What are the three histological vascular derangements in DBR?

1) Pericyte loss
2) BM thickening → ↓ lumen diameter
3) Loss of endothelial barrier function
What are the three histological vascular derangements in DBR?

1) Pericyte loss

2) BM thickening $\rightarrow$ ↓ lumen diameter

3) Loss of endothelial barrier function

$BM = \text{Basement membrane}$
What are the three histological vascular derangements in DBR?

1) Pericyte loss
2) BM thickening $\rightarrow$ lumen diameter
3) Loss of endothelial barrier function
What are the three histological vascular derangements in DBR?

1) **Pericyte loss**
2) BM thickening $\rightarrow$ ↓ lumen diameter
3) Loss of endothelial barrier function
Trypsin mount of normal retina--low and high mag

(The dark nuclei belong to pericytes; the lighter, to endothelial cells)
Trypsin mount of DBR retina--low and high mag

Note the relative paucity of pericytes c/w normal retina
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
What are the three histological vascular derangements in DBR?

1) Pericyte loss
2) BM thickening $\rightarrow$ ↓ lumen diameter
3) **Loss of endothelial barrier function**

*Loss of endothelial barrier function leads to what pathologic event?*
What are the three histological vascular derangements in DBR?

1) Pericyte loss
2) BM thickening $\rightarrow$ ↓ lumen diameter
3) **Loss of endothelial barrier function**

*Loss of endothelial barrier function leads to what pathologic event? Leaching of serum into the retina*
What are the three histological vascular derangements in DBR?

1) Pericyte loss
2) BM thickening $\rightarrow$ ↓ lumen diameter
3) **Loss of endothelial barrier function**

*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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1) Pericyte loss
2) BM thickening $\rightarrow$ ↓ lumen diameter
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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?*
Retinal edema
What are the three histological vascular derangements in DBR?

1) Pericyte loss
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3) Loss of endothelial barrier function

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?

Retinal edema

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

Thiazolidinediones, AKA the glitazones

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!
What are the three histological vascular derangements in DBR?

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Q/A

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Leaching of serum into the retina

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

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Retinal edema
What are the three histological vascular derangements in DBR?

1) Pericyte loss

2) BM thickening \[\rightarrow\text{↓lumen diameter}\]

3) Loss of endothelial barrier function

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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Diabetic Retinopathy: Diabetic Macular Edema

Two systems for classifying DME

?  ?
Diabetic Retinopathy: Diabetic Macular Edema

Two systems for classifying DME

Primary intervention: *Pharmacologic*

Primary intervention: *Laser surgery*
Primary intervention: **Pharmacologic**

Primary intervention: **Laser surgery**

*Why must the classification of DME be adjusted for the type of primary intervention being contemplated?*
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
Primary intervention: Pharmacologic

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’?
Primary intervention: **Pharmacologic**

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.
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: **Pharmacologic**

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?
--?
--?
--?
--?
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: Pharmacologic

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

--Pegaptanib (And pegaptanib. But because no one uses it, and the BCSC Retina book barely mentions it, we won’t discuss it further.)
Diabetic Retinopathy: Diabetic Macular Edema

**Primary intervention:**

*Pharmacologic*

---

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’?

**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.
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: Pharmacologic

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
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?
-- ?
-- ?
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:

**Pharmacologic**

- 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?**
- Focal macular laser (FML)
- Grid macular laser (GML)
Diabetic Retinopathy: Diabetic Macular Edema

**Primary intervention:**

*Pharmacologic*

Two types of DME

**Primary intervention:**

*Laser surgery*

*In this classification system, there are two types of DME. What are they?*
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: **Pharmacologic**

Center-involved

Non-center-involved

Two types of DME

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

Primary intervention: **Pharmacologic**

- 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?
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:

**Pharmacologic**

- 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?
By OCT
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?*
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*In this system, what findings signal that treatment is indicated?*
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: **Pharmacologic**

- 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?
By OCT

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

**Primary intervention:**

*Pharmacologic*

- Center-involved
- Non-center-involved

**Primary intervention:**

*Laser surgery*

---

*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?*

Interference with VEGF activity

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

Center-involving DME + decreased visual acuity
Primary intervention: Pharmacologic

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?

By OCT

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

Center-involving DME + decreased visual acuity

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?

--Afibercept
--Ranibizumab
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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
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: **Pharmacologic**

- Center-involved
- Non-center-involved

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

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
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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)
Primary intervention: **Pharmacologic**

- 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?

- By OCT

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

- Center-involving DME + decreased visual acuity

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

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)
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: **Pharmacologic**

- 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?

- By OCT

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

- Center-involving DME + decreased visual acuity

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? Interference with VEGF activity

Let’s drill down on VEGF…

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
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

Broadly speaking, what is it?

\[
\text{VEGF-A}_{165}
\]
What does VEGF stand for?
Vascular endothelial growth factor

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

VEGF-A\textsubscript{165}
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-A\textsubscript{165}
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?
Yes, it also is a potent vasodilator (it was known originally as **vascular permeability factor**)

**VEGF-A**₁₆₅
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?
Yes, it also is a potent vasodilator (it was known originally as **vascular permeability factor**)

How potent?

**VEGF-A**₁₆₅
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? Yes, it also is a potent vasodilator (it was known originally as vascular permeability factor)

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

VEGF-A\textsubscript{165}
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?
Yes, it also is a potent vasodilator (it was known originally as vascular permeability factor)

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

VEGF-A\textsubscript{165}

This property accounts for VEGF’s role in the development of diabetic macular edema, and explains why anti-VEGF meds can treat this condition!
What does VEGF stand for?
Vascular endothelial growth factor

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

How does VEGF work?

VEGF-A_{165}
What does VEGF stand for?
Vascular endothelial growth factor

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

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR), which are transmembrane receptor tyrosine kinase (RTK) structures.
What does VEGF stand for?
Vascular endothelial growth factor

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

How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR), which are transmembrane receptor tyrosine kinase (RTK) structures.
What does VEGF stand for? Vascular endothelial growth factor

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

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

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 subfamily designation, it is understood to mean VEGF-A.
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is it?
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What does 165 signify?

VEGF-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

**How does VEGF work?**
Extracellular VEGF binds to VEGF receptors (VEGFR), which are transmembrane receptor tyrosine kinase (RTK) structures.

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 the **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.
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: **Pharmacologic**

- 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?

By OCT.

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

Center-involving DME + decreased visual acuity.

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?

Yes, multiple studies have established them to be safe and effective.
Primary intervention: *Pharmacologic*

- 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

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Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: **Pharmacologic**

- 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?

- By OCT

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

- Center-involving DME + decreased visual acuity

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?

Yes, although they are less effective, and have a worse side-effect profile.
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: Pharmacologic

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
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--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
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
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?
By OCT

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

Two types of DME

Clinically significant

Not clinically significant
Diabetic Retinopathy: Diabetic Macular Edema

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

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

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

Pharmacologic

Center-involved Non-center-involved

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 DFE

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 DFE

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

The presence of CSME
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: Pharmacologic

Primary intervention: Laser surgery

Center-involved Non-center-involved

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
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

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

What does CSME stand for?
'Clinically significant macular edema'
Primary intervention: Pharmacologic

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?
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

That which qualifies as ‘clinically significant,’ and that which does not

What does CSME stand for?
‘Clinically significant macular edema’
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:

- **Pharmacologic**
  - Center-involved
  - Non-center-involved

- **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 shortly).

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

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**
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 qualifies as ‘clinically significant,’ and that which does not

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

- By OCT

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

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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
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**Why is pharmacologic first-line?**
- Because it beat laser head-to-head in several clinical trials
- Beat it how, ie, what outcome measure was used? **Visual acuity at 1- and/or 2-years post-tx**

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

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What outcome measure was used?

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**In this system, what findings signal that treatment is indicated?**
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Three important studies demonstrated the superiority of anti-VEGF tx—what are they?
- Protocol I: Intravitreal ranibizumab > laser for center-involved DME
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In this classification system, there are two types of DME. What are they?

- That which involves the center (foveal) region, and everything else.
- Center-involved DME + decreased visual acuity

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

In this system, what findings signal that treatment is indicated? The presence of CSME.
**Diabetic Retinopathy: Diabetic Macular Edema**

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**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
Diabetic Retinopathy: Diabetic Macular Edema

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By the way: How is CSME defined?
CSME
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By the way: How is CSME defined?

That’s the subject of the next section…

By the way: How is CSME defined?

The presence of CSME
**CSME**

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

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What does DD stand for?
**CSME**

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**What does DD stand for?**
Disc diameter
**Diabetic Retinopathy: Diabetic Macular Edema**

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---

**What does DD stand for?**
- Disc diameter

**How big is \(1/3\) DD in microns?**
- 500 microns
Diabetic Retinopathy: Diabetic Macular Edema

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*What does DD stand for? Disc diameter*

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Diabetic Retinopathy: Diabetic Macular Edema

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  *or*
  - An area of retinal thickening **in size**, any part of which is within **.
Diabetic Retinopathy: Diabetic Macular Edema

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Diabetic Retinopathy: Diabetic Macular Edema

Retinal thickening $\geq 1$DD in area, any portion of which is w/in 1DD of the foveal center
In this case, the area is too far away to qualify under the ‘any thickening w/in 500µm’ 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
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CSME
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What landmark clinical trial provided this definition of CSME?
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**What 3 questions did this study seek to answer?**
1)  
2)  
3)
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1. Is laser effective in treating diabetic macular edema?
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What modality of laser (ie, type of energy) was employed in the ETDRS? Argon.

What two approaches/strategies for laser application were employed? Focal macular laser (FML) and grid macular laser (GML).

FML:
- Energy applied directly to individual leaking microaneurysms (MAs).

GML:
- Energy applied to areas of diffuse leakage when offending MAs are not readily identifiable.
**CSME**

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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.

What is the definition of MVL?
Doubling of the baseline visual angle (e.g., 20/40 → 20/80).

Is there a qualifier on the effectiveness of laser for diabetic macular edema?
Yes. It was effective only if the edema met CSME criteria (that's why the criteria are what they are).
**Diabetic Retinopathy: Diabetic Macular Edema**

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

Is there a qualifier on the effectiveness of laser for diabetic macular edema?
Yes. It was effective only if the edema met CSME criteria (that’s why the criteria are what they are).
**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.
  
  **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?
    - Yes: it cut the risk of moderate vision loss (MVL) by 50%, as well as increased the likelihood of gaining vision.
  - 2) Is PRP effective for treating early NPDR?
    - Yes.
  - 3) Is ASA effective in preventing the progression of DRB?
    - Yes. It was effective only if the edema met CSME criteria (that's why the criteria are what they are)

**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!
CSME

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

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

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

*So, what was the answer to the question?*
PRP reduced the risk of severe vision loss in pts with *severe NPDR*, but not with *mild or moderate NPDR*
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What was the answer to this question?
No. However, it didn’t worsen it either; therefore, DBR is not a contraindication for ASA use.
**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
- 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

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

**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 by 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)
Diabetic Retinopathy: Diabetic Macular Edema

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

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

The presence of CSME

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