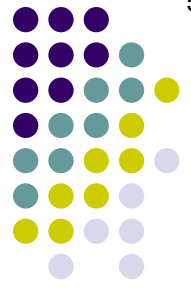
- What are the three histological vascular derangements in DBR?
 - 1) **Pericyte loss** *BM = Basement membrane*
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**Q**

Diabetic Retinopathy: Diabetic Macular Edema

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With respect to the structure of retinal arterioles and capillaries, how are pericytes and endothelial cells related to one another?



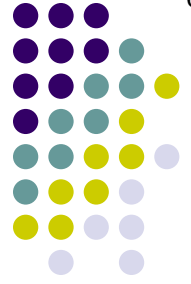
Q/A

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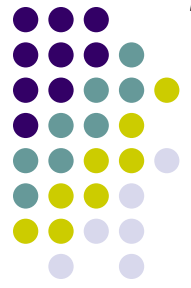
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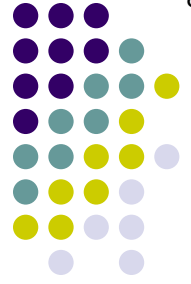
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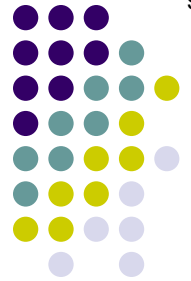
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The **endothelial** cells line the lumen of the vessel. They are surrounded by their BM. They are **nonfenestrated** .



Q

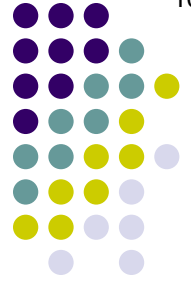
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four words



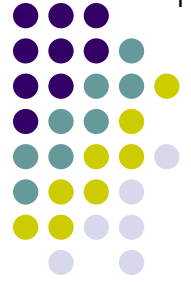
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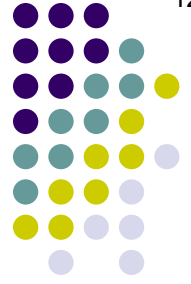
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Q

Diabetic Retinopathy: Diabetic Macular Edema

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Do retinal vessels have an intimal lining?

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A

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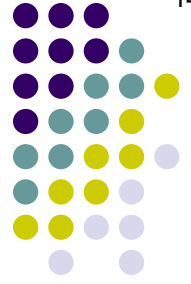
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Do they possess a muscular wall?

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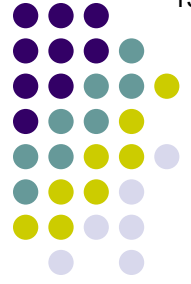
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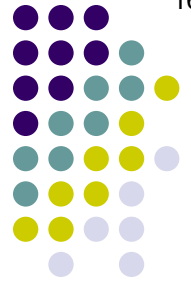
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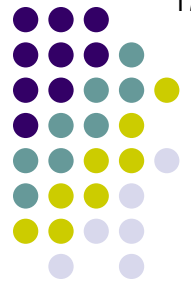
Do retinal vessels have an intimal lining?

No

Do they possess a muscular wall?

No

With what nearby vascular bed do they share the lack of these features?



A

Diabetic Retinopathy: Diabetic Macular Edema

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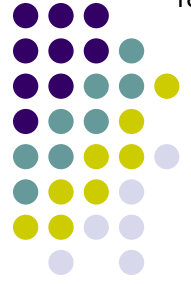
Do retinal vessels have an intimal lining?
No

Do they possess a muscular wall?
No

With what nearby vascular bed do they share the lack of these features?
The cerebral vasculature (which makes sense, because *the retina is in essence an extension of the CNS*)

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Q

Diabetic Retinopathy: Diabetic Macular Edema

- What are the three histological vascular derangements in DBR?
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That this is known as the inner blood-retina barrier implies the existence of what?

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...nded by their

BM. They are **nontenestrated**. Tight junctions between cells form the so-called **inner blood-retina barrier**. The pericytes surround the vessel, and are embedded in the BM of the endothelial cells.



A

Diabetic Retinopathy: Diabetic Macular Edema

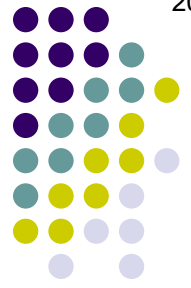
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An **outer** blood-retina barrier

How are

bounded by their

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Q

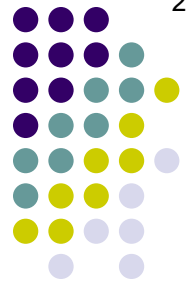
Diabetic Retinopathy: Diabetic Macular Edema

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*That this is known as the inner blood-retina barrier implies the existence of what?
An **outer** blood-retina barrier*

Yup. What forms the outer blood-retina barrier?

*BM. They are **nontenestrated**. Tight junctions between cells form the so-called **inner blood-retina barrier**. The pericytes surround the vessel, and are embedded in the BM of the endothelial cells.*



Q/A

Diabetic Retinopathy: Diabetic Macular Edema

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An **outer** blood-retina barrier

Yup. What forms the outer blood-retina barrier?
Tight junctions between **three words** cells

inner blood-retina barrier. The pericytes surround the vessel, and are embedded in the BM of the endothelial cells.



A

Diabetic Retinopathy: Diabetic Macular Edema

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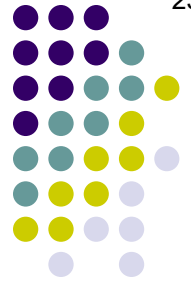
That this is known as the inner blood-retina barrier implies the existence of what?

An **outer** blood-retina barrier

Yup. What forms the outer blood-retina barrier?

Tight junctions between retinal pigment epithelium (RPE) cells

BM. They are **nontenestrated**. Tight junctions between cells form the so-called **inner blood-retina barrier**. The pericytes surround the vessel, and are embedded in the BM of the endothelial cells.



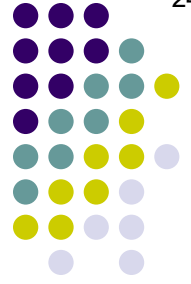
Q

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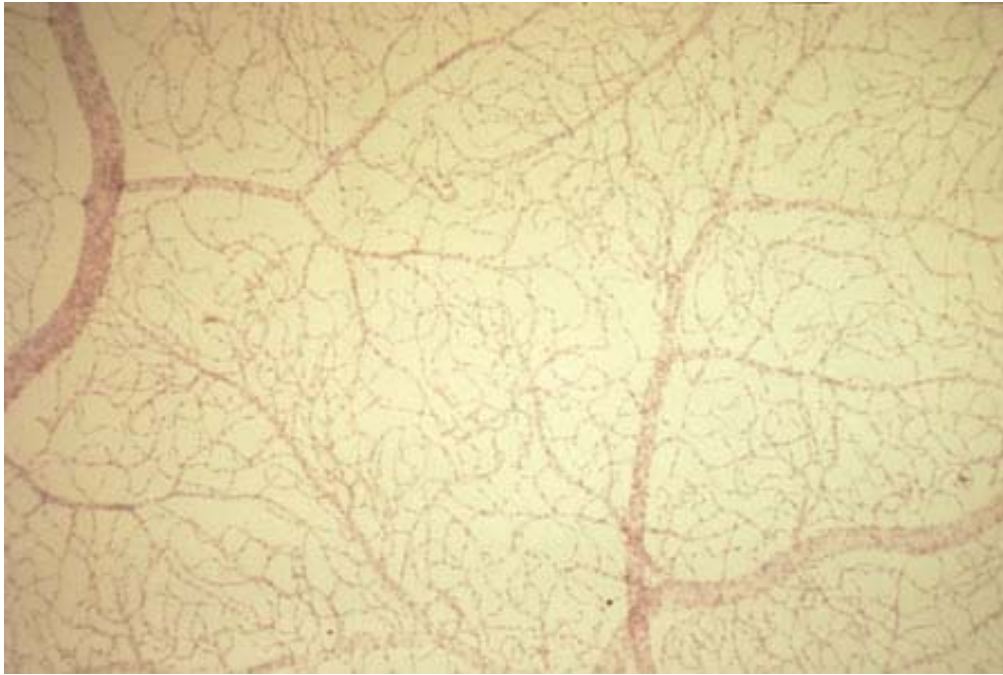
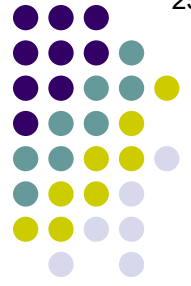
Which occurs first?

A

Diabetic Retinopathy: Diabetic Macular Edema

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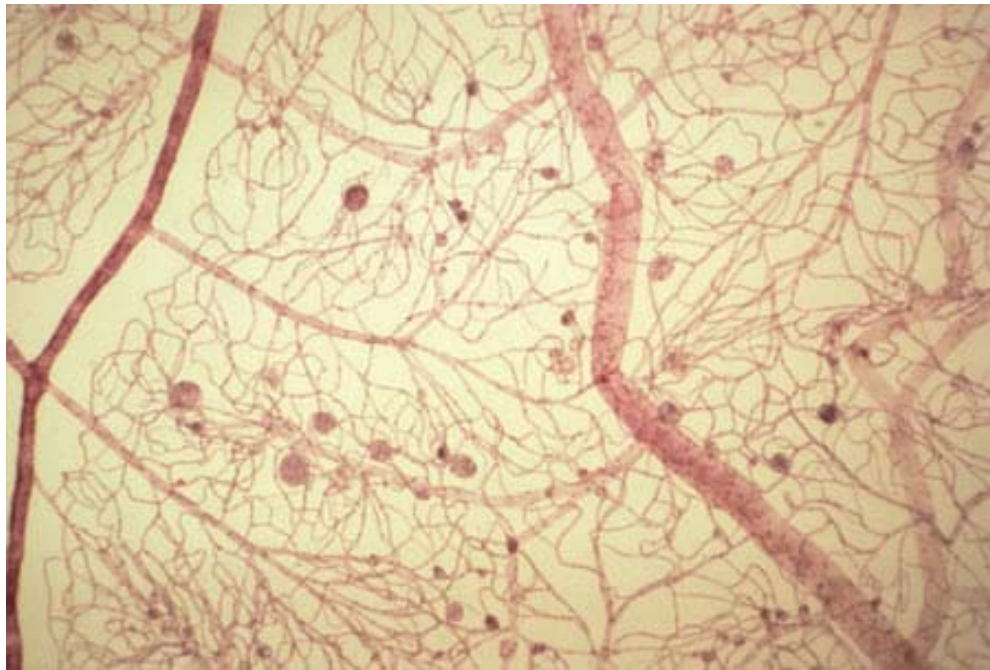
Which occurs first?
Pericyte loss



*Trypsin mount of normal retina--
low and high mag*

The dark nuclei belong to pericytes;
the lighter, to endothelial cells.
*Note that the ratio between them is
roughly 1:1.*

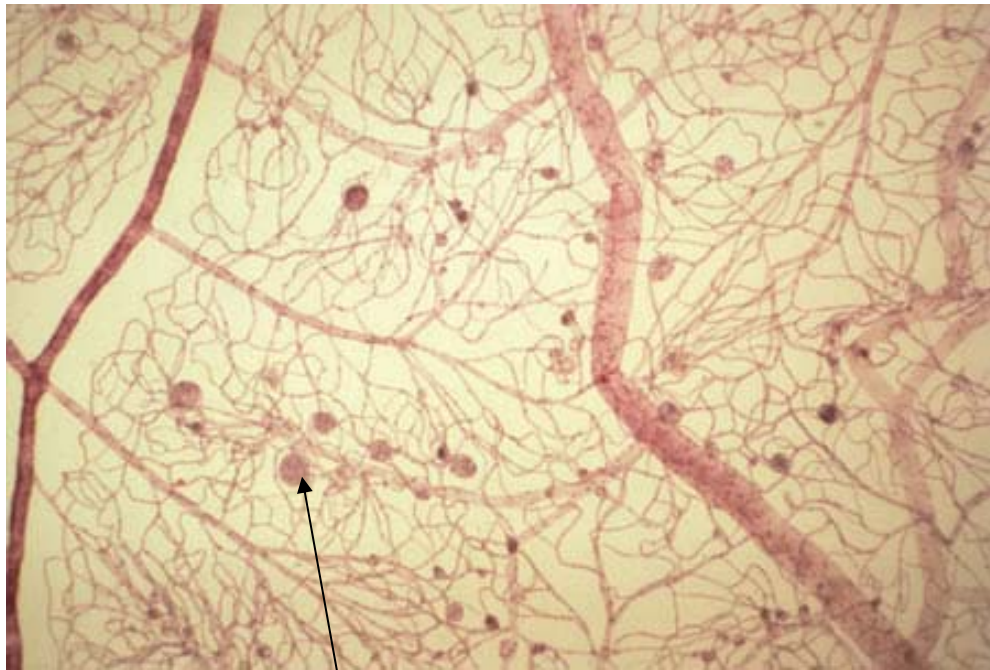




*Trypsin mount of **DBR** retina--
low and high mag*

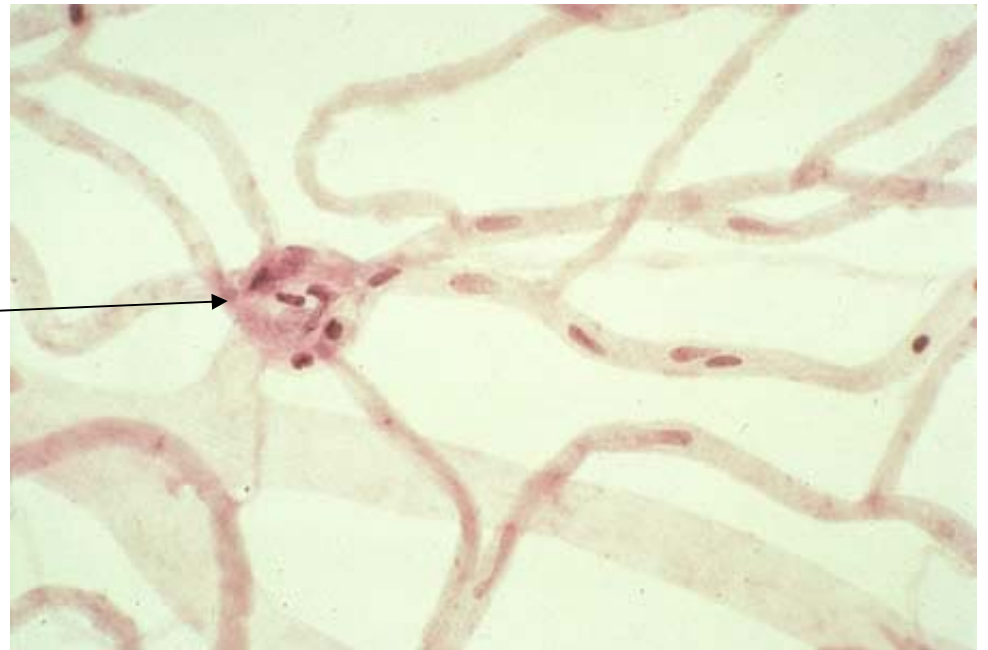
But in a retina that with damage 2ndry to diabetes, the ratio of endothelial cells to pericytes is **many-to-one**.

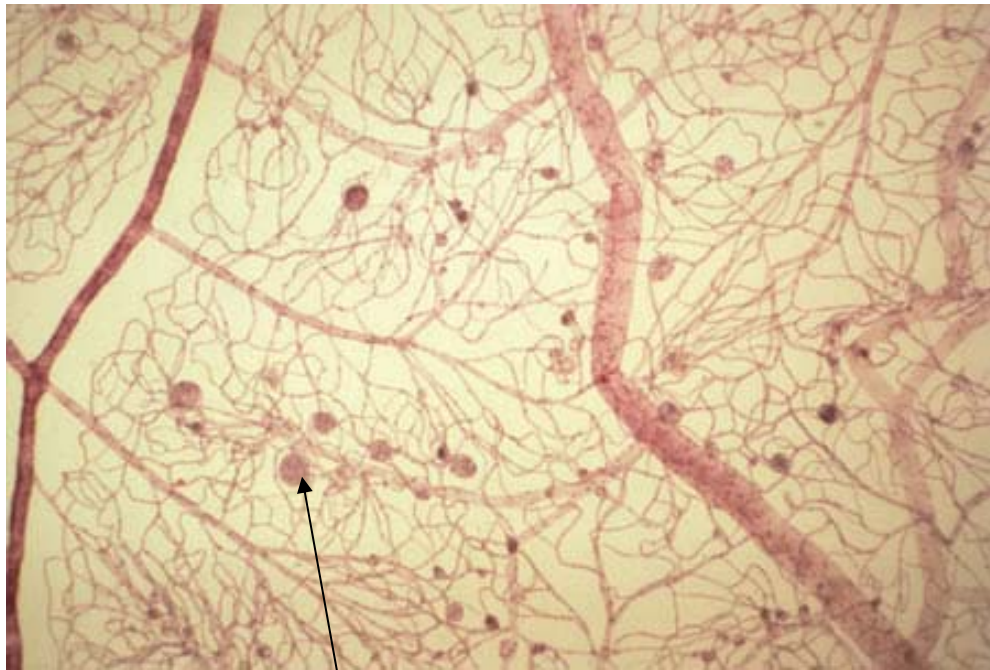
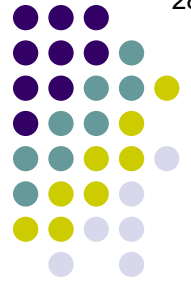




*Trypsin mount of **DBR** retina--
low and high mag*

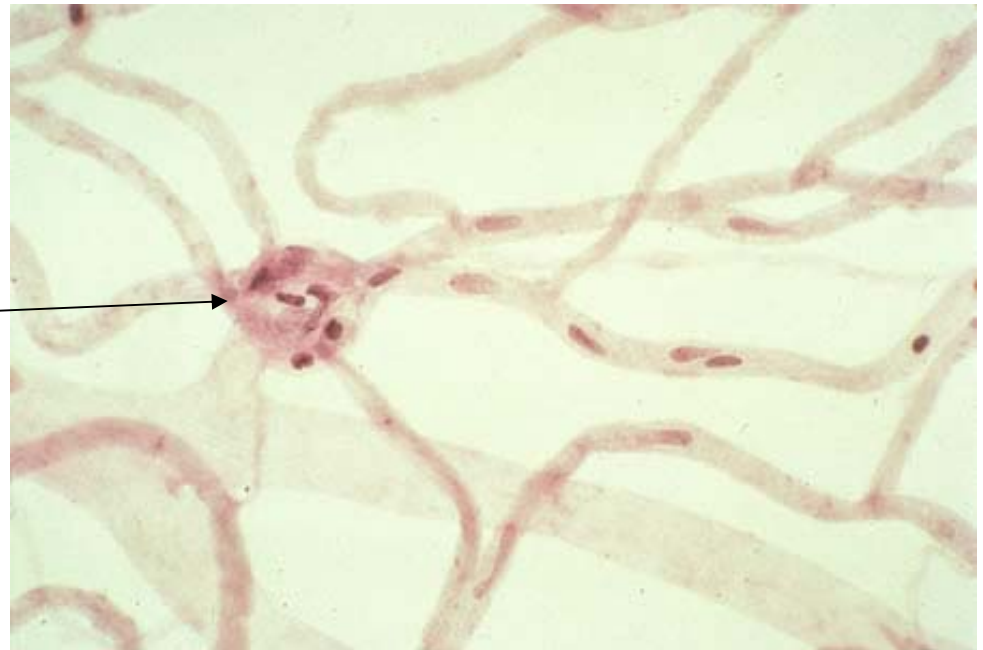
What are these things?

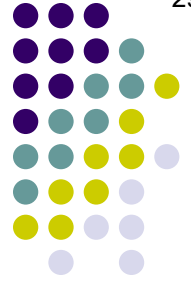




*Trypsin mount of **DBR** retina--
low and high mag*

What are these things?
Microaneurysms



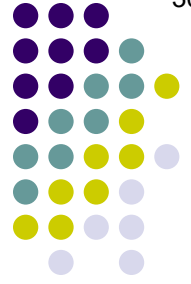


Q

Diabetic Retinopathy: Diabetic Macular Edema

- What are the three histological vascular derangements in DBR?
 - 1) Pericyte loss
 - 2) BM thickening → ↓ lumen diameter
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Loss of endothelial barrier function leads to what pathologic event?

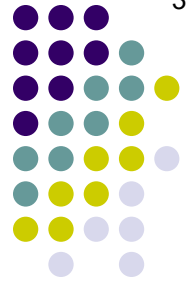


A

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Loss of endothelial barrier function leads to what pathologic event?
Leaching of serum into the retina



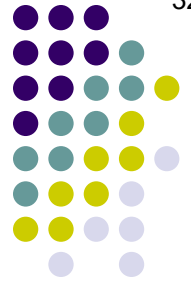
Q

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Loss of endothelial barrier function leads to what pathologic event?
Leaching of serum into the retina

Leaching of serum into the retina leads to what pathological state?



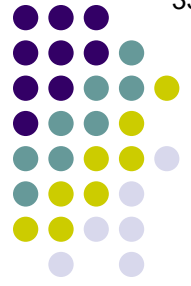
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Loss of endothelial barrier function leads to what pathologic event?
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Leaching of serum into the retina leads to what pathological state?
Retinal edema



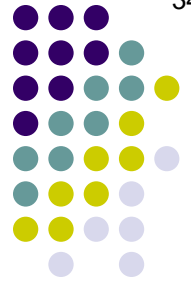
Q

Diabetic Retinopathy: Diabetic Macular Edema

- What are the three histological vascular derangements in DBR?
 - 1) Pericyte loss

What commonly-prescribed class of PO diabetes medicine is notorious for causing or exacerbating diabetic macular edema?

Retinal edema



A

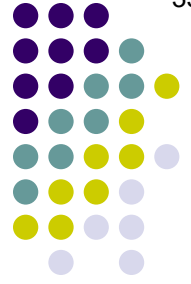
Diabetic Retinopathy: Diabetic Macular Edema

- What are the three histological vascular derangements in DBR?
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What commonly-prescribed class of PO diabetes medicine is notorious for causing or exacerbating diabetic macular edema?

The **thiazolidinediones**, AKA the **glitazones**

Retinal edema



Q

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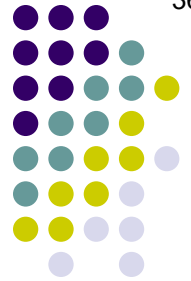
The **thiazolidinediones**, AKA the **glitazones**

Two such meds are commonly prescribed in the US. What are they?

--

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Retinal edema



Q/A

Diabetic Retinopathy: Diabetic Macular Edema

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Two such meds are commonly prescribed in the US. What are they?

--Pioglitazone (brand name)

--Rosiglitazone (brand name)

Retinal edema



A

Diabetic Retinopathy: Diabetic Macular Edema

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What commonly-prescribed class of PO diabetes medicine is notorious for causing or exacerbating diabetic macular edema?

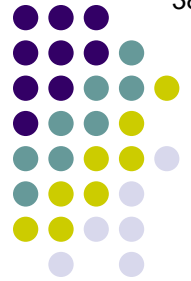
The **thiazolidinediones**, AKA the **glitazones**

Two such meds are commonly prescribed in the US. What are they?

--Pioglitazone (brand name Actos)

--Rosiglitazone (brand name Avandia)

Retinal edema



Diabetic Retinopathy: Diabetic Macular Edema

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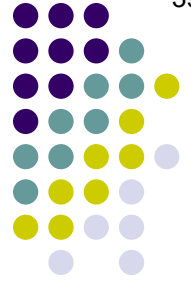
Two such meds are commonly prescribed in the US. What are they?

--Pioglitazone (brand name Actos)

--Rosiglitazone (brand name Avandia)

Always inquire whether your DME pt is on one of these meds!

Retinal edema



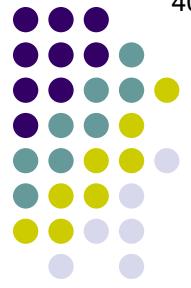
Q

Diabetic Retinopathy: Diabetic Macular Edema

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?

With respect to its clinical management, there are two ways to think about/classify DME. On what basis is this division made?



A

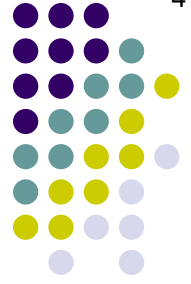
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention

Primary intervention

With respect to its clinical management, there are two ways to think about/classify DME. On what basis is this division made?

It is made on the basis of the type of intervention being contemplated



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
?

Primary intervention:
?

With respect to its clinical management, there are two ways to think about/classify DME. On what basis is this division made?

It is made on the basis of the type of intervention being contemplated

What are the two types of intervention?

**A**

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

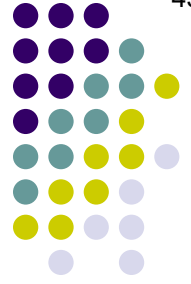
Primary intervention:
Laser surgery

With respect to its clinical management, there are two ways to think about/classify DME. On what basis is this division made?

It is made on the basis of the type of intervention being contemplated

What are the two types of intervention?

Intravitreal anti-VEGF injection, and laser



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

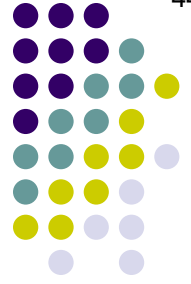
With respect to its clinical management, there are two ways to think about/classify DME. On what basis is this division made?

It is made on the basis of the type of intervention being contemplated

What are the two types of intervention?

Intravitreal anti-VEGF injection, and laser

Why must the classification of DME be adjusted for the type of primary intervention being contemplated?

**A**

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Why must the classification of DME be adjusted for the type of primary intervention being contemplated?

Because the factors influencing treatment appropriateness and success differ between the modalities



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

Why must the classification of DME be adjusted for the type of primary intervention being contemplated?

Because the factors influencing treatment success differ between the modalities

In the present context, what is being referred to by the term 'pharmacologic intervention'?

**A****Diabetic Retinopathy: Diabetic Macular Edema**

Primary intervention:
Pharmacologic

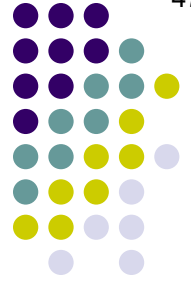
Primary intervention:
Laser surgery

Why must the classification of DME be adjusted for the type of primary intervention being contemplated?

Because the factors influencing treatment success differ between the modalities

In the present context, what is being referred to by the term 'pharmacologic intervention'?

Intravitreal injection of a pharmacologic agent



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

Why must the classification of DME be adjusted for the type of primary intervention being contemplated?

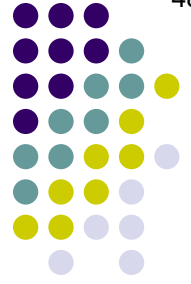
Because the factors influencing treatment success differ between the modalities

In the present context, what is being referred to by the term 'pharmacologic intervention'?

Intravitreal injection of a pharmacologic agent

What specific pharmacologic agents are available?

- ?
- ?
- ?
- ?



A

Diabetic Retinopathy: Diabetic Macular Edema

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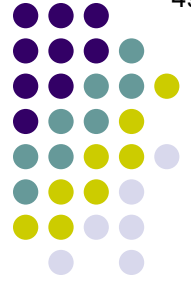
--Aflibercept

--Ranibizumab

--Bevacizumab

--Triamcinolone

--*Pegaptanib* (And *pegaptanib*. But because no one uses it, and the BCSC *Retina* book barely mentions it, we won't discuss it further.)



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

Why must the classification of DME be adjusted for the type of primary intervention being contemplated?

Because the factors influencing treatment success differ between the modalities

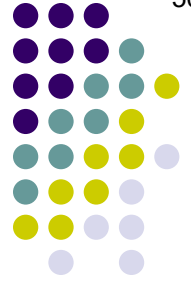
In the present context, what is being referred to by the term 'pharmacologic intervention'?

Intravitreal injection of a pharmacologic agent

What specific pharmacologic agents are available?

- Aflibercept
- Ranibizumab
- Bevacizumab
- Triamcinolone

In the present context, what is being referred to by the term 'laser surgery'?



A

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

Why must the classification of DME be adjusted for the type of primary intervention being contemplated?

Because the factors influencing treatment success differ between the modalities

In the present context, what is being referred to by the term 'pharmacologic intervention'?

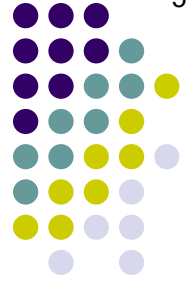
Intravitreal injection of a pharmacologic agent

What specific pharmacologic agents are available?

- Aflibercept
- Ranibizumab
- Bevacizumab
- Triamcinolone

In the present context, what is being referred to by the term 'laser surgery'?

Lasering the edematous regions of the retina



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

Why must the classification of DME be adjusted for the type of primary intervention being contemplated?

Because the factors influencing treatment success differ between the modalities

In the present context, what is being referred to by the term 'pharmacologic intervention'?

Intravitreal injection of a pharmacologic agent

What specific pharmacologic agents are available?

- Aflibercept
- Ranibizumab
- Bevacizumab
- Triamcinolone

In the present context, what is being referred to by the term 'laser surgery'?

Lasering the edematous regions of the retina

What specific laser procedures are available?

- ?
- ?



A

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

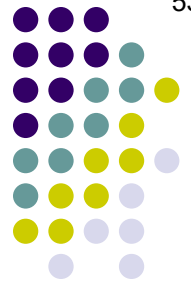
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In the present context, what is being referred to by the term 'pharmacologic intervention'?
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What specific pharmacologic agents are available?
--Aflibercept
--Ranibizumab
--Bevacizumab
--Triamcinolone

In the present context, what is being referred to by the term 'laser surgery'?
Lasering the edematous regions of the retina

What specific laser procedures are available?
--Focal macular laser (FML)
--Grid macular laser (GML)



Q

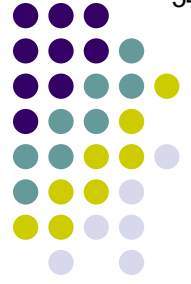
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery



In this classification system, there are two types of DME. What are they?

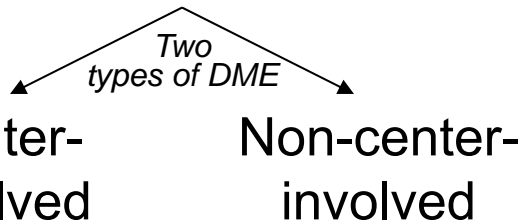


A

Diabetic Retinopathy: Diabetic Macular Edema

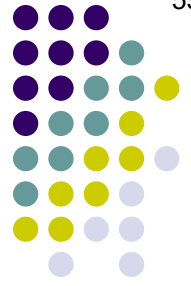
Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery



In this classification system, there are two types of DME. What are they?
That which involves the center (foveal) region, and everything else

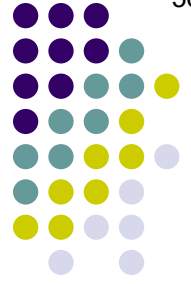
Diabetic Retinopathy: Diabetic Macular Edema



DME: Center-involved



DME: Not center-involved



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

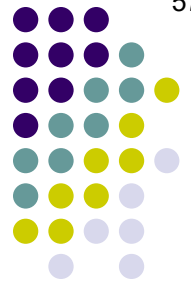
Center-
involved

Non-center-
involved

In this classification system, there are two types of DME. What are they?

That which involves the center (foveal) region, and everything else

By what technique is the retina evaluated for the presence of DME?



A

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

Center-
involved

Non-center-
involved

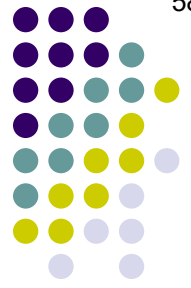
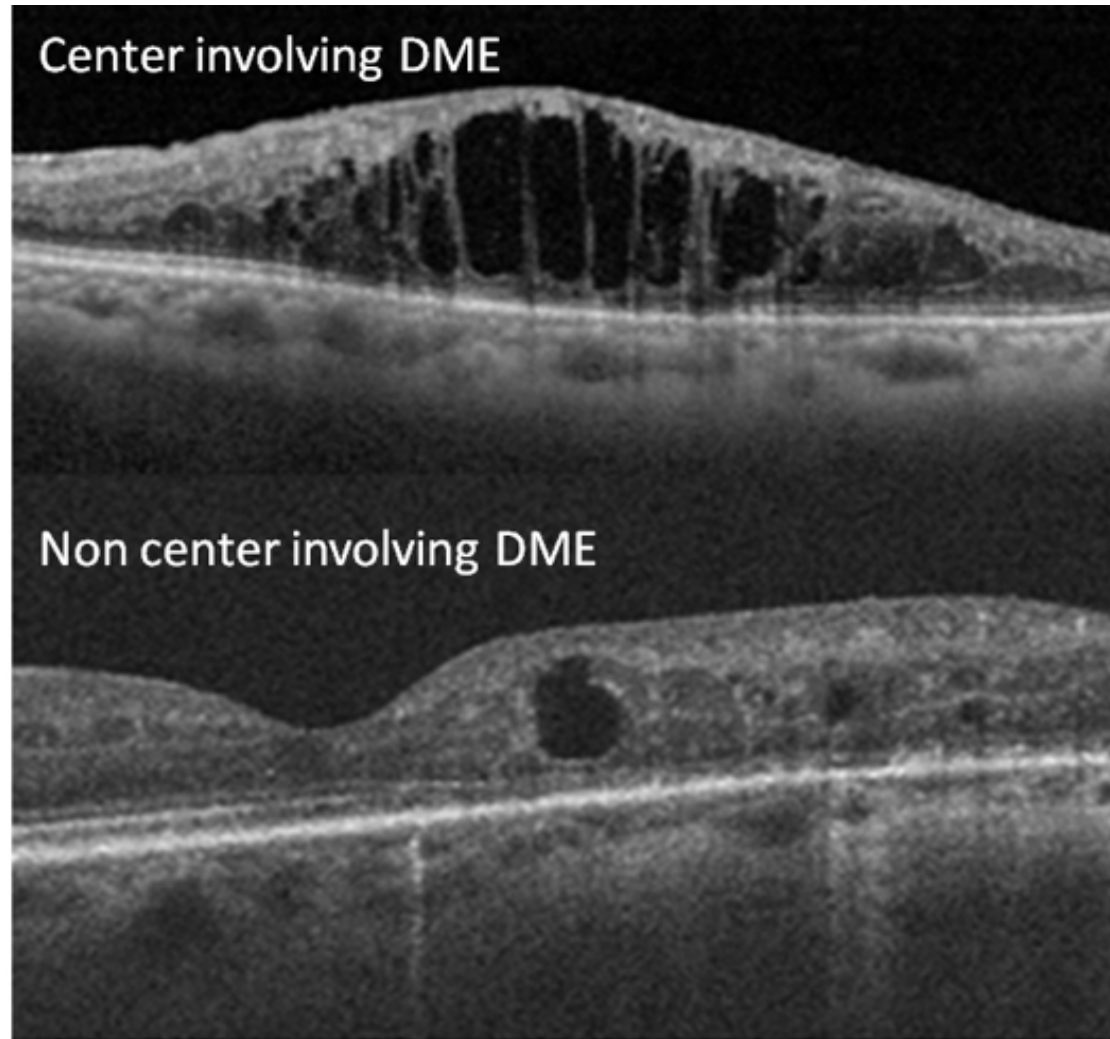
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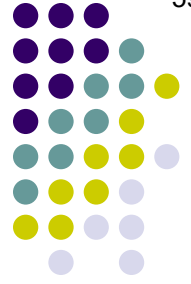
That which involves the center (foveal) region, and everything else

By what technique is the retina evaluated for the presence of DME?

By OCT

Diabetic Retinopathy: Diabetic Macular Edema





Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

Center-
involved

Non-center-
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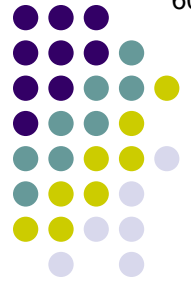
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Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

Center-
involved

Non-center-
involved

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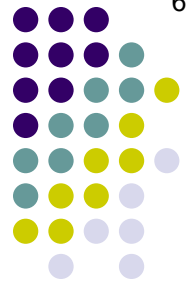
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By OCT

In this system, what findings signal that treatment is indicated?

Center-involving DME + decreased visual acuity



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

Center-
involved

Non-center-
involved

In the present context, what is being referred to by the term 'pharmacologic intervention'?

Intravitreal injection of a pharmacologic agent

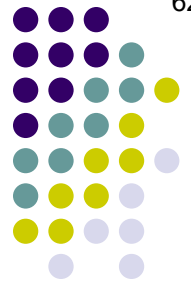
What specific pharmacologic agents are available?

- Aflibercept
- Ranibizumab
- Bevacizumab
- Triamcinolone

Broadly, what is the mechanism of action for these meds?

*In this system, what findings signal that **treatment** is indicated?*

Center-involving DME + decreased visual acuity



A

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

Center-
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Non-center-
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In the present context, what is being referred to by the term 'pharmacologic intervention'?
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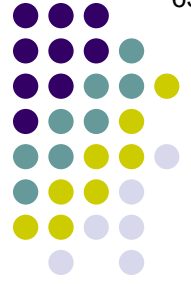
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Broadly, what is the mechanism of action for these meds? Interference with VEGF activity

*In this system, what findings signal that **treatment** is indicated?*

Center-involving DME + decreased visual acuity



Q

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Primary intervention:
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Center-
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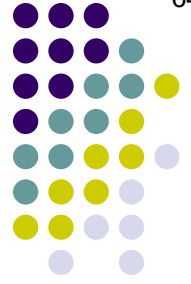
--**Triamcinolone**

Broadly, what is the mechanism of action for these meds? Interference with VEGF activity

Broadly, what is the mechanism of action for triamcinolone?

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A

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Primary intervention:
Laser surgery

Center-
involved

Non-center-
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In the present context, what is being referred to by the term 'pharmacologic intervention'?

Intravitreal injection of a pharmacologic agent

What specific pharmacologic agents are available?

--Aflibercept

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--**Triamcinolone**

Broadly, what is the mechanism of action for these meds? Interference with VEGF activity

Broadly, what is the mechanism of action for triamcinolone? Anti-inflammatory (it's a steroid)

*In this system, what findings signal that **treatment** is indicated?*

Center-involving DME + decreased visual acuity



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Primary intervention:
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*Broadly, what is the mechanism of action for these meds? Interference with **VEGF** activity*

Broadly, what is the mechanism of action for triamcinolone? Anti-inflammatory (it's a steroid)

Let's drill down on VEGF...

*In this system, what findings signal that **treatment** is indicated?*

Center-involving DME + decreased visual acuity

**Q**

Diabetic Retinopathy: Diabetic Macular Edema

What does **VEGF** stand for?

VEGF-A₁₆₅



A

Diabetic Retinopathy: Diabetic Macular Edema

What does **VEGF** stand for?
Vascular endothelial growth factor

VEGF-A₁₆₅



Q

Diabetic Retinopathy: Diabetic Macular Edema

What does **VEGF** stand for?
Vascular endothelial growth factor

Broadly speaking, what is it?

VEGF-A₁₆₅



A

Diabetic Retinopathy: Diabetic Macular Edema

*What does **VEGF** stand for?*
Vascular endothelial growth factor

Broadly speaking, what is it?
An extracellular signaling protein
involved in vascular development

VEGF-A₁₆₅



Q

Diabetic Retinopathy: Diabetic Macular Edema

What does **VEGF** stand for?
Vascular endothelial growth factor

Broadly speaking, what is it?
An extracellular signaling protein
involved in **vascular development**

Does VEGF do anything besides grow new blood vessels?

VEGF-A₁₆₅



A

Diabetic Retinopathy: Diabetic Macular Edema

What does **VEGF** stand for?
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Broadly speaking, what is it?
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Does *VEGF* do anything besides grow new blood vessels?
Yes, it also is a potent vasodilator (it was known originally as *vascular permeability factor*)

VEGF-A₁₆₅



Q

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How potent?

VEGF-A₁₆₅



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How potent?
About 10,000x more potent than histamine!

VEGF-A₁₆₅



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VEGF-A₁₆₅

This property accounts for VEGF's role in the development of diabetic macular edema, and explains why anti-VEGF meds can treat this condition!



Q

Diabetic Retinopathy: Diabetic Macular Edema

*What does **VEGF** stand for?*
Vascular endothelial growth factor

Broadly speaking, what is it?
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How does VEGF work?

VEGF-A₁₆₅



A

Diabetic Retinopathy: Diabetic Macular Edema

*What does **VEGF** stand for?*
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Broadly speaking, what is it?
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How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR), which are transmembrane receptor tyrosine kinase (RTK) structures.

VEGF-A₁₆₅



Q

Diabetic Retinopathy: Diabetic Macular Edema

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VEGF-A₁₆₅





A

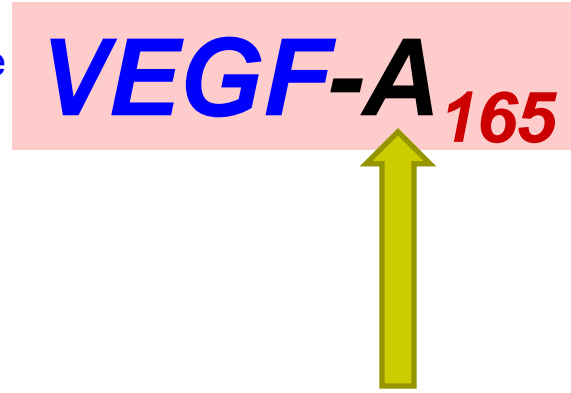
Diabetic Retinopathy: Diabetic Macular Edema

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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.





Q

Diabetic Retinopathy: Diabetic Macular Edema

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VEGF-A₁₆₅



*What does **165** signify?*



A

Diabetic Retinopathy: Diabetic Macular Edema

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When the term *VEGF* is used in the ophthalmology literature without a sub-family designation, it is understood to mean VEGF-A.

VEGF-A₁₆₅



*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.



Q

Diabetic Retinopathy: Diabetic Macular Edema

*What does **VEGF** stand for?*
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Broadly speaking, what is it?
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VEGF-A **165**



*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?



A

Diabetic Retinopathy: Diabetic Macular Edema

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Broadly speaking, what is it?
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How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR), which are transmembrane receptor tyrosine kinase (RTK) structures.

VEGF-A₁₆₅ ←

*What does the **A** signify?*

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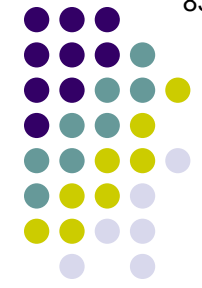
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*What does **165** signify?*

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.



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

Center-
involved

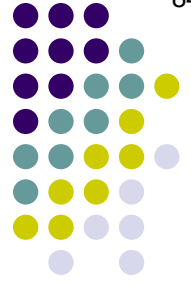
Non-center-
involved

In the present context, what is being referred to by the term 'pharmacologic intervention'?
Intravitreal injection of a pharmacologic agent

What specific pharmacologic agents are available?
--**Aflibercept**
--**Ranibizumab**
--**Bevacizumab**
--Triamcinolone

Does good clinical trial data exist justifying the use of these anti-VEGF agents in treating DME?

*In this system, what findings signal that **treatment** is indicated?*
Center-involving DME + decreased visual acuity



A

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

Center-
involved

Non-center-
involved

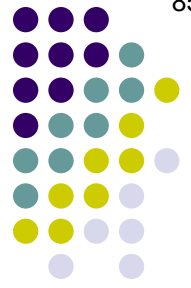
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What specific pharmacologic agents are available?

- Aflibercept
- Ranibizumab
- Bevacizumab
- Triamcinolone

Does good clinical trial data exist justifying the use of these anti-VEGF agents in treating DME?
Yes, multiple studies have established them to be safe and effective

*In this system, what findings signal that **treatment** is indicated?*
Center-involving DME + decreased visual acuity



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

Center-
involved

Non-center-
involved

In the present context, what is being referred to by the term 'pharmacologic intervention'?
Intravitreal injection of a pharmacologic agent

What specific pharmacologic agents are available?

- Aflibercept
- Ranibizumab
- Bevacizumab
- Triamcinolone**

Does good clinical trial data exist justifying the use of intravitreal steroids in treating DME?

*In this system, what findings signal that **treatment** is indicated?*

Center-involving DME + decreased visual acuity



A

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Primary intervention:
Laser surgery

Center-
involved

Non-center-
involved

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Intravitreal injection of a pharmacologic agent

What specific pharmacologic agents are available?

--Aflibercept

--Ranibizumab

--Bevacizumab

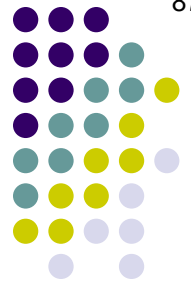
--**Triamcinolone**

Does good clinical trial data exist justifying the use of intravitreal steroids in treating DME?

Yes, although they are less effective, and have a worse side-effect profile

*In this system, what findings signal that **treatment** is indicated?*

Center-involving DME + decreased visual acuity



Q

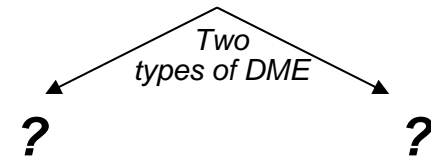
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-
involved

Non-center-
involved

Primary intervention:
Laser surgery



In this classification system, there are two types of DME. What are they?

That which involves the center (foveal) region, and everything else

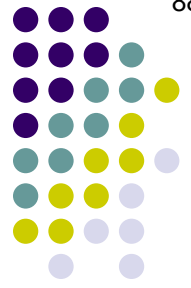
By what technique is the retina evaluated for the presence of DME?

By OCT

In this system, what findings signal that treatment is indicated?

Center-involving DME + decreased visual acuity

In this classification system, there are two types of DME. What are they?



A

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-
involved

Non-center-
involved

Primary intervention:
Laser surgery

Clinically
significant

Not clinically
significant

In this classification system, there are two types of DME. What are they?

That which involves the center (foveal) region, and everything else

By what technique is the retina evaluated for the presence of DME?

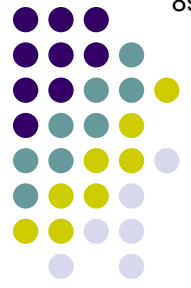
By OCT

In this system, what findings signal that treatment is indicated?

Center-involving DME + decreased visual acuity

In this classification system, there are two types of DME. What are they?

That which qualifies as 'clinically significant,' and that which does not



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
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Center-
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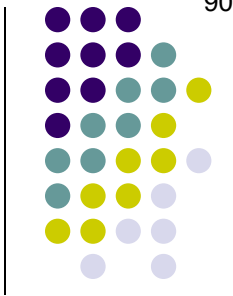
By what technique is the retina evaluated for the presence of DME?

By OCT

By what technique is the retina evaluated for the presence of DME?

In this system, what findings signal that treatment is indicated?

Center-involving DME + decreased visual acuity



A

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-
involved

Non-center-
involved

**Primary intervention:
*Laser surgery***

Clinically
significant

Not clinically
significant

In this classification system, there are two types of DME. What are they?

That which involves the center (foveal) region, and everything else

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That which qualifies as 'clinically significant,' and that which does not

By what technique is the retina evaluated for the presence of DME?

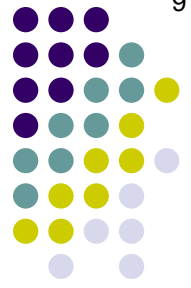
By OCT

By what technique is the retina evaluated for the presence of DME?

By DFE

In this system, what findings signal that treatment is indicated?

Center-involving DME + decreased visual acuity



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-involved

Non-center-involved

Primary intervention:
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In this classification system, there are two types of DME. What are they?

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Primary intervention:
Pharmacologic

Center-
involved

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In this classification system, there are two types of DME. What are they?

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By what technique is the retina evaluated for the presence of DME?

By OCT

In this system, what findings signal that treatment is indicated?

Center-involving DME + decreased visual acuity

Primary intervention:
Laser surgery

Clinically
significant

Not clinically
significant

In this classification system, there are two types of DME. What are they?

That which qualifies as 'clinically significant,' and that which does not

By what technique is the retina evaluated for the presence of DME?

By DFE

In this system, what findings signal that treatment is indicated?

The presence of CSME



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-involved

Non-center-involved

Primary intervention:
Laser surgery

Clinically significant

Not clinically significant

In this classification system, there are two types of DME. What are they?

That which involves the center (foveal) region, and everything else

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By OCT

In this system, what findings signal that treatment is indicated?

Center-involving DME + decreased visual acuity

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That which qualifies as 'clinically significant,' and that which does not

By what technique is the retina evaluated for the presence of DME?

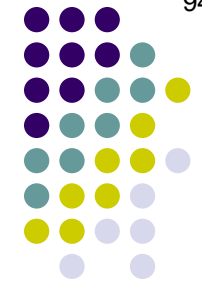
By DFE

What does CSME stand for?

In this system, what findings signal that treatment is indicated?

The presence of **CSME**

CSME



A

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-involved

Non-center-involved

**Primary intervention:
*Laser surgery***

Clinically significant

Not clinically significant

In this classification system, there are two types of DME. What are they?

That which involves the center (foveal) region, and everything else

By what technique is the retina evaluated for the presence of DME?

By OCT

In this system, what findings signal that treatment is indicated?

Center-involving DME + decreased visual acuity

In this classification system, there are two types of DME. What are they?

That which qualifies as 'clinically significant,' and that which does not

By what technique is the retina evaluated for the presence of DME?

By DFF

**What does CSME stand for?
'Clinically significant macular edema'**

treatment is indicated?

The presence of

CSME



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-involved

Non-center-involved

> ? <

Primary intervention:
Laser surgery

Clinically significant

Not clinically significant

Of the two approaches to treating DME, which is considered first-line?

In this classification system, there are two types of DME. What are they? That which involves the center (foveal) region, and everything else

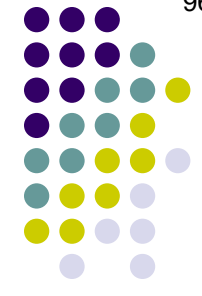
There are two types of DME. What are they? That which qualifies as 'clinically significant,' and that which does not

By what technique is the retina evaluated for the presence of DME?
By OCT

By what technique is the retina evaluated for the presence of DME?
By DFE

In this system, what findings signal that treatment is indicated?
Center-involving DME + decreased visual acuity

In this system, what findings signal that treatment is indicated?
The presence of CSME



A

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-involved

Non-center-involved

>>>

Primary intervention:
Laser surgery

Clinically significant

Not clinically significant

Of the two approaches to treating DME, which is considered first-line?
Pharmacologic, but not in every case (we'll revisit this issue later)

In this classification system, DME is divided into two types: center-involved DME, which involves the center (foveal) region, and non-center-involved DME, which involves the peripheral macula and everything else.

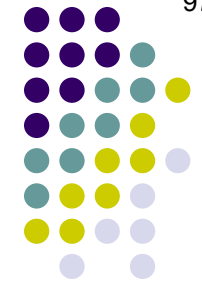
There are two types of DME: clinically significant macular edema (CSME), which is defined as DME that is clinically significant, and non-clinically significant macular edema (NCSME), which is defined as DME that is not clinically significant.

*By what technique is the retina evaluated for the presence of DME?
By OCT*

*By what technique is the retina evaluated for the presence of DME?
By DFE*

*In this system, what findings signal that treatment is indicated?
Center-involving DME + decreased visual acuity*

*In this system, what findings signal that treatment is indicated?
The presence of CSME*



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-involved

Non-center-involved

>>>

Primary intervention:
Laser surgery

Clinically significant

Not clinically significant

Pharmacologic

Of the two approaches to treating DME, which is considered first-line? (we'll revisit this issue later)

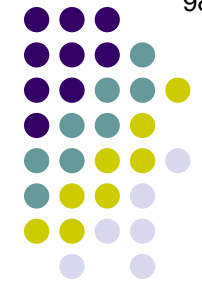
Why is pharmacologic first-line?

By what technique is the retina evaluated for the presence of DME?
By OCT

In this system, what findings signal that treatment is indicated?
Center-involving DME + decreased visual acuity

By what technique is the retina evaluated for the presence of DME?
By DFE

In this system, what findings signal that treatment is indicated?
The presence of CSME



A

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-involved

Non-center-involved

>>>

Primary intervention:
Laser surgery

Clinically significant

Not clinically significant

Pharmacologic

Of the two approaches to treating DME, which is considered first-line? but not in every case (we'll revisit this issue later)

Why is pharmacologic first-line?
Because it beat laser head-to-head in several clinical trials

In this class...

of DME. Which approach is preferred?

That which involves the center (foveal) region, and everything else

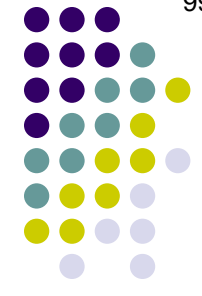
By what technique is the retina evaluated for the presence of DME?
By OCT

In this system, what findings signal that treatment is indicated?
Center-involving DME + decreased visual acuity

...two types of DME: center-involving and non-center-involving. Which is clinically significant, and that which does not?

...technique is the retina evaluated for the presence of DME?
By DFE

In this system, what findings signal that treatment is indicated?
The presence of CSME



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-involved

Non-center-involved

>>>

Primary intervention:
Laser surgery

Clinically significant

Not clinically significant

Pharmacologic

Of the two approaches to treating DME, which is considered first-line? but not in every case (we'll revisit this issue later)

Why is pharmacologic first-line?

Because it beat laser head-to-head in several clinical trials

What outcome measure was used?

In this class... of DME. Wh... That which... and everything else

By what techn... presence of DM... By OCT

In this system, what findings signal that treatment is indicated?
Center-involving DME + decreased visual acuity

... two types... are they?... clinically significant... and that which does not

... technique is the retina evaluated for the presence of DME?
By DFE

In this system, what findings signal that treatment is indicated?
The presence of CSME



A

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-involved

Non-center-involved

>>>

Primary intervention:
Laser surgery

Clinically significant

Not clinically significant

Pharmacologic

Of the two approaches to treating DME, which is considered first-line? but not in every case (we'll revisit this issue later)

Why is pharmacologic first-line?
Because it beat laser head-to-head in several clinical trials

What outcome measure was used?
Visual acuity (VA) at 1- and/or 2-years post-tx

In this class of DME. Which approach is preferred? That which involves the center (foveal) region, and everything else. In this system, what findings signal that treatment is indicated? Center-involving DME + decreased visual acuity

Of the two types of DME, what are they? 'Clinically significant,' and that which does not. In this system, what findings signal that treatment is indicated? The presence of CSME

By what technique is the retina evaluated for the presence of DME? By OCT

By what technique is the retina evaluated for the presence of DME? By DFE



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-involved Non-center-involved

>>>

Primary intervention:
Laser surgery

Clinically significant Not clinically significant

Pharmacologic

Protocol I : Intravitreal ranibizumab > laser

tl;dr it for me, bro—what did the studies show?

clinical trials

VIVID & VISTA : Intravitreal aflibercept > laser for center-involved DME

In this class of DME. Which of the two approaches to treating DME, which is considered first-line? Of the two types of DME, which are they? That which involves the center (macular) region, 'clinically significant,' and everything else. Why is pharmacologic first-line? Because it beat laser head-to-head. By what technique? By OCT. In this system, what findings signal that treatment is indicated? Center-involving DME + decreased visual acuity



A

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-involved

Non-center-involved

>>>

Primary intervention:
Laser surgery

Clinically significant

Not clinically significant

Pharmacologic

Protocol I : Intravitreal ranibizumab > laser

tl;dr it for me, bro—what did the studies show?
That laser was effective for **maintaining** VA,
but intravitreal anti-VEGF tx **improved** VA

clinical trials

VIVID & VISTA : Intravitreal aflibercept > laser
for center-involved DME

In this class...
of DME. Wh...
That which involves the center (foveal) region, and everything else

By what technique...
presence of DME

By OCT

In this system, what findings signal that treatment is indicated?
Center-involving DME + decreased visual acuity

...two types...
...are they?

...significant,

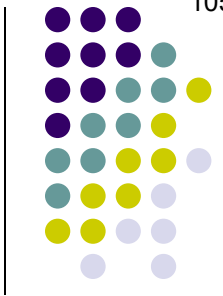
...not

...for the
DME?

...DME

...that
treatment is indicated?

The presence of CSME



Q

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

Center-involved

Non-center-involved

Primary intervention:
Laser surgery

Clinically significant

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In this classification system, there are two types of DME. What are they?

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In this classification system, there are two types of DME. What are they?

That which qualifies as 'clinically significant,' and that which does not

By what technique is the retina evaluated for the presence of DME?

By DFE

By the way: How is CSME defined?

treatment is indicated?

The presence of **CSME**



A

Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:
Pharmacologic

**Primary intervention:
*Laser surgery***

Center-
involved

Non-center-
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**Clinically
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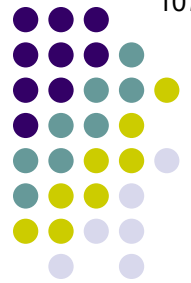
By DFE

In this system, what findings signal that treatment is indicated?

Center-involving DME + decreased visual acuity

**By the way: How is CSME defined?
That's the subject of the next section...**

*treatment is indicated?
The presence of* **CSME**



Q

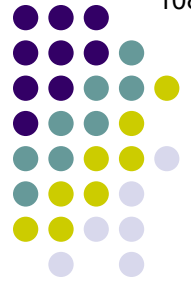
Diabetic Retinopathy: Diabetic Macular Edema

● CSME

- Acronym for *clinically significant macular edema*
- Definition has three components:
 - Any retinal thickening within

A

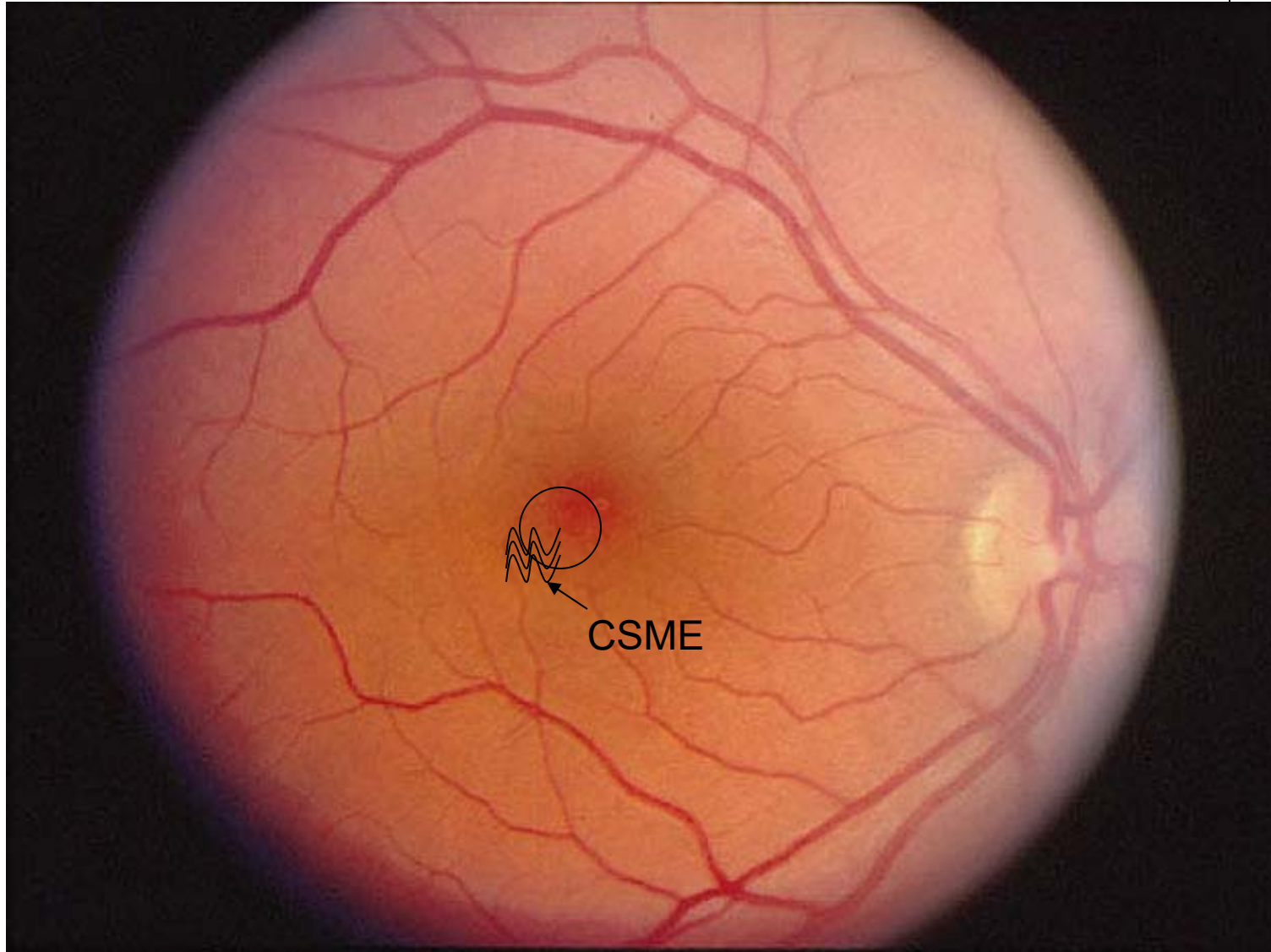
Diabetic Retinopathy: Diabetic Macular Edema



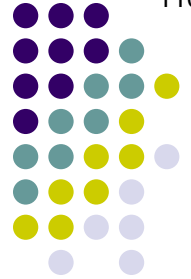
- **CSME**

- Acronym for *clinically significant macular edema*
- Definition has three components:
 - Any retinal thickening within $1/3$ DD of the foveal center

Diabetic Retinopathy: Diabetic Macular Edema



CSME: Any retinal thickening within 1/3 DD of the foveal center



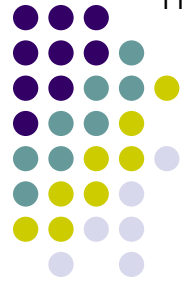
Q

Diabetic Retinopathy: Diabetic Macular Edema

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 - Any retinal thickening within $1/3$ **DD** of the foveal center

What does DD stand for?



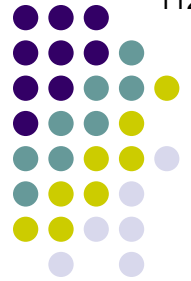
A

Diabetic Retinopathy: Diabetic Macular Edema

● CSME

- Acronym for *clinically significant macular edema*
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 - Any retinal thickening within $1/3$ **DD** of the foveal center

What does DD stand for?
Disc diameter



Q

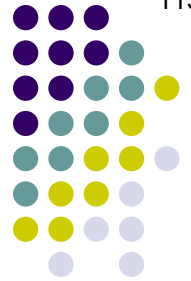
Diabetic Retinopathy: Diabetic Macular Edema

● CSME

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- Definition has three components:
 - Any retinal thickening within $1/3$ **DD** of the foveal center

What does DD stand for?
Disc diameter

How big is 1/3 DD in microns?



A

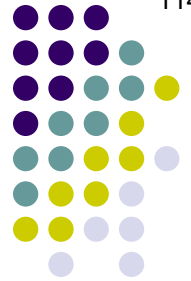
Diabetic Retinopathy: Diabetic Macular Edema

● CSME

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 - Any retinal thickening within $1/3$ **DD** of the foveal center

What does DD stand for?
Disc diameter

How big is 1/3 DD in microns?
500

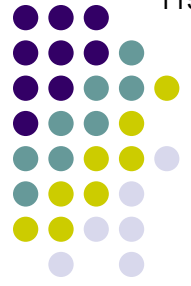


Q

Diabetic Retinopathy: Diabetic Macular Edema

● CSME

- Acronym for *clinically significant macular edema*
- Definition has three components:
 - Any retinal thickening within $1/3$ DD of the foveal center;
or
 - that are associated with adjacent retinal thickening



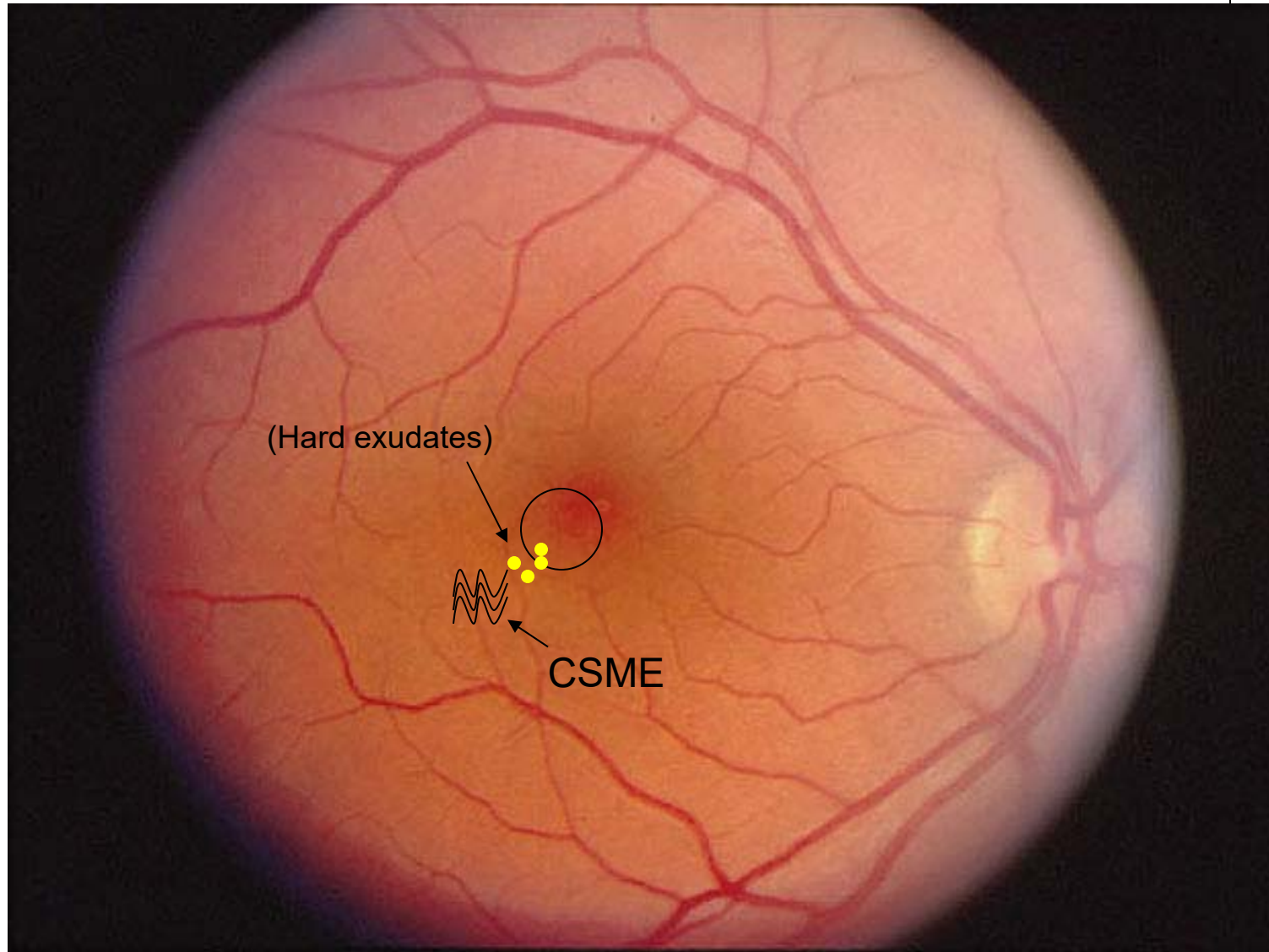
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Diabetic Retinopathy: Diabetic Macular Edema

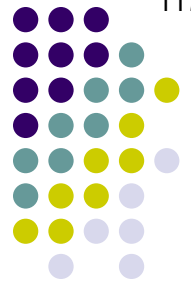
● CSME

- Acronym for *clinically significant macular edema*
- Definition has three components:
 - Any retinal thickening within $1/3$ DD of the foveal center;
or
 - Hard exudates within $1/3$ DD of the foveal center that are associated with adjacent retinal thickening

Diabetic Retinopathy: Diabetic Macular Edema



HE within 1/3 DD of the foveal center that are associated with adjacent retinal thickening

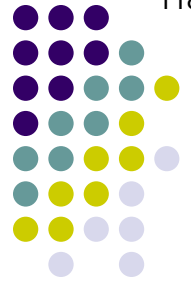


Q

Diabetic Retinopathy: Diabetic Macular Edema

● CSME

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or
 - Hard exudates within $1/3$ DD of the foveal center that are associated with adjacent retinal thickening;
or
 - An area of retinal thickening [] in size, any part of which is within []



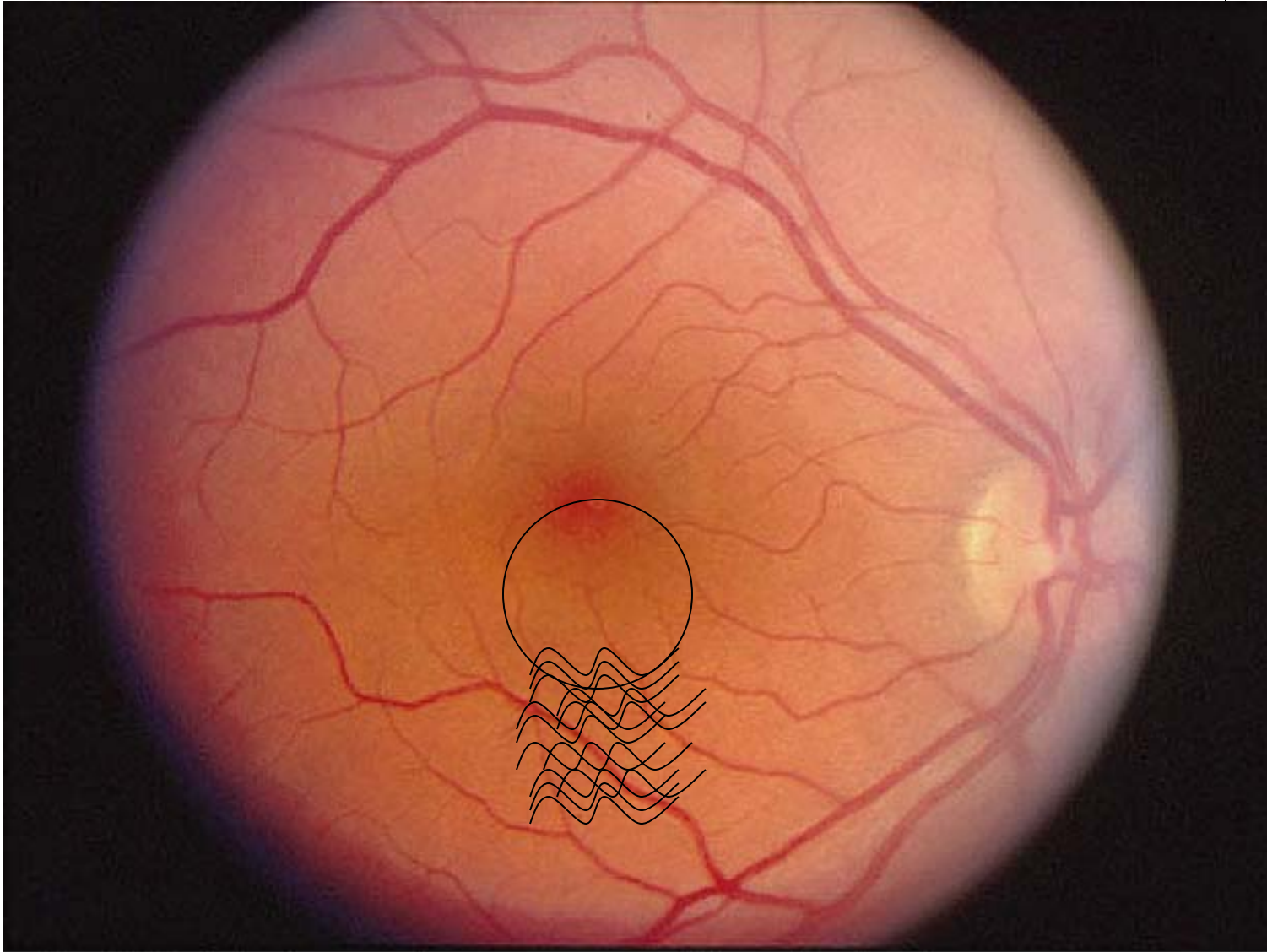
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Diabetic Retinopathy: Diabetic Macular Edema

● CSME

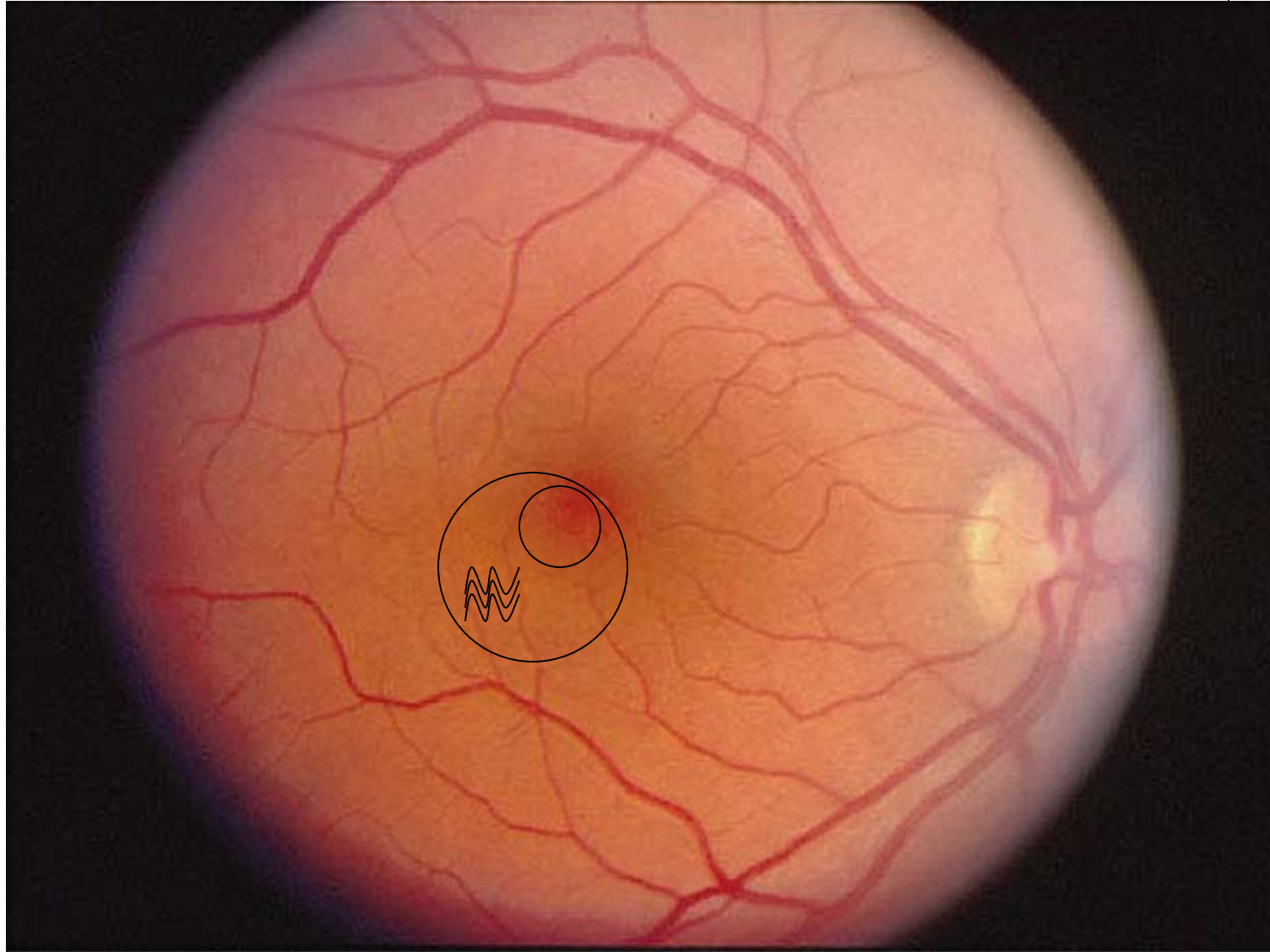
- Acronym for *clinically significant macular edema*
- Definition has three components:
 - Any retinal thickening within $1/3$ DD of the foveal center;
or
 - Hard exudates within $1/3$ DD of the foveal center that are associated with adjacent retinal thickening;
or
 - An area of retinal thickening 1 DD or larger in size, any part of which is within 1 DD of the foveal center

Diabetic Retinopathy: Diabetic Macular Edema



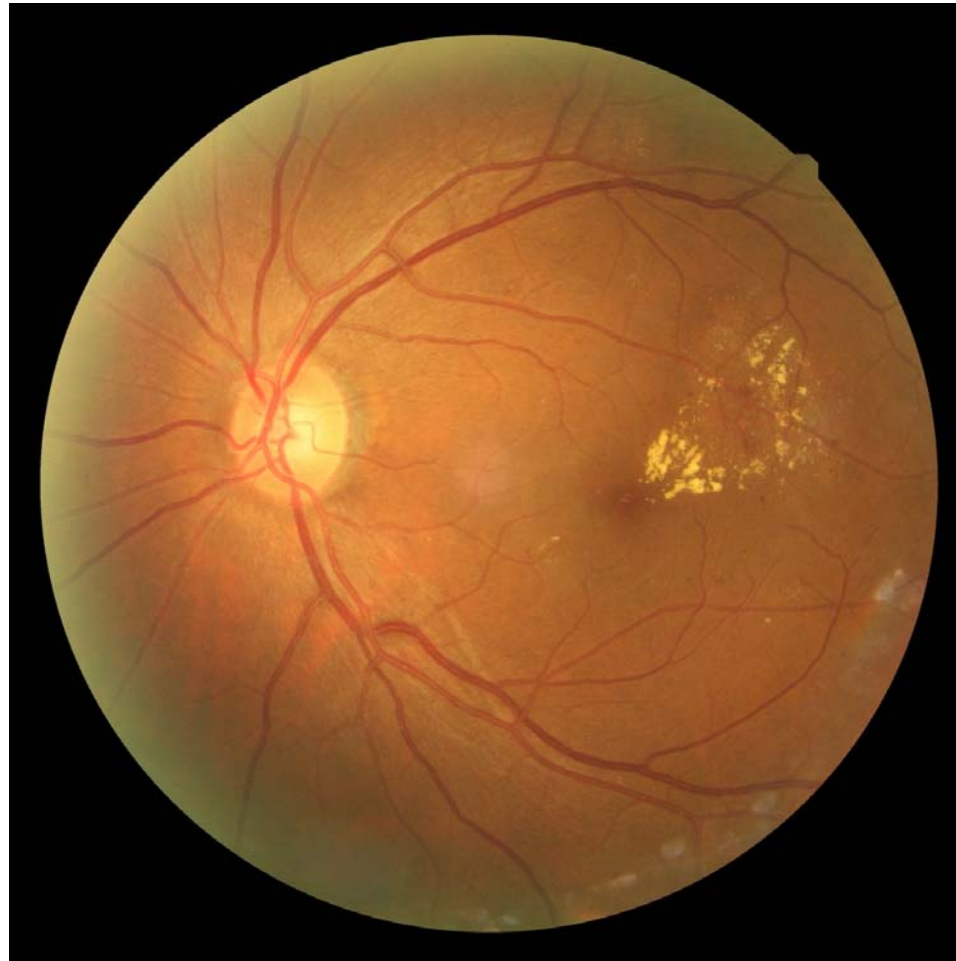
Retinal thickening $\geq 1\text{DD}$ in area, any portion of which is w/in 1DD of the foveal center

Diabetic Retinopathy: Diabetic Macular Edema



In this case, the area is too far away to qualify under the 'any thickening w/in 500 μ m' rule, and too small to qualify under the '1DD area w/in 1DD of the central fovea' rule. This is DME, but *not* CSME.

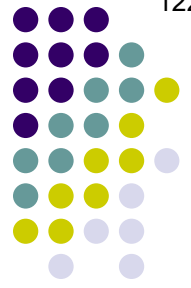
Diabetic Retinopathy: Diabetic Macular Edema



CSME

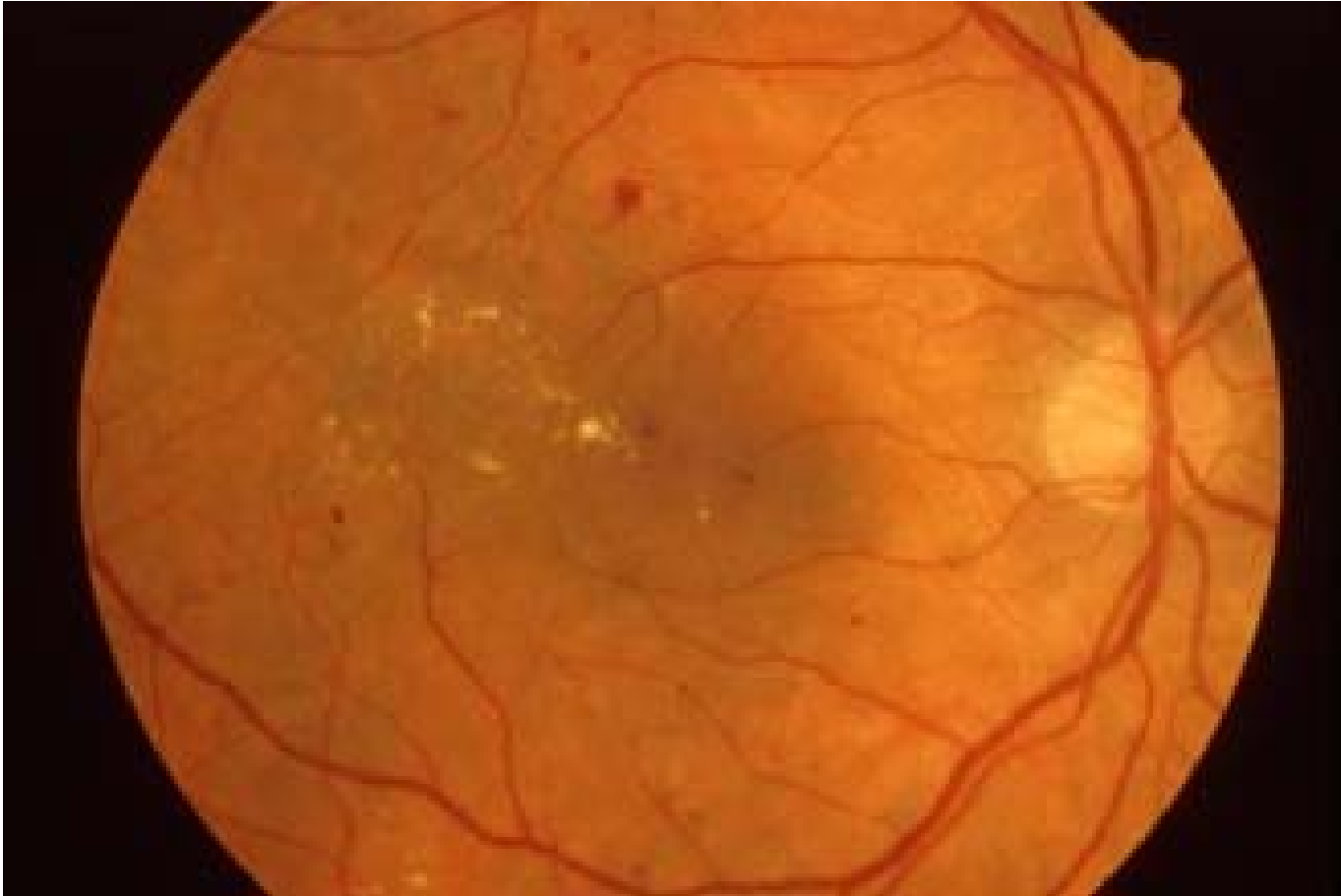


Diabetic Retinopathy: Diabetic Macular Edema

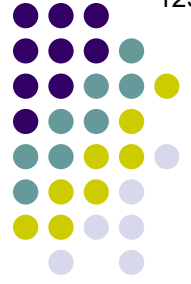


CSME

Diabetic Retinopathy: Diabetic Macular Edema



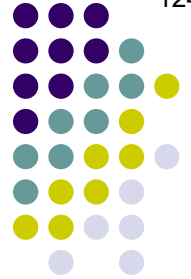
CSME

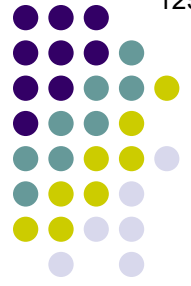


Diabetic Retinopathy: Diabetic Macular Edema



CSME





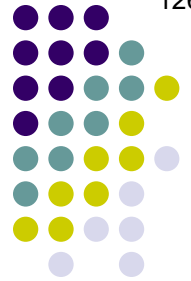
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- Acronym for *clinically significant macular edema*
- Definition has three components:
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or
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What landmark clinical trial provided this definition of CSME?



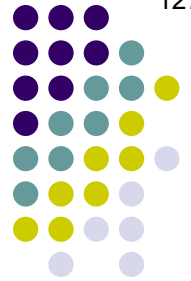
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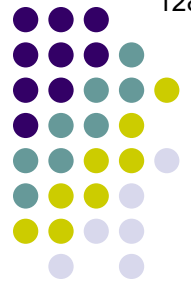
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- 1)
- 2)
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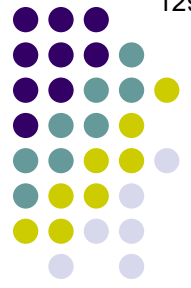
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- 1) Is laser effective in treating diabetic macular edema?
- 2) Is PRP effective for treating early NPDR?
- 3) Is ASA effective in preventing the progression of DBR?

PRP = Pan-retinal
 photocoagulation

ASA = aspirin

NPDR = Non-
 proliferative
 diabetic
 retinopathy



Q

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● Any *or*

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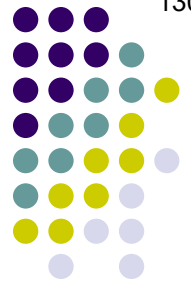
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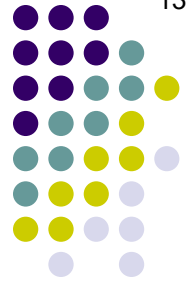
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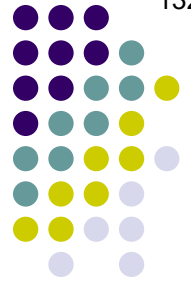
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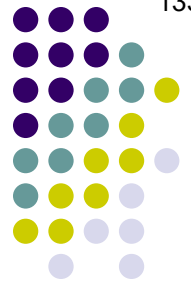
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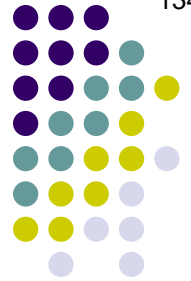
- H *What is the basic technique for each?*
a *FML:*
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or *GML:*

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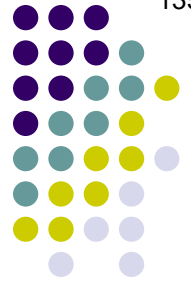
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GML:

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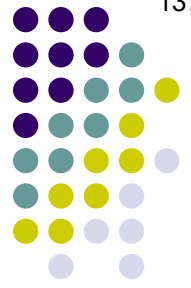
- H *What is the basic technique for each?*
a *FML: Energy applied directly to individual leaking microaneurysms (MAs)*
or *GML: Energy applied to areas of diffuse leakage when offending MAs are not readily identifiable*

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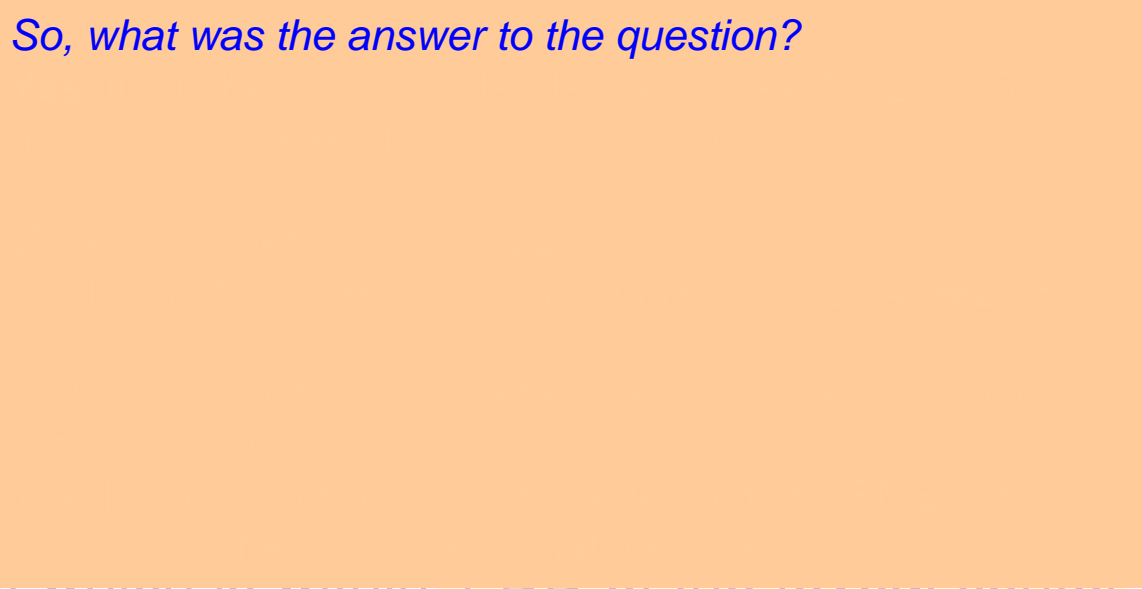
● Acronym for *clinically significant macular edema*

● Definition has three components:

● Any retinal thickening or leakage of fluid in the macular center;

● Hard exudates in the macula or within 500 micrometers of the center that are associated with retinal thickening; *or*

● An area of retinal thickening that is at least 500 micrometers in size, any part of which is within 1 mm of the foveal center.

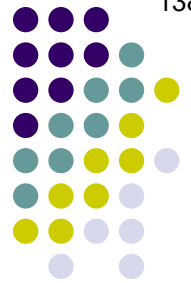


So, what was the answer to the question?



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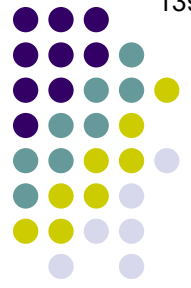
So, what was the answer to the question?

Yes; it cut the risk of moderate vision loss (MVL) by 50%, as well as increased the likelihood of gaining vision

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What is the definition of MVL?

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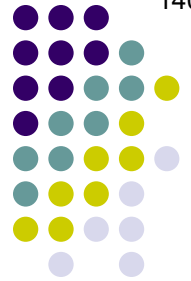
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- Hard exudates associated with macular thickening or
- An area of retinal thickening, part of which is within 1 DD of the foveal center

So, what was the answer to the question?

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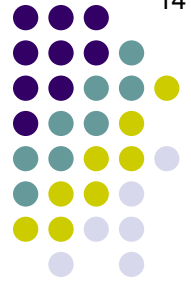
What is the definition of MVL?

Doubling of the baseline visual angle (e.g., 20/40 → 20/80)

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Is there a qualifier on the effectiveness of laser for diabetic macular edema?

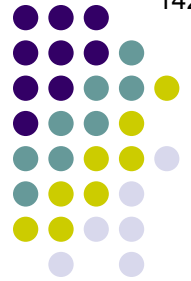
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- Any reduction in visual acuity to less than 20/40 in the better eye at the study center;

- Hard exudates in the macula or that are associated with a reduction in visual acuity to less than 20/40 in the better eye;

- An area of retinal thickening in the macula, in which the width of the thickening is greater than 500 micrometers, and any part of which is within 1 DD of the foveal center.

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Doubling of the baseline visual angle (e.g., 20/40 → 20/80)

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Yes. It was effective only if the edema met CSME criteria (that's why the criteria are what they are)

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- Definition has three components:

So, what was the answer to the question?

Yes: it cut the risk of moderate vision loss (MVL) by 50%

Take note of this! The byzantine definition of CSME is what it is because it delineates the sort of DME that will respond favorably to laser treatment. The point being, if a pt's DME fails to meet the ETDRS definition of CSME, don't laser it!

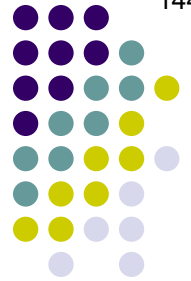
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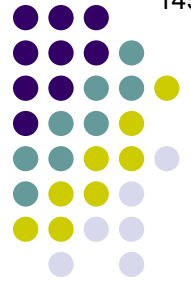
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 - An area of retinal thickening in size, any part of which is within 1/3 DD of the foveal center

What does NPDR stand for in this context?

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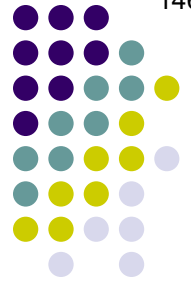
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Nonproliferative diabetic retinopathy

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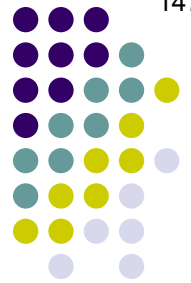
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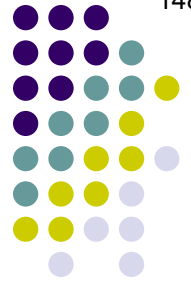
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What does NPDR stand for in this context?
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So, what was the answer to the question?
PRP reduced the risk of severe vision loss in pts with *in size, any* **severe** NPDR, but not with **mild** or **moderate** NPDR *center*

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- Def: If you're unsure what is entailed by the terms *mild*, *moderate* and *severe NPDR*, check out slide-set R31 (*Diabetic retinopathy: The basics*)

- Hard exudates within 1/3 DD of the foveal center that are

What does NPDR stand for in this context?
Nonproliferative diabetic retinopathy

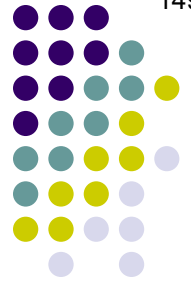
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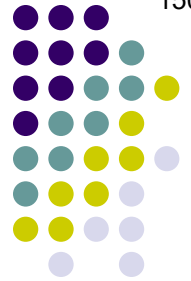
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 - Any retinal thickening within 1/3 DD of the foveal center, any part of which is within 1/3 DD of the foveal center

What was the answer to **this** question?

No. However, it didn't worsen it either; therefore, **DBR is not a contraindication for ASA use.**

What landmark clinical trial provided this definition of CSME?
The **Early Treatment of Diabetic Retinopathy Study (ETDRS)**

What 3 questions did this study seek to answer?

1) Is laser effective in treating diabetic macular edema?

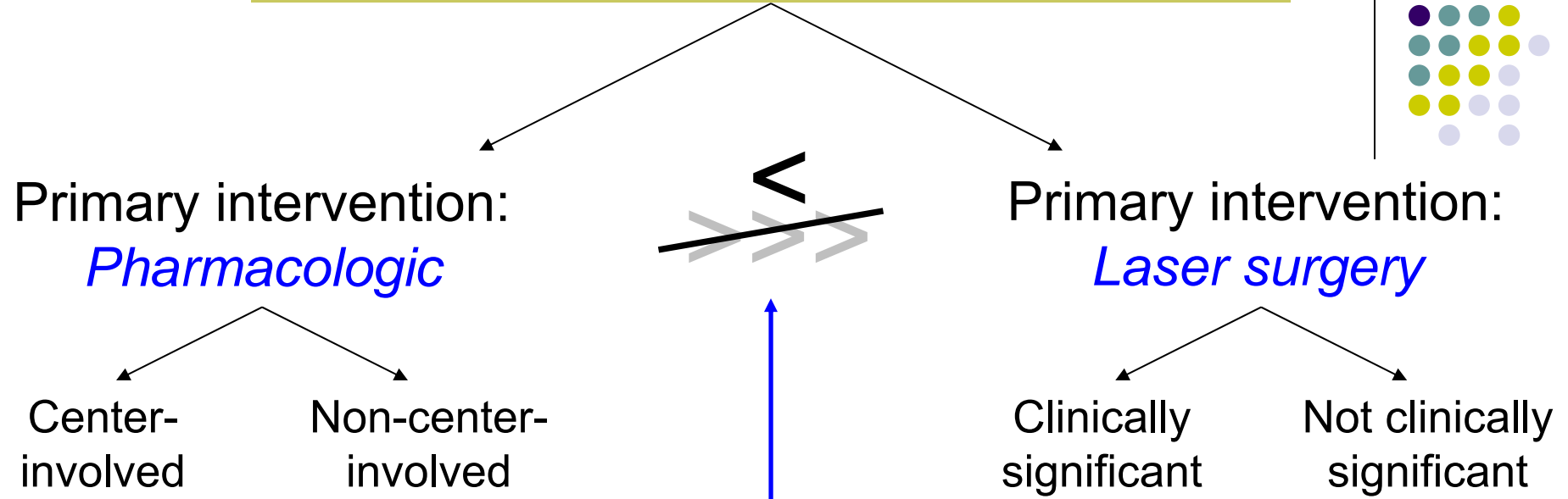
2) Is PRP effective for treating early NPDR?

3) Is ASA effective in preventing the progression of DBR?



Q

Diabetic Retinopathy: Diabetic Macular Edema



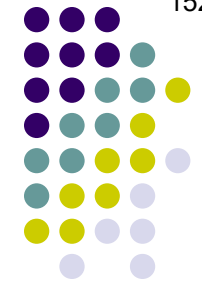
Of the two approaches to treating DME, which is considered first-line? Pharmacologic, but not in every case (we'll revisit this issue later)

Time to revisit this issue. Under what circumstances might laser be the preferred treatment modality?

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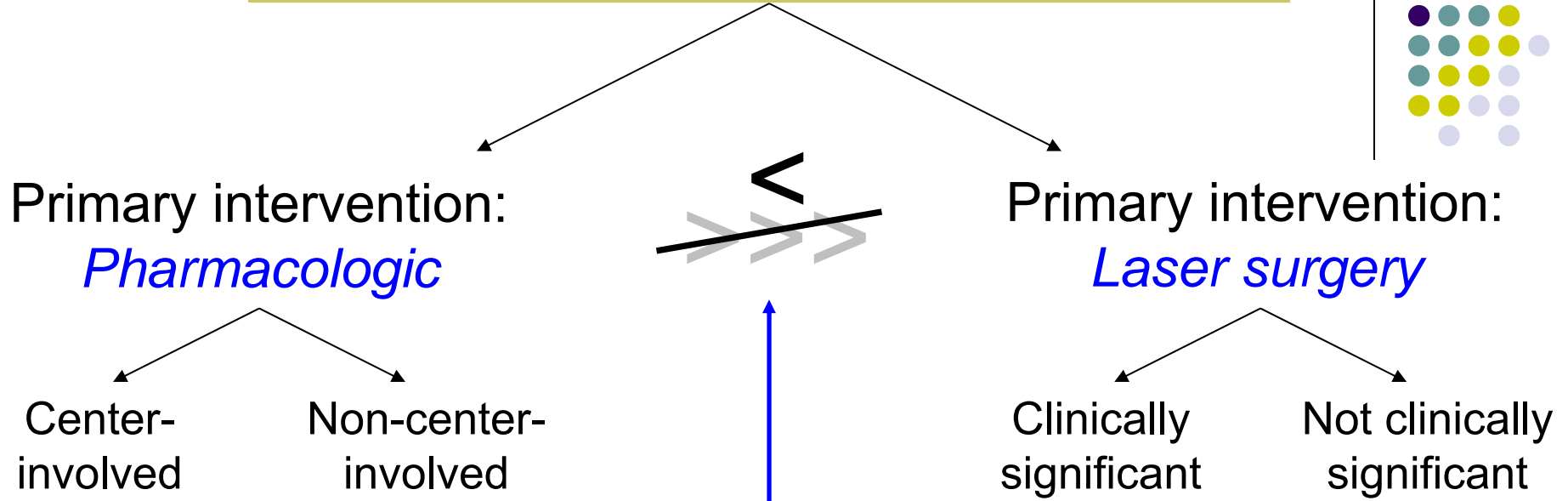
Center-involving DME + decreased visual acuity

The presence of CSME



A

Diabetic Retinopathy: Diabetic Macular Edema



Of the two approaches to treating DME, which is considered first-line? Pharmacologic, but not in every case (we'll revisit this issue later)

Time to revisit this issue. Under what circumstances might laser be the preferred treatment modality?

- If there is an obvious, easily-lased microaneurysm that is the source of the edema (that meets CSME criteria of course); or
- If there is reason to doubt the pt will comply with the demands imposed by a pharmacologic treatment regimen (eg, monthly visits).

Center-involving DME + decreased visual acuity

The presence of CSME

Diabetic Retinopathy: Diabetic Macular Edema



Primary intervention:
Pharmacologic

Center-involved

Non-center-involved



Primary intervention:
Laser surgery

Clinically significant

Not clinically significant

Of the two approaches to treating DME, which is considered first-line?
Pharmacologic, but not in every case (we'll revisit this issue later)

Time to revisit this issue. Under what circumstances might laser be the preferred treatment modality?

--If there is an obvious, easily-lased microaneurysm that is the source of the edema (that meets CSME criteria of course); or

--If there is reason to doubt the pt will comply with the demands imposed by a pharmacologic treatment regimen (eg, monthly visits).

Additionally, some clinicians opt for laser if a pt presents with DME but has good VA (recall from the 'anti-VEGF-vs-laser trials' tl;dr that laser is effective for **maintaining** VA)

Center-involving DME + decreased visual acuity

The presence of CSME