What are the three histological vascular derangements in DBR?

1) Pericyte loss
2) BM thickening
3)

Diabetic Retinopathy: Diabetic Macular Edema
What are the three histological vascular derangements in DBR?

1) Pericyte loss
2) BM thickening → ↓ lumen diameter
3) Loss of endothelial barrier function

BM = Basement membrane
What are the three histological vascular derangements in DBR?

1) **Pericyte loss**

2) **BM thickening** → ↓ lumen diameter

3) **Loss of endothelial barrier function**

*BM = Basement membrane*
What are the three histological vascular derangements in DBR?

1) Pericyte loss
2) BM thickening $\rightarrow$ ↓ lumen diameter
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With respect to the structure of retinal arterioles and capillaries, how are pericytes and endothelial cells related to one another?
What are the three histological vascular derangements in DBR?

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

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

The endothelial cells line the lumen of the vessel. They are surrounded by their BM.
What are the three histological vascular derangements in DBR?

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

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

The endothelial cells line the lumen of the vessel. They are surrounded by their BM.
What are the three histological vascular derangements in DBR?

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

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

The **endothelial** cells line the lumen of the vessel. They are surrounded by their **BM**. They are **fenestrated or non-**.
What are the three histological vascular derangements in DBR?

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

*With respect to the structure of retinal arterioles and capillaries, how are pericytes and endothelial cells related to one another?*  
The endothelial cells line the lumen of the vessel. They are surrounded by their BM. They are nonfenestrated.
What are the three histological vascular derangements in DBR?

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

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

The endothelial cells line the lumen of the vessel. They are surrounded by their BM. They are nonfenestrated. Tight junctions between cells form the so-called four words.
What are the three histological vascular derangements in DBR?

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

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

The endothelial cells line the lumen of the vessel. They are surrounded by their BM. They are nonfenestrated. Tight junctions between cells form the so-called *inner blood-retina barrier.*
What are the three histological vascular derangements in DBR?

1) Pericyte loss
2) BM thickening $\rightarrow$ ↓ lumen diameter
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With respect to the structure of retinal arterioles and capillaries, how are pericytes and endothelial cells related to one another?

The endothelial cells line the lumen of the vessel. They are surrounded by their BM. They are nonfenestrated. 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.
Diabetic Retinopathy: Diabetic Macular Edema

What are the three histological vascular derangements in DBR?

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

*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)
What are the three histological vascular derangements in DBR?

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

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**Q**

Diabetic Retinopathy: Diabetic Macular Edema

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  - 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 and is embedded by their BM)
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That this is known as the inner blood-retina barrier implies the existence of what?

BM, They are nonfenestrated. 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.
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1) Pericyte loss
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That this is known as the inner blood-retina barrier implies the existence of what? An outer blood-retina barrier

Diabetic Retinopathy: Diabetic Macular Edema

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

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

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?

**inner blood-retina barrier**
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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Yup. What forms the **outer blood-retina barrier**?
Tight junctions between **retinal pigment epithelium (RPE)** cells

The pericytes surround the vessel, and are embedded in the **BM** of the endothelial cells.
What are the three histological vascular derangements in DBR?

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inner blood-retina barrier
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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. 
*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
What are the three histological vascular derangements in DBR?

1) Pericyte loss
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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
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*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?

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

1) Pericyte loss

2) BM thickening → ↓ lumen diameter

3) Loss of endothelial barrier function

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: Pioglitazone (brand name Actos) and 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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Retinal edema
What are the three histological vascular derangements in DBR?

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Retinal edema
Diabetic Retinopathy: Diabetic Macular Edema

With respect to its clinical management, there are two ways to think about/classify DME. On what basis is this division made?
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.
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?
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
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?
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?*
Because the factors influencing treatment appropriateness and success differ between the modalities.
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’?
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.

Primary intervention:  
**Laser surgery**
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?

--Afibercept
--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.)

Primary intervention:

**Laser surgery**
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’?

Primary intervention: 
Laser surgery
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

Primary intervention: Laser surgery
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?
--Afibercept
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--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)
Primary intervention: **Pharmacologic**

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

**Primary intervention:**

- **Pharmacologic**
  - Two types of DME
    - 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*
Diabetic Retinopathy: Diabetic Macular Edema

DME: Center-involved

DME: Not center-involved
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

Primary intervention: **Laser surgery**
Diabetic Retinopathy: Diabetic Macular Edema

Center involving DME

Non center involving DME
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: **Pharmacologic**

- 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?
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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

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
-- 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
Diabetic Retinopathy: Diabetic Macular Edema

**Primary intervention:**

- **Pharmacologic**
  - Center-involved
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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

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

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- Aflibercept
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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**

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Broadly, what is the mechanism of action for triamcinolone? Anti-inflammatory (it’s a steroid)
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:

**Pharmacologic**

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- Non-center-involved

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

By OCT

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Center-involve DME + decreased visual acuity

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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-involve 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?

VEGF-A
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is it?
An extracellular signaling protein involved in vascular development
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$_{165}$
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)
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?
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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**

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? 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$_{165}$

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-A165
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?
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How does VEGF work?
Extracellular VEGF binds to VEGF receptors (VEGFR), which are transmembrane receptor tyrosine kinase (RTK) structures.

What does the A signify?

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 [PIGF], 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?**
An extracellular signaling protein involved in vascular development

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

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What does 165 signify?

**VEGF-A**

79
What does VEGF stand for?
Vascular endothelial growth factor

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

VEGF-A

What does 165 signify?
VEGF-A is not a single entity either. At least 4 isoforms exist; these differ in the number of peptides they contain, and that number is used as a subscript to identify specific isoforms.
**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 165 signify?**
VEGF-A is not a single entity either. At least 4 isoforms exist; these differ in the number of peptides they contain, and that number is used as a subscript to identify specific isoforms.

**Why focus on isoform 165?**
What does VEGF stand for?
Vascular endothelial growth factor

Broadly speaking, what is 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 [PIGF], 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 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.
**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?**

- OCT

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

- Center-involving DME + decreased visual acuity

**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
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:

**Pharmacologic**

- Center-involved
- Non-center-involved

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

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**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
- 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
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:

**Pharmacologic**

- Center-involved
- Non-center-involved

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

**OCT**

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

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

Primary intervention:

- Pharmacologic
- Laser surgery

Center-involved
Non-center-involved

Two types of DME

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
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: Pharmacologic

- Center-involved
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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
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:

Pharmacologic

Laser surgery

Primary intervention:

Clinically significant

Not clinically significant

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

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 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?
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?*
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 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 and DFE.

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

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

What does CSME stand for?
‘Clinically significant macular edema’

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 shortly)

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
- The presence of CSME

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

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- By DFE
- By OCT

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

- Center-involving DME + decreased visual acuity
- The presence of CSME

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

**Pharmacologic**

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
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: Pharmacologic
- Center-involved
- Non-center-involved

Primary intervention: Laser surgery
- Clinically significant
- Not clinically significant

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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?**

- 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?**

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**Q**

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Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention:

- **Pharmacologic**
  - Center-involved
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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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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
- The presence of CSME

Why is pharmacologic first-line?

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What outcome measure was used?

Visual acuity (VA) at 1- and/or 2-years post-tx
Diabetic Retinopathy: Diabetic Macular Edema

Primary intervention: **Pharmacologic**

- Center-involved
- Non-center-involved

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Primary intervention: **Laser surgery**

- Clinically significant
- Not clinically significant

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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 DFE
- By OCT

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

- The presence of CSME
- Center-involving DME + decreased visual acuity

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

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

What outcome measure was used to evaluate for the superiority of anti-VEGF tx—what are they?

- Visual acuity (VA) at 1- and/or 2-years post-tx

Three important studies demonstrated the superiority of anti-VEGF tx—what are they?

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

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One study: Intravitreal ranibizumab > laser for center-involved DME

Two studies: Intravitreal aflibercept > laser for center-involved DME
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?

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

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- By OCT

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

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What outcome measure was used to evaluate for the presence of DME?

Visual acuity (VA) at 1- and/or 2-years post-tx

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

Of the two approaches to treating DME, which is considered first-line?
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Three important studies demonstrated the superiority of anti-VEGF tx—what are they?
- VIVID & VISTA
- PROGRESS
- VISION

**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

Primary intervention: **Pharmacologic**

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- Non-center-involved

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- Not clinically significant

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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

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 DFE

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 the way: How is CSME defined?
The presence of CSME
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 DFE

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

Primary intervention: **Laser surgery**

Clinically significant Not clinically significant

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

CSME

- Acronym for *clinically significant macular edema*
- Definition has three components:
  - Any retinal thickening within \( \frac{1}{3} \text{DD} \) of the foveal center

What does DD stand for?

Diabetic Retinopathy: Diabetic Macular Edema
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

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

CSME

- Acronym for *clinically significant macular edema*
- Definition has three components:
  - Any retinal thickening within \( \frac{1}{3} \text{DD} \) of the foveal center

What does DD stand for?
Disc diameter

How big is \( \frac{1}{3} \text{DD} \) in microns?
CSME

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

*What does DD stand for?*
Disc diameter

*How big is $1/3$ DD in microns?*
500
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*;
  - Hard exudates within *1/3 DD of the foveal center* that are associated with adjacent retinal thickening
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
**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 in size, any part of which is within **
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
Retinal thickening ≥1DD 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 500\(\mu\)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
CSME

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  - **Hard exudates within 1/3 DD of the foveal center** that are associated with adjacent retinal thickening;
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What landmark clinical trial provided this definition of CSME?
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)*
CSME

Acronym for *clinically significant macular edema*

Definition has three components:

- Any retinal thickening within 1/3 DD of the foveal center;
- Hard exudates within 1/3 DD of the foveal center that are associated with adjacent retinal thickening;
- 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)
2)
3)
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**
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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?

PRP = Pan-retinal photocoagulation  
ASA = aspirin  
NPDR = Non-proliferative diabetic retinopathy
**CSME**

- Acronym for **clinically significant macular edema** (CSME)
- Definition has three components:
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What modality of laser (ie, type of energy) was employed in the ETDRS?
Argon laser

What two approaches/strategies for laser application were employed?

**FML (focal macular laser)**: Energy applied directly to individual leaking microaneurysms (MAs)

**GML (grid macular laser)**: Energy applied to areas of diffuse leakage when offending MAs are not readily identifiable.
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What is the definition of MVL?

Doubling of the baseline visual angle (e.g., 20/40 $\rightarrow$ 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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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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*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**
- **Laser surgery**

**Center-involved**
- Clinically significant
- Not clinically significant

**Non-center-involved**
- Clinically significant
- Not clinically significant

*In this classification system, there are two types of DME. What are they?*
- That which qualifies as 'clinically significant,'
- 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

**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)

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Center-involving DME + decreased visual acuity

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The presence of CSME

By OCT

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