How many American adults are diabetic or pre-diabetic?
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Over 100M!
How many American adults are diabetic or pre-diabetic?
Over 100M!

Of the ~30M or so adults with full-blown diabetes, what proportion don’t even know they have it?
How many American adults are diabetic or pre-diabetic?
Over 100M!

Of the ~30M or so adults with full-blown diabetes, what proportion don’t even know they have it?
About 25%!
How many American adults are diabetic or pre-diabetic? Over 100M!

Of the ~30M or so adults with full-blown diabetes, what proportion don’t even know they have it? About 25%!

Does diabetes prevalence vary with age?
How many American adults are diabetic or pre-diabetic?
Over 100M!

Of the ~30M or so adults with full-blown diabetes, what proportion don’t even know they have it?
About 25%!

Does diabetes prevalence vary with age?
Yes, it increases with advancing age
How many American adults are diabetic or pre-diabetic?
Over 100M!

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Does diabetes prevalence vary with age?
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Does diabetes prevalence vary with ethnicity?
How many American adults are diabetic or pre-diabetic? Over 100M!

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Does diabetes prevalence vary with age? Yes, it increases with advancing age

Does diabetes prevalence vary with ethnicity? Yes. It is highest among Native Americans and Alaskan Natives, followed in order by non-Hispanic blacks, and Hispanics, Asians and non-Hispanic whites
How many American adults are diabetic or pre-diabetic? 
Over 100M!

Of the ~30M or so adults with full-blown diabetes, what proportion don’t even know they have it? 
About 25%!

Does diabetes prevalence vary with age? 
Yes, it increases with advancing age

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Does diabetes prevalence vary with education level?
Diabetic Retinopathy: The Basics

How many American adults are diabetic or pre-diabetic?
Over 100M!

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Does diabetes prevalence vary with education level?
Yes, rates are twice as high among individuals with less than a high-school education
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Yes, rates are twice as high among individuals with less than a high-school education

What proportion of diabetics receive screening eye exams at recommended intervals?
How many American adults are diabetic or pre-diabetic?
Over 100M!

Of the ~30M or so adults with full-blown diabetes, what proportion don’t even know they have it?
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Does diabetes prevalence vary with education level?
Yes, rates are twice as high among individuals with less than a high-school education

What proportion of diabetics receive screening eye exams at recommended intervals?
Only about 60%
Worldwide, what proportion of diabetics have retinopathy?
Worldwide, what proportion of diabetics have retinopathy?
About a third
Worldwide, what proportion of diabetics have retinopathy?
About a third

Of those diabetics with retinopathy, what proportion have vision-threatening retinopathy?
**Diabetic Retinopathy: The Basics**

*Worldwide, what proportion of diabetics have retinopathy?*
About a third

*Of those diabetics with retinopathy, what proportion have vision-threatening retinopathy?*
Again, about a third
Worldwide, what proportion of diabetics have retinopathy?
About a third

Of those diabetics with retinopathy, what proportion have vision-threatening retinopathy?
Again, about a third

Per the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), what proportion of Type 2 diabetics have at least some retinopathy after 20 years?
Worldwide, what proportion of diabetics have retinopathy?
About a third

Of those diabetics with retinopathy, what proportion have vision-threatening retinopathy?
Again, about a third

Per the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), what proportion of Type 2 diabetics have at least some retinopathy after 20 years? 60%
Worldwide, what proportion of diabetics have retinopathy?
About a third

Of those diabetics with retinopathy, what proportion have vision-threatening retinopathy?
Again, about a third

Per the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), what proportion of Type 2 diabetics have at least some retinopathy after 20 years?
60%

Per the WESDR, what proportion of Type 1 diabetics have at least some retinopathy after 20 years?
**Diabetic Retinopathy: The Basics**

*Worldwide, what proportion of diabetics have retinopathy?*
About a third

*Of those diabetics with retinopathy, what proportion have vision-threatening retinopathy?*
Again, about a third

*Per the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), what proportion of Type 2 diabetics have at least some retinopathy after 20 years?*
60%

*Per the WESDR, what proportion of Type I diabetics have at least some retinopathy after 20 years?*
99%! 
Worldwide, what proportion of diabetics have retinopathy? About a third.

Of those diabetics with retinopathy, what proportion have vision-threatening retinopathy? Again, about a third.

Per the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), what proportion of Type 2 diabetics have at least some retinopathy after 20 years? 60%.

Per the WESDR, what proportion of Type 1 diabetics have at least some retinopathy after 20 years? 99%!
Diabetic Retinopathy: The Basics

Worldwide, what proportion of diabetics have retinopathy?
About a third

Of those diabetics with retinopathy, what proportion have vision-threatening retinopathy?
Again, about a third

Per the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), what proportion of Type 2 diabetics have at least some retinopathy after 20 years?
60%

Per the WESDR, what proportion of Type 1 diabetics have at least some retinopathy after 20 years?
99%

Per the WESDR, what proportion of Type 2 diabetics have proliferative retinopathy (PDR) after 20 years?
25%
Worldwide, what proportion of diabetics have retinopathy? About a third

Of those diabetics with retinopathy, what proportion have vision-threatening retinopathy? Again, about a third

Per the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), what proportion of Type 2 diabetics have at least some retinopathy after 20 years? 60%

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Diabetic Retinopathy: The Basics

Worldwide, what proportion of diabetics have retinopathy? About a third

Of those diabetics with retinopathy, what proportion have vision-threatening retinopathy? Again, about a third

Per the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), what proportion of Type 2 diabetics have at least some retinopathy after 20 years? 60%

Per the WESDR, what proportion of Type 1 diabetics have at least some retinopathy after 20 years? 99%!

Per the WESDR, what proportion of Type 2 diabetics have proliferative retinopathy (PDR) after 20 years? 25%

Per the WESDR, what proportion of Type 1 diabetics have proliferative retinopathy (PDR) after 20 years? 50%!
Diabetic Retinopathy: The Basics

Worldwide, what proportion of diabetics have retinopathy?
About a third

Of those diabetics with retinopathy, what proportion have vision-threatening retinopathy?
Again, about a third

Per the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), what proportion of Type 2 diabetics have at least some retinopathy after 20 years?
60%

Per the WESDR, what proportion of Type 1 diabetics have at least some retinopathy after 20 years?
99%!

Per the WESDR, what proportion of Type 2 diabetics have proliferative retinopathy (PDR) after 20 years?
25%

Per the WESDR, what proportion of Type 1 diabetics have proliferative retinopathy (PDR) after 20 years?
50%

(If you’re not sure what proliferative retinopathy is, no worries—it’ll be covered in this slide-set)
What are the three histological vascular derangements in DBR?

1)

2)

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

1) Pericyte loss

2) BM thickening $\rightarrow$ ↓ lumen diameter

3) Loss of endothelial barrier function

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

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

1) Pericyte loss
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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 → ↓ 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
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) Pericycle 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-fenestrated.
What are the three histological vascular derangements in DBR?

1) Pericyte loss
2) BM thickening → ↓ 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 → ↓ 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 four words.
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. 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 → ↓ 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 *inner blood-retina barrier*. The pericytes surround the vessel, and are embedded in the BM of the endothelial cells.
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?

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

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Do retinal vessels have an intimal lining?  
No

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Do retinal vessels have a muscular wall?  
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What are the three histological vascular derangements in DBR?

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**Diabetic Retinopathy: The Basics**
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?**
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**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?

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

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

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.
What are the three histological vascular derangements in DBR?

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

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

**Q**

*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?

1) Pericyte loss
2) BM thickening $\rightarrow$ 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?

Tight junctions between retinal pigment epithelium (RPE) cells

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

1) **Pericyte** loss
2) **BM** thickening $\rightarrow$ ↓ 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?

Tight junctions between **retinal pigment epithelium (RPE)** cells

**inner blood-retina barrier**

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

1) Pericyte loss
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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.*
But in a retina with damage secondary 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

2) BM thickening $\rightarrow$ ↓ lumen diameter

3) Loss of endothelial barrier function

What pathological state is the endpoint of decreasing lumen diameter?

Occlusion of the retinal vessel

Vessel occlusion leads to what pathological event?

Ischemia of the retinal area serviced by the vessel

Retinal ischemia leads to what pathological state?

Hypoxia of the affected retinal cells
● 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 pathological state is the endpoint of decreasing lumen diameter? Occlusion of the retinal vessel
What are the three histological vascular derangements in DBR?

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What pathological state is the endpoint of decreasing lumen diameter?
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Ischemia of the retinal area serviced by the vessel
What are the three histological vascular derangements in DBR?

1) Pericyte loss

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

3) Loss of endothelial barrier function

*What pathological state is the endpoint of decreasing lumen diameter?*
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Hypoxia of the affected retinal cells
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Occlusion of the retinal vessel

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Ischemia of the retinal area serviced by the vessel

Retinal ischemia leads to what pathological state?
Hypoxia of the affected retinal cells

Hypoxic retinal cells release a signaling molecule that is central to the pathogenesis of DBR. What is that signaling molecule?
What are the three histological vascular derangements in DBR?

1) Pericyte loss

2) BM thickening $\rightarrow$ ↓ lumen diameter

What pathological state is the endpoint of decreasing lumen diameter?
Occlusion of the retinal vessel

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Ischemia of the retinal area serviced by the vessel

Retinal ischemia leads to what pathological state?
Hypoxia of the affected retinal cells

Hypoxic retinal cells release a signaling molecule that is central to the pathogenesis of DBR. What is that signaling molecule?
**VEGF** (we will have much more to say about VEGF shortly)
What are the three histological vascular derangements in DBR?

1) Pericyte loss
2) BM thickening ➔ ↓ 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 → ↓ 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?*
What are the three histological vascular derangements in DBR?

1) Pericyte loss
2) BM thickening → ↓ 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
Classification of diabetic retinopathy

Two broad categories of DBR

Nonproliferative diabetic retinopathy (NPDR)
- Mild
- Moderate
- Severe: Any of the 4:2:1 rule
  - 15% chance of high-risk PDR within 1 year
- Very severe: Any 2 of the 4:2:1 rule
  - 45% chance of high-risk PDR within 1 year

Pre-proliferative:
- Severe or very severe NPDR + CWS

Proliferative diabetic retinopathy (PDR)
- High-risk PDR
  - Any NVD associated with vitreous heme (VH)
  - Large (at least ¼ DD) area of NVD with or without VH
  - Large (at least ½ DD) area of NVE with VH
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - Mild
  - Moderate
  - Severe
  - Very severe

- Proliferative diabetic retinopathy (PDR)
  - High-risk PDR
    - Any NVD associated with vitreous heme (VH)
    - Large (at least ¼ DD) area of NVD with or without VH
    - Large (at least ½ DD) area of NVE with VH

Two broad categories of DBR

Diabetic Retinopathy: The Basics
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - Mild
  - Moderate
  - Severe: Any of the 4:2:1 rule
    - 15% chance of high-risk PDR within 1 year
  - Very severe: Any 2 of the 4:2:1 rule
    - 45% chance of high-risk PDR within 1 year
  - Pre-proliferative: Severe or very severe NPDR + CWS

- Proliferative diabetic retinopathy (PDR)
  - High-risk PDR
    - Any NVD associated with vitreous heme (VH)
    - Large (at least ¼ DD) area of NVD with or without VH
    - Large (at least ½ DD) area of NVE with VH

Two broad categories of DBR

What is the histological definition of proliferation in this context?
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - Mild
  - Moderate
  - Severe
  - Very severe
    - Any 2 of the 4:2:1 rule
      - 15% chance of high-risk PDR within 1 year
    - Any 3 of the 4:2:1 rule
      - 45% chance of high-risk PDR within 1 year
  - Pre-proliferative
    - Severe or very severe NPDR + CWS

- Proliferative diabetic retinopathy (PDR)
  - High-risk PDR
    - Any NVD associated with vitreous heme (VH)
    - Large (at least ¼ DD) area of NVD with or without VH
    - Large (at least ½ DD) area of NVE with VH

What is the histological definition of proliferation in this context?
Retinal neovascularization that breaks through the internal limiting membrane (ILM)
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - Three basic levels of NPDR

- Proliferative diabetic retinopathy (PDR)
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)
- Mild
- Moderate
- Severe

Proliferative diabetic retinopathy (PDR)
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - Mild
  - Moderate
  - Severe

- Proliferative diabetic retinopathy (PDR)

Three basic levels of NPDR

One more level (not universally used)
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)
- Mild
- Moderate
- Severe

Very severe

Three basic levels of NPDR

Proliferative diabetic retinopathy (PDR)
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)

- Mild
- Moderate
- Severe

Very severe

Three basic levels of NPDR

Proliferative diabetic retinopathy (PDR)

One level of concern

One more level (not universally used)
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - Mild
  - Moderate
  - Severe
  - Very severe

Three basic levels of NPDR

- Very severe

One more level (not universally used)

- Proliferative diabetic retinopathy (PDR)
  - High-risk PDR

One level of concern
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - Mild
  - Moderate
  - Severe
  - Very severe

- Proliferative diabetic retinopathy (PDR)
  - High-risk PDR

What landmark clinical trial provided this system of DBR classification?

The Early Treatment of Diabetic Retinopathy Study.
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)
- Mild
- Moderate
- Severe
- Very severe

Proliferative diabetic retinopathy (PDR)
- High-risk PDR

What landmark clinical trial provided this system of DBR classification? The Early Treatment of Diabetic Retinopathy Study. Note that the ETDRS is one of the studies you are expected to be familiar with by name.
Diabetic Retinopathy: The Basics

Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - Mild
  - Moderate
  - Severe
  - Very severe

- Proliferative diabetic retinopathy (PDR)
  - High-risk PDR

How are mild and moderate NPDR defined?
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)
- Mild
- Moderate
- Severe

Very severe

Proliferative diabetic retinopathy (PDR)
- High-risk PDR
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - **Mild:** Any DBR < moderate
  - **Moderate**
  - **Severe**
  - **Very severe**

- Proliferative diabetic retinopathy (PDR)
  - **High-risk PDR**
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)
- **Mild**: Any DBR < moderate
- Moderate
- Severe
- Very severe

Proliferative diabetic retinopathy (PDR)
- High-risk PDR
Mild nonproliferative diabetic retinopathy
Classification of diabetic retinopathy

- **Nonproliferative diabetic retinopathy (NPDR)**
  - **Mild:** Any DBR < moderate
  - **Moderate:** (definition)
  - **Severe**
  - **Very severe**

- **Proliferative diabetic retinopathy (PDR)**
  - **High-risk PDR**
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)

- **Mild**: Any DBR < moderate
- **Moderate**: DBR > mild but < severe
- **Severe**
- **Very severe**

Proliferative diabetic retinopathy (PDR)

- **High-risk PDR**
Diabetic Retinopathy: The Basics

Moderate nonproliferative diabetic retinopathy
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)

- **Mild:** Any DBR < moderate
- **Moderate:** DBR > mild but < severe
- **Severe:** Presence of any 1 of the 4:2:1 rule
  - 15% chance of high-risk PDR within 1 year
- **Very severe:** Any 2 of the 4:1:2 rule
  - 45% chance of high-risk PDR within 1 year

- Severe or very severe NPDR + CWS

Proliferative diabetic retinopathy (PDR)

- High-risk PDR
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)
- Mild: Any DBR < moderate
- Moderate: DBR > mild but < severe
- Severe: Presence of any 1 of the 4:2:1 rule

Very severe

Proliferative diabetic retinopathy (PDR)
- High-risk PDR
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - **Mild**: Any DBR < moderate
  - **Moderate**: DBR > mild but < severe
  - **Severe**: Presence of any 1 of the 4:2:1 rule
    - 15% chance of high-risk PDR within 1 year
  - **Very severe**: Any 2 of the 4:2:1 rule
    - 45% chance of high-risk PDR within 1 year

- Proliferative diabetic retinopathy (PDR)

**What is the 4:2:1 rule?**

- 4 retinal quadrants of extensive retinal hemorrhages
- 2 retinal quadrants of venous beading
- 1 retinal quadrant of IRMA
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)
- **Mild**: Any DBR < moderate
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- **Severe**: Presence of any 1 of the 4:2:1 rule
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Very severe:
- Any 2 of the 4:2:1 rule
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Proliferative diabetic retinopathy (PDR)

What is the 4:2:1 rule?
- 4 retinal quadrants of...
- 2 retinal quadrants of...
- 1 retinal quadrant of...
Classification of diabetic retinopathy

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Proliferative diabetic retinopathy (PDR)
Severe nonproliferative diabetic retinopathy:
Extensive hemorrhages
Classification of diabetic retinopathy

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Proliferative diabetic retinopathy (PDR)

What is the 4:2:1 rule?
- 4 retinal quadrants of...
- extensive retinal hemorrhages
- 2 retinal quadrants of...
- 1 retinal quadrant of...

Diabetic Retinopathy: The Basics
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - Mild: Any DBR < moderate
  - Moderate: DBR > mild but < severe
  - Severe: Presence of any 1 of the 4:2:1 rule

  What is the 4:2:1 rule?
  - 4 retinal quadrants of...extensive retinal hemorrhages
  - 2 retinal quadrants of...venous beading
  - 1 retinal quadrant of...

- Very severe

- Proliferative diabetic retinopathy (PDR)
Severe nonproliferative diabetic retinopathy:
Venous beading
Classification of diabetic retinopathy

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- Proliferative diabetic retinopathy (PDR)

What is the 4:2:1 rule?
--4 retinal quadrants of...extensive retinal hemorrhages
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--1 retinal quadrant of...
Classification of diabetic retinopathy

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  - 4 retinal quadrants of extensive retinal hemorrhages
  - 2 retinal quadrants of venous beading
  - 1 retinal quadrant of IRMA

Very severe:

Proliferative diabetic retinopathy (PDR)
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
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- Proliferative diabetic retinopathy (PDR)

**What does IRMA stand for?**
- Intraretinal microvascular anomalies
- Think of it as neovascularization that has not broken through the ILM
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - Mild: Any DBR < moderate
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- Proliferative diabetic retinopathy (PDR)

What does IRMA stand for?
Intraretinal microvascular anomalies

4:2:1 rule
- 4 retina quadrants of extensive retinal hemorrhages
- 2 retina quadrants of venous beading
- 1 retina quadrant of IRMA

What does IRMA mean?
Think of it as neovascularization that has not broken through the ILM.
Classification of diabetic retinopathy

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Proliferative diabetic retinopathy (PDR)

What does IRMA stand for? Intraretinal microvascular anomalies

What does that mean? IRMA
Classification of diabetic retinopathy

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Proliferative diabetic retinopathy (PDR)

What does IRMA stand for?
Intraretinal microvascular anomalies

What does that mean?
Think of it as neovascularization that has not broken through the ILM

What is the histological definition of proliferation in this context?
Retinal neovascularization that breaks through the internal limiting membrane (ILM) hasn’t broken
Diabetic Retinopathy: The Basics

4 patches of IRMA (Airlie House Slide 6a). Note that they are more visible in the right-hand red-free image.

Severe nonproliferative diabetic retinopathy: IRMA
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)

- **Mild**: Any DBR < moderate
- **Moderate**: DBR > mild but < severe
- **Severe**: Presence of any 1 of the 4:2:1 rule

- **Very severe**: Severe or very severe NPDR + CWS

Proliferative diabetic retinopathy (PDR)

- **High-risk PDR**
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)

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Classification of diabetic retinopathy

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- **High-risk PDR**
Classification of diabetic retinopathy

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  - 15% chance of high-risk PDR within 1 year
- **Very severe**: Any 2 of the 4:2:1 rule

What % of **very** severe NPDR cases will progress to high-risk PDR in 1 year?

Proliferative diabetic retinopathy (PDR)

- **High-risk PDR**
Classification of diabetic retinopathy

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- **High-risk PDR**
Classification of diabetic retinopathy

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- **Very severe:** Any 2 of the 4:2:1 rule
  - 45% chance of high-risk PDR within 1 year
- **Pre-proliferative:** Severe or very severe NPDR + CWS

Proliferative diabetic retinopathy (PDR)

How should NPDR be managed?

There is a clear role for controlling three systemic risk factors:
- Blood glucose
- Blood pressure
- Lipid profile

What's less clear (at the time of this writing) is the role of two modalities that have shown considerable potential:
- Intravitreal anti-VEGF injections
- Intravitreal steroids

There is good clinical-trial data demonstrating that these interventions can lessen the severity of NPDR—substantially so in some cases. What is uncertain at this time is whether the cost/benefit ratio of these interventions is favorable enough to warrant mandating their use. Trials addressing this issue are ongoing.
Classification of diabetic retinopathy

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Pre-proliferative:
- Severe or very severe NPDR + CWS

Proliferative diabetic retinopathy (PDR)

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**Classification of diabetic retinopathy**

**Nonproliferative diabetic retinopathy (NPDR)**

- **Mild**: Any DBR < moderate

  - How should NPDR be managed?
  - There is a clear role for controlling three systemic risk factors:
    - Blood glucose
    - Blood pressure
    - Lipid profile

- **Moderate**: DBR > mild but < severe

- **Severe**: Presence of any 1 of the 4:2:1 rule
  - 15% chance of high-risk PDR within 1 year

- **Very severe**: Any 2 of the 4:2:1 rule
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**Proliferative diabetic retinopathy (PDR)**

**Diabetic Retinopathy: The Basics**
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)

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- **Moderate:** DBR > mild but < severe
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  - 45% chance of high-risk PDR within 1 year

Pre-proliferative:
- Severe or very severe NPDR + CWS

Proliferative diabetic retinopathy (PDR)

How should NPDR be managed?
- There is a clear role for controlling three systemic risk factors:
  - Blood glucose
  - Blood pressure
  - Lipid profile
- What’s less clear (at the time of this writing) is the role of two modalities that have shown considerable potential:
  - Intravitreal steroids
  - ...
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)

- **Mild**: Any DBR < moderate
- **Moderate**: DBR > mild but < severe
- **Severe**: Presence of any 1 of the 4:2:1 rule
  - 15% chance of high-risk PDR within 1 year
- **Very severe**: Any 2 of the 4:2:1 rule
  - 45% chance of high-risk PDR within 1 year
- **Pre-proliferative**: Severe or very severe NPDR + CWS

Proliferative diabetic retinopathy (PDR)

How should NPDR be managed?

There is a clear role for controlling three systemic risk factors:

- Blood glucose
- Blood pressure
- Lipid profile

What’s less clear (at the time of this writing) is the role of two modalities that have shown considerable potential:

- Intravitreal anti-VEGF injections
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Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)

Mild: Any DBR < moderate

How should NPDR be managed?
- There is a clear role for controlling three systemic risk factors:
  - Blood glucose
  - Blood pressure
  - Lipid profile

What's less clear (at the time of this writing) is the role of two modalities that have shown considerable potential:
- Intravitreal anti-VEGF injections
- Intravitreal steroids

There is good clinical-trial data demonstrating that these interventions can lessen the severity of NPDR—substantially so in some cases. What is uncertain at this time is whether the cost/benefit ratio of these interventions is favorable enough to warrant mandating their use. (Trials addressing this issue are ongoing.)
**Classification of diabetic retinopathy**

- **Nonproliferative diabetic retinopathy (NPDR)**
  - *Mild:* Any DBR < *moderate*
  - *Moderate:* DBR > *mild* but < *severe*
  - *Severe:* Presence of any 1 of the 4:2:1 rule
    - 15% chance of high-risk PDR within 1 year
  - *Very severe:* Any 2 of the 4:2:1 rule
    - 45% chance of high-risk PDR within 1 year

- **Proliferative diabetic retinopathy (PDR)**
  - *High-risk PDR*
    - OR
      - definition 1
    - OR
      - definition 2
    - OR
      - definition 3
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)

- **Mild**: Any DBR < moderate
- **Moderate**: DBR > mild but < severe
- **Severe**: Presence of any 1 of the 4:2:1 rule
  
  - 15% chance of high-risk PDR within 1 year
- **Very severe**: Any 2 of the 4:2:1 rule
  
  - 45% chance of high-risk PDR within 1 year

Proliferative diabetic retinopathy (PDR)

- **High-risk PDR**
  
  - Any NVD associated with vitreous heme (VH), OR
  - Large (at least ¼ DD) area of NVD with or without VH, OR
  - Large (at least ½ DD) area of NVE with VH

**NVD** = Neovascularization of the disc

**definition 2**

**definition 3**
Diabetic Retinopathy: The Basics

High-risk proliferative diabetic retinopathy: NVD + vitreous hemorrhage
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - **Mild**: Any DBR < **moderate**
  - **Moderate**: DBR > **mild** but < **severe**
  - **Severe**: Presence of any 1 of the 4:2:1 rule
    - 15% chance of high-risk PDR within 1 year
  - **Very severe**: Any 2 of the 4:2:1 rule
    - 45% chance of high-risk PDR within 1 year

- Proliferative diabetic retinopathy (PDR)
  - **High-risk PDR**
    - Any NVD associated with vitreous heme (VH), **OR**
    - Large (at least ¼ DD) area of NVD with or without VH, **OR**

\[ DD = \text{Disc diameter} \]

**definition 3**
High-risk proliferative diabetic retinopathy:
Extensive NVD
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)
- Mild: Any DBR < moderate
- Moderate: DBR > mild but < severe
- Severe: Presence of any 1 of the 4:2:1 rule
  - 15% chance of high-risk PDR within 1 year
- Very severe: Any 2 of the 4:2:1 rule
  - 45% chance of high-risk PDR within 1 year

Proliferative diabetic retinopathy (PDR)
- High-risk PDR
  - Any NVD associated with vitreous heme (VH), OR
  - Large (at least ¼ DD) area of NVD with or without VH, OR
  - Large (at least ½ DD) area of NVE with VH

NVE = Neovascularization elsewhere (ie, anywhere but the disc)
High-risk proliferative diabetic retinopathy: Large area NVE + associated vitreous heme
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - **Mild:** Any DBR < moderate
  - **Moderate:** DBR > mild but < severe
  - **Severe:** Presence of any 1 of the 4:2:1 rule
    - 15% chance of high-risk PDR within 1 year
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- Proliferative diabetic retinopathy (PDR)
  - **High-risk PDR**
    - Any NVD associated with vitreous heme (VH), OR
    - Large (at least ¼ DD) area of NVD without VH, OR
    - Large (at least ½ DD) area of NVE with VH

How big is a DD in microns?

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Diabetic Retinopathy: The Basics
Classification of diabetic retinopathy

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Proliferative diabetic retinopathy (PDR)
- **High-risk PDR**
  - Any NVD associated with vitreous heme (VH), **OR**
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How big is a DD in microns?

1500 (1.5 mm)
**Classification of diabetic retinopathy**

- **Nonproliferative diabetic retinopathy (NPDR)**
  - **Mild:** Any DBR < *moderate*
  - **Moderate:** DBR > *mild* but < *severe*
  - **Severe:** Presence of any *1* of the *4:2:1* rule
    - 15% chance of high-risk PDR within 1 year
  - **Very severe:** Any *2* of the *4:2:1* rule
    - 45% chance of high-risk PDR within 1 year

---

**Circling back for a minute…**
We said that PDR consists of retinal neovascularization. What sequence of events leads to retinal neovascularization?

**Retinal neovascularization**

- **Large (at least ½ DD) area of NVE with VH**
Classification of diabetic retinopathy

What pathological state is the endpoint of decreasing lumen diameter?
Occlusion of the retinal vessel

Vessel occlusion leads to what pathological event?
Ischemia of the retinal area serviced by the vessel

Retinal ischemia leads to what pathological state?
Hypoxia of the affected retinal cells

Hypoxic retinal cells release a signaling molecule that is central to the pathogenesis of DBR. What is that signaling molecule? VEGF (we will have much more to say about VEGF shortly)

Circling back for a minute…We said that PDR consists of retinal neovascularization. What sequence of events leads to retinal neovascularization?
The answer can be found in this set of questions/answers from earlier in the slide-set:

What is the histological definition of proliferation in this context?
Retinal neovascularization

- Any NVD associated with vitreous heme (VH), OR
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High-risk PDR

- 15% chance of high-risk PDR within 1 year
- 45% chance of high-risk PDR within 1 year
Classification of diabetic retinopathy

What pathological state is the endpoint of decreasing lumen diameter?
- Occlusion of the retinal vessel

Vessel occlusion leads to what pathological event?
- To summarize: Occlusive vasculopathy secondary to diabetic derangements produces retinal ischemia.

Pathogenesis of DBR. What is that signaling molecule?
- VEGF (we will have much more to say about VEGF shortly)

Circling back for a minute…We said that PDR consists of retinal neovascularization. What sequence of events leads to retinal neovascularization?
The answer can be found in this set of questions/answers from earlier in the slide-set:

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Eye Disease and Retinal Pathology (PDR)

Diabetic Retinopathy: The Basics
Classification of diabetic retinopathy

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- **High-risk PDR**
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---

**Diabetic Retinopathy: The Basics**

What pathological state is the endpoint of decreasing lumen diameter?
- Occlusion of the retinal vessel

Vessel occlusion leads to what pathological event?

To summarize: Occlusive vasculopathy secondary to diabetic derangements produces retinal ischemia. In a desperate attempt to recruit a blood supply, hypoxic retinal cells release **VEGF**, which diffuses throughout the vitreous cavity promoting neovascularization.

What pathological state is the endpoint of decreasing lumen diameter?
- Occlusion of the retinal vessel

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- The answer can be found in this set of questions/answers from earlier in the slide-set:

What is the histological definition of proliferation in this context?
- Retinal neovascularization that breaks through the internal limiting membrane (ILM)
  - Large (at least ½ DD) area of NVE with VH

---
**Classification of diabetic retinopathy**

What pathological state is the endpoint of decreasing lumen diameter? Occlusion of the retinal vessel

Vessel occlusion leads to what pathological event?

To summarize: Occlusive vasculopathy secondary to diabetic derangements produces retinal ischemia. In a desperate attempt to recruit a blood supply, hypoxic retinal cells release **VEGF**, which diffuses throughout the vitreous cavity promoting neovascularization. Unfortunately, the resulting new fibrovascular tissue is highly abnormal—it is prone to bleeding and contraction, leading to vitreous hemorrhages and/or tractional retinal detachment.

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To summarize: Occlusive vasculopathy secondary to diabetic derangements produces retinal ischemia. In a desperate attempt to recruit a blood supply, hypoxic retinal cells release VEGF, which diffuses throughout the vitreous cavity promoting neovascularization. Unfortunately, the resulting new fibrovascular tissue in the vitreous is abnormal—it is prone to bleeding and contraction, leading to vitreous hemorrhages and/or tractional retinal detachment.

Obviously, VEGF plays a central role in the pathogenesis of DBR. Let’s take a closer look at it.

Circling back for a minute…We said that PDR consists of retinal neovascularization. What sequence of events leads to retinal neovascularization?
The answer can be found in this set of questions/answers from earlier in the slide-set:

What is the histological definition of proliferation in this context?
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1:5% chance of high-risk PDR within 1 year

Very severe: Any 2 of the 4:2:1 rule
• 45% chance of high-risk PDR within 1 year

Pre-proliferative:
Severe or very severe NPDR + CWS

Proliferative diabetic retinopathy (PDR)

Diabetic Retinopathy: The Basics
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?
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\textsuperscript{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-A165
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-A165
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!
What does VEGF stand for?
Vascular endothelial growth factor

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)

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!

(Diabetic macular edema is addressed in slide-set R32)
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
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.

"Diabetic Retinopathy: The Basics"
What does VEGF stand for?
Vascular endothelial growth factor

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.

What does the A signify?
VEGF-A

Diabetic Retinopathy: The Basics
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

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

VEGF-A

What does 165 signify?

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?
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.

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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.
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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?
What does VEGF stand for?
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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.
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - Mild: Any DBR < moderate
  - Moderate: DBR > mild but < severe
  - Severe: Presence of any 1 of the 4:2:1 rule
    - 15% chance of high-risk PDR within 1 year
  - Very severe: Any 2 of the 4:2:1 rule
    - 45% chance of high-risk PDR within 1 year

- Pre-proliferative diabetic retinopathy (PDR)
  - Severe or very severe NPDR + CWS

- Proliferative diabetic retinopathy (PDR)
  - High-risk PDR
    - Any NVD associated with vitreous heme (VH), OR
    - Large (at least ¼ DD) area of NVD with or without VH, OR
    - Large (at least ½ DD) area of NVE with VH

Diabetic Retinopathy: The Basics

What landmark clinical trial provided this system of PDR classification?

The Diabetic Retinopathy Study (DRS)

What question did the DRS seek to answer?

'MIs PRP effective in treating PDR/severe NPDR?'

And the answer was…?

We'll get to that in a few slides
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**And the answer was…?**
We'll get to that in a few slides

**What does PRP stand for in this context?**
Panretinal photocoagulation
Classification of diabetic retinopathy

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Diabetic Retinopathy: The Basics

*First, let’s talk about laser-tissue interaction…*
What are the five modes of laser-tissue interaction?
What are the five modes of laser-tissue interaction?

- Photo-chemical, aka photoactivation
- Thermal
- Photo-ablation
- Plasma-induced ablation
- Photo-disruption, aka plasma-induced disruption
The five modes of laser-tissue interaction

- Photo-chemical (aka photoactivation)
- Thermal
- Photo-ablation
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Which mode is PRP an exemplar of?
Diabetic Retinopathy: The Basics

The five modes of laser-tissue interaction

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Which mode is PRP an exemplar of?
Thermal
The five modes of laser-tissue interaction

- Photo-chemical
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*Thermal effects on tissue exist on a continuum. What are the five degrees (see what I did there?) of tissue effects?*
Thermal effects on tissue exist on a continuum. What are the five degrees (see what I did there?) of tissue effects?

--Hyperthermia
--Coagulation
--Vaporization
--Carbonization
--Melting
Thermal effects on tissue exist on a continuum. What are the five degrees (see what I did there?) of tissue effects?

--Hyperthermia?
--Coagulation?
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--Carbonization?
--Melting?

Which thermal effect is employed most frequently?
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Which thermal effect is employed most frequently?
Coagulation
Thermal effects on tissue exist on a continuum. What are the five degrees? --Hyperthermia--Coagulation--Vaporization--Carbonization--Melting

Which thermal mode is employed most frequently? Coagulation

What does it mean to say that tissue has 'coagulated'?

It means the proteins have been denatured.

What does it mean to say a protein has been 'denatured'?

It means the protein has been forced out of its native conformation by some sort of applied stress (in this case, heat).

Because a protein's function is inextricably tied to its shape, denatured proteins do not behave as they do in their native form.

Can you give an example of protein denaturation?

Consider egg albumin. In its native state, it's a clear liquid. But if sufficient heat is applied, it becomes a white solid. (And if sufficient salsa is applied to the white solid, it becomes delish.)
Thermal effects on tissue exist on a continuum. What are the five degrees (see what I did there?) of tissue effects?

--Hyperthermia--
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The five modes of laser-tissue interaction

- Photo-chemical ablation (aka photoactivation)
- Thermal effects
  - Hyperthermia
  - Coagulation
  - Vaporization
  - Carbonization
  - Melting
- Plasma-induced ablation
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Consider egg albumin. In its native state, it’s a clear liquid. But if sufficient heat is applied, it becomes a white solid. (And if sufficient salsa is applied to the white solid, it becomes delish.)

At what temperature does retinal tissue start to coagulate?

65°C
Thermal effects on tissue exist on a continuum. What are the five degrees?
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For more info on lasers, see slide-set FELT26
Which laser is used to perform PRP?
Which laser is used to perform PRP? Argon green or blue-green
Q

- Which laser is used to perform PRP? Argon green or blue-green
- How many shots constitute a full compliment of PRP?
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Which laser is used to perform PRP? Argon green or blue-green

How many shots constitute a full compliment of PRP? About 1200-1400

What spot size should be used?
• Which laser is used to perform PRP? Argon green or blue-green
• How many shots constitute a full compliment of PRP? About 1200-1400
• What spot size should be used? 500 μm
Which laser is used to perform PRP? Argon green or blue-green
How many shots constitute a full compliment of PRP? About 1200-1400
What spot size should be used? 500 μm
How much power?
Q/A

- Which laser is used to perform PRP? Argon green or blue-green
- How many shots constitute a full compliment of PRP? About 1200-1400
- What spot size should be used? 500 \( \mu m \)
- How much power? Enough to produce a gray or light cream-colored burn
• Which laser is used to perform PRP? Argon green or blue-green
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How many shots constitute a full compliment of PRP? About 1200-1400

What spot size should be used? 500 \( \mu m \)

How much power? Enough to produce a gray or light cream-colored burn

How much distance between burns?
Which laser is used to perform PRP?
Argon green or blue-green

How many shots constitute a full compliment of PRP?
About 1200-1400

What spot size should be used?
500 μm

How much power?
Enough to produce a gray or light cream-colored burn

How much distance between burns?
About half a burn’s width
Diabetic Retinopathy: The Basics

PRP
Which laser is used to perform PRP? Argon green or blue-green

How many shots constitute a full compliment of PRP? About 1200-1400

What spot size should be used? 500 μm

How much power? Enough to produce a gray or light cream-colored burn

How much distance between burns? About half a burn’s width

Should it be done in one, or multiple sessions?
Which laser is used to perform PRP? Argon green or blue-green

How many shots constitute a full compliment of PRP? About 1200-1400

What spot size should be used? 500 μm

How much power? Enough to produce a gray or light cream-colored burn

How much distance between burns? About half a burn’s width

Should it be done in one, or multiple sessions? It doesn’t matter
What are known complications of PRP?

- Reduced vision
- Reduced contrast sensitivity
- Loss of 1-2 lines BCVA

Effects on vision
What are known complications of PRP?

- Reduced *peripheral* vision
- Reduced *color* vision
- Reduced *contrast sensitivity*
- Loss of 1-2 lines BCVA

*Diabetic Retinopathy: The Basics*
What are known complications of PRP?

- Reduced peripheral vision
- Reduced color vision
- Reduced contrast sensitivity
- Loss of 1-2 lines BCVA
- Decreased parasympathetic function
- Decreased two words
What are known complications of PRP?

- Reduced *peripheral* vision
- Reduced *color* vision
- Reduced *contrast sensitivity*
- Loss of 1-2 lines BCVA
- Decreased *accommodation*
- Decreased *corneal sensitivity*
What are known complications of PRP?
- Reduced peripheral vision
- Reduced color vision
- Reduced contrast sensitivity
- Loss of 1-2 lines BCVA
- Decreased accommodation
- Decreased corneal sensitivity

What do accommodation and corneal sensitivity have in common?
What are known complications of PRP?

- Reduced peripheral vision
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- Loss of 1-2 lines BCVA
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- Decreased corneal sensitivity

What do accommodation and corneal sensitivity have in common? Both are mediated by the long ciliary nerves.
What are known complications of PRP?

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What do accommodation and corneal sensitivity have in common?
Both are mediated by the long ciliary nerves

OK, but what do the long ciliary nerves have to do with PRP?
What are known complications of PRP?

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What do accommodation and corneal sensitivity have in common?
Both are mediated by the long ciliary nerves.

OK, but what do the long ciliary nerves have to do with PRP?
The long ciliary nerves run pretty deep (ie, just under the choroid) in the horizontal meridian.
What are known complications of PRP?

- Reduced peripheral vision
- Reduced color vision
- Reduced contrast sensitivity
- Loss of 1-2 lines BCVA
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The long ciliary nerves run pretty deep (i.e., just under the choroid) in the horizontal meridian.
What are known complications of PRP?

- Reduced *peripheral* vision
- Reduced *color* vision
- Reduced *contrast* sensitivity
- Loss of 1-2 lines BCVA
- Decreased *accommodation*
- Decreased *corneal sensitivity*

*What do accommodation and corneal sensitivity have in common?*
Both are mediated by the *long ciliary nerves.*

*OK, but what do the long ciliary nerves have to do with PRP?*
The long ciliary nerves run pretty deep (ie, just under the choroid) in the *horizontal meridian.* Because of their location, they are vulnerable to damage during PRP.
What are known complications of PRP?

- Reduced peripheral vision
- Reduced color vision
- Reduced contrast sensitivity
- Loss of 1-2 lines BCVA
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What do accommodation and corneal sensitivity have in common?
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OK, but what do the long ciliary nerves have to do with PRP?
The long ciliary nerves run pretty deep (ie, just under the choroid) in the horizontal meridian. Because of their location, they are vulnerable to damage during PRP.

How can one minimize the risk to the long ciliary nerves?
What are known complications of PRP?

- Reduced peripheral vision
- Reduced color vision
- Reduced contrast sensitivity
- Loss of 1-2 lines BCVA
- Decreased accommodation
- Decreased corneal sensitivity

What do accommodation and corneal sensitivity have in common? Both are mediated by the long ciliary nerves.

OK, but what do the long ciliary nerves have to do with PRP? The long ciliary nerves run pretty deep (i.e., just under the choroid) in the horizontal meridian. Because of their location, they are vulnerable to damage during PRP.

How can one minimize the risk to the long ciliary nerves? By avoiding the horizontal meridian during PRP.
What are known complications of PRP?

- Reduced *peripheral* vision
- Reduced *color* vision
- Reduced *contrast sensitivity*
- Loss of 1-2 lines BCVA
- Decreased *accommodation*
- Decreased *corneal sensitivity*
- Macular
- Inadvertent burn
What are known complications of PRP?

- Reduced peripheral vision
- Reduced color vision
- Reduced contrast sensitivity
- Loss of 1-2 lines BCVA
- Decreased accommodation
- Decreased corneal sensitivity
- Macular edema
- Inadvertent foveal burn
What are known complications of PRP?

- Reduced peripheral vision
- Reduced color vision
- Reduced contrast sensitivity
- Loss of 1-2 lines BCVA
- Decreased accommodation
- Decreased corneal sensitivity
- Macular edema
- Inadvertent foveal burn
- Choroidal edema
What are known complications of PRP?

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- Reduced color vision
- Reduced contrast sensitivity
- Loss of 1-2 lines BCVA
- Decreased accommodation
- Decreased corneal sensitivity
- Macular edema
- Inadvertent foveal burn
- Choroidal detachment
What are known complications of PRP?

- Reduced peripheral vision
- Reduced color vision
- Reduced contrast sensitivity
- Loss of 1-2 lines BCVA
- Decreased accommodation
- Decreased corneal sensitivity
- Macular edema
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- Choroidal detachment
- Iatrogenic break in Bruch’s
What are known complications of PRP?

- Reduced **peripheral** vision
- Reduced **color** vision
- Reduced **contrast sensitivity**
- Loss of **1-2 lines BCVA**
- Decreased **accommodation**
- Decreased **corneal sensitivity**
- Macular **edema**
- Inadvertent **foveal** burn
- Choroidal **detachment**
- Iatrogenic break in Bruch’s → **CNVM**

*(CNVM = Choroidal neovascular membrane)*
**Diabetic Retinopathy: The Basics**

What does the term high-risk PDR mean? High risk of what?

- **Proliferative diabetic retinopathy (PDR)**
  - **High-risk PDR**
    - Any NVD associated with vitreous heme (VH), OR
    - Large (at least ¼ DD) area of NVD with or without VH, OR
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In the DRS, patients with this level of neovascularization were found to be at high risk of severe vision loss (SVL).

What was the definition of SVL in the DRS?

Snellen acuity ≤ 5/200 (20/800)

Why was this level of vision chosen as the benchmark?

At or below 5/200, visually-guided ambulation becomes problematic.

What is the clinical implication of finding high-risk PDR in a patient?

High-risk PDR is the formal justification for performing PRP (I say 'formal' because many clinicians will offer PRP at lesser levels of DBR if they feel it is warranted).

To answer an earlier question: Per the DRS, is PRP effective at preventing SVL?

Indeed it is--it reduces the risk by 50% at 5 years post-treatment.
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)

Mild: Any DBR < moderate

Moderate: DBR > mild but < severe

Severe: Presence of any 1 of the 4:2:1 rule
  - 15% chance of high-risk PDR within 1 year

Very severe: Any 2 of the 4:2:1 rule
  - 45% chance of high-risk PDR within 1 year

Pre-proliferative: Severe or very severe NPDR + CWS

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Diabetic Retinopathy: The Basics

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What was the definition of SVL in the DRS?

Snellen acuity ≤ 5/200 (20/800)

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At or below 5/200, visually-guided ambulation becomes problematic.

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High-risk PDR is the formal justification for performing PRP (I say ‘formal’ because many clinicians will offer PRP at lesser levels of DBR if they feel it is warranted).

To answer an earlier question: Per the DRS, is PRP effective at preventing SVL?

Indeed it is—it reduces the risk by 50% at 5 years post-treatment.

There is another ‘informal’ justification for PRP that has yet to be mentioned—what is it?

There is another ‘informal’ justification for performing PRP (I say ‘formal’ because many clinicians will offer PRP at lesser levels of DBR if they feel it is warranted).

The presence of extensive neovascularization of the iris (NVI), or any neovascularization of the angle (NVA) is the informal justification for PRP.

What is the concern vis a vis extensive NVI, or NVA?

Their presence is very worrisome for the development of neovascular glaucoma (NVG), a potentially blinding condition.

In very general terms, what type of glaucoma is NVG, ie, what causes the IOP elevation?

It is a type of angle-closure glaucoma.
There is another ‘informal’ justification for PRP that has yet to be mentioned—what is it?
The presence of extensive neovascularization of the iris, or any neovascularization of the angle, or any other extensive neovascularization is the informal justification for performing PRP (I say ‘formal’ because many clinicians will offer PRP at lesser levels of DBR if they feel it is warranted).

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Diabetic Retinopathy: The Basics

Extensive NVI
**Classification of diabetic retinopathy**

- Nonproliferative diabetic retinopathy (NPDR)
  - **Mild:** Any DBR < **moderate**
  - **Moderate:** DBR > **mild** but < **severe**
  - **Severe:** Presence of any 1 of the 4:2:1 rule
    - 15% chance of high-risk PDR within 1 year
  - **Very severe:** Any 2 of the 4:2:1 rule
    - 45% chance of high-risk PDR within 1 year

- Pre-proliferative:
  - Severe or very severe NPDR + CWS

- Proliferative diabetic retinopathy (PDR)
  - **High-risk PDR**
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**Diabetic Retinopathy: The Basics**

*There is another ‘informal’ justification for PRP that has yet to be mentioned—what is it? The presence of extensive neovascularization of the iris (NVI), or any neovascularization of the angle (NVA)*

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- **Proliferative diabetic retinopathy (PDR)**
classification of diabetic retinopathy

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  - mild: any dbr < moderate
  - moderate: dbr > mild but < severe
  - severe: presence of any of the 4:2:1 rule
    - 15% chance of high-risk pdr within 1 year
  - very severe: any 2 of the 4:2:1 rule
    - 45% chance of high-risk pdr within 1 year
- proliferative diabetic retinopathy (pdr)
  - high-risk pdr
    - any nvd associated with vitreous heme (vh), or
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My diabetic pt has a small area of NVI at the pupillary margin—should I PRP him?

Not necessarily. So-called ‘tufts’ of NVI are a common occurrence in diabetics, and do not of themselves warrant PRP. That said, they do warrant a careful evaluation of the retina (consider wide-field FA to assess for extensive nonperfusion and/or subtle NVE), as well as close follow up (including frequent undilated gonioscopy to assess for NVA).

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Pupillary vascular tufts
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NVI/NVA is the informal justification for performing PRP (I say ‘formal’ because many clinicians will offer PRP at lesser levels of DBR if they feel it is warranted).

LPI? No!

I’m confused—if extensive NVI or NVA is concerning for the development of angle-closure glaucoma, shouldn’t I be performing laser peripheral iridotomy (LPI) rather than PRP?

No. LPI is effective only if/when the mechanism of angle closure is pupillary block. In NVA, the mechanism of angle closure is occlusion via peripheral anterior synechiae (PAS).

LPI? No!

In very general terms, what type of glaucoma is NVG, ie, what causes the IOP elevation?

It is a type of angle-closure glaucoma.

NVI/NVA is the informal justification for performing PRP (I say ‘formal’ because many clinicians will offer PRP at lesser levels of DBR if they feel it is warranted).

To answer an earlier question: Per the DRS, is PRP effective at preventing SVL?

Indeed it is—it reduces the risk by 50% at 5 years post-treatment.

- Proliferative diabetic retinopathy (PDR)
  - High-risk PDR
    - Any NVD associated with vitreous heme (VH), OR
    - Large (at least ¼ DD) area of NVD with or without VH, OR
    - Large (at least ½ DD) area of NVE with VH
Diabetic Retinopathy: The Basics

There is another ‘informal’ justification for PRP that has yet to be mentioned—what is it? The presence of extensive neovascularization of the iris (NVI), or any neovascularization of the angle (NVA)

I’m confused—if extensive NVI or NVA is concerning for the development of angle-closure glaucoma, shouldn’t I be performing laser peripheral iridotomy (LPI) rather than PRP? No. LPI is effective only if/when the mechanism of angle closure is pupillary block. In NVA, the mechanism of angle closure is occlusion via peripheral anterior synechiae, PAS.

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● Proliferative diabetic retinopathy (PDR)

High-risk PDR

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Diabetic Retinopathy: The Basics

There is another ‘informal’ justification for PRP that has yet to be mentioned—what is it? The presence of extensive neovascularization of the iris (NVI), or any

My diabetic pt has a small area of NVI at the pupillary margin—should I PRP him?

I’m confused—if extensive NVI or NVA is concerning for the development of angle-closure glaucoma, shouldn’t I be performing laser peripheral iridotomy (LPI) rather than PRP?

No. LPI is effective only if/when the mechanism of angle closure is pupillary block. In NVA, the mechanism of angle closure is occlusion via peripheral anterior synechiae, PAS. (If you’re unclear on the difference between the two, it’s really important that you review slide-set G16 in the not-too-distant future.)

In very general terms, what type of glaucoma is NVG, ie, what causes the IOP elevation? It is a type of angle-closure glaucoma

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Diabetic Retinopathy: The Basics

What does the term high-risk PDR mean? High risk of what?
In the DRS, patients with this level of neovascularization were found to be at high risk of severe vision loss (SVL)

What is the goal of PRP, ie, what are we trying to do?

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What is the goal of PRP; ie, what are we trying to do?
The goal is to kill most of the cells in the peripheral retina.

To answer an earlier question: Per the DRS, is PRP effective at preventing SVL? Indeed it is—it reduces the risk by 50% at 5 years post-treatment.

**Proliferative diabetic retinopathy (PDR)**

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The goal is to kill most of the cells in the peripheral retina

What is the therapeutic rationale? Why kill the peripheral retina?

To answer an earlier question: Per the DRS, is PRP effective at preventing SVL? Indeed it is—it reduces the risk by 50% at 5 years post-treatment

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**What is the goal of PRP, ie, what are we trying to do?**
The goal is to kill most of the cells in the peripheral retina.

**What is the therapeutic rationale? Why kill the peripheral retina?**
As stated several times now: DBR renders portions of the retina hypoxic, and hypoxic cells release VEGF, initiating a cascade of deleterious events.

To answer an earlier question: Per the DRS, is PRP effective at preventing SVL? Indeed it is—**it reduces the risk by 50%** at 5 years post-treatment.

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The goal is to kill most of the cells in the peripheral retina

What is the therapeutic rationale? Why kill the peripheral retina?
As stated several times now: DBR renders portions of the retina hypoxic, and hypoxic cells release VEGF, initiating a cascade of deleterious events. OTOH, dead cells do not release VEGF. So by euthanizing the hypoxic retina, the intraocular VEGF burden is reduced, neovascularization is halted, and SVL is avoided.

To answer an earlier question: Per the DRS, is PRP effective at preventing SVL? Indeed it is— it reduces the risk by 50% at 5 years post-treatment

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  - Any NVD associated with vitreous heme (VH)
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Proliferative diabetic retinopathy (PDR)

What was the definition of SVL in the DRS?
Snellen acuity ≤ 5/200 (20/800)

Why was this level of vision chosen as the benchmark?
At or below 5/200, visually-guided ambulation becomes problematic

What is the clinical implication of finding high-risk PDR in a patient?
High-risk PDR is the formal justification for performing PRP (I say 'formal' because many clinicians will offer PRP at lesser levels of DBR if they feel it is warranted)
What does the term high-risk PDR mean? High risk of what?
In the DRS, patients with this level of neovascularization were found to be at high risk of severe vision loss (SVL)

What is the goal of PRP, ie, what are we trying to do?
The goal is to kill most of the cells in the peripheral retina

PRP has two other salutary effects on oxygen tension in the retina—what are they?
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To answer an earlier question: Per the DRS, is PRP effective at preventing SVL?
Indeed it is— it reduces the risk by 50% at 5 years post-treatment

Proliferative diabetic retinopathy (PDR)

High-risk PDR

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Classification of diabetic retinopathy

**Nonproliferative diabetic retinopathy (NPDR)**

- **Mild:** Any DBR < moderate
- **Moderate:** DBR > mild but < severe
- **Severe:** Presence of any 1 of the 4:2:1 rule
  - 15% chance of high-risk PDR within 1 year

- **Very severe:** Any 2 of the 4:2:1 rule
  - 45% chance of high-risk PDR within 1 year

**Pre-proliferative:** Severe or very severe NPDR + CWS

**Proliferative diabetic retinopathy (PDR)**

- **High-risk PDR**
  - Any NVD associated with vitreous heme (VH), OR
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**Diabetic Retinopathy: The Basics**

**What does the term high-risk PDR mean? High risk of what?**

In the DRS, patients with this level of neovascularization were found to be at high risk of severe vision loss (SVL)

**What is the goal of PRP, i.e., what are we trying to do?**

The goal is to kill most of the cells in the peripheral retina

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**PrP has two other salutary effects on oxygen tension in the retina—what are they?**

- By decreasing the number of living retinal cells competing for oxygen, the remaining ones receive a greater portion of the oxygen delivered to the retina
- The peripheral VEGF burden is reduced, neovascularization is halted, and CWS is avoided.

**To answer an earlier question: Per the DRS, is PRP effective at preventing SVL?**

Indeed it is—it reduces the risk by 50% at 5 years post-treatment

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**Proliferative diabetic retinopathy (PDR)**

**High-risk PDR**

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**What was the definition of SVL in the DRS?**

Snellen acuity ≤ 5/200 (20/800)

**Why was this level of vision chosen as the benchmark?**

At or below 5/200, visually-guided ambulation becomes problematic

**What is the goal of PRP, i.e., what are we trying to do?**

The goal is to kill most of the cells in the peripheral retina

**What is the therapeutic rationale? Why kill the peripheral retina?**

As stated several times now: DBR renders portions of the retina hypoxic, and hypoxic cells release VEGF, initiating a cascade of deleterious events.

OTOH, dead cells do not release VEGF. So by euthanizing the hypoxic retina, the intraocular VEGF burden is reduced, neovascularization is halted, and CWS is avoided.

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**Diabetic Retinopathy: The Basics**

*What does the term high-risk PDR mean? High risk of what?*

In the DRS, patients with this level of neovascularization were found to be at high risk of severe vision loss (SVL).

*What is the goal of PRP, ie, what are we trying to do?*

The goal is to kill most of the cells in the peripheral retina.

**PRP has two other salutary effects on oxygen tension in the retina—what are they?**

--By decreasing the number of living retinal cells competing for oxygen, the remaining ones receive a greater portion of the oxygen delivered to the retina.

--The PRP scars facilitate the diffusion of oxygen from the choroidal circulation into the retinal space.

To answer an earlier question, per the DRS, is PRP effective at preventing SVL? Indeed it is—**it reduces the risk by 50%** at 5 years post-treatment.

**Proliferative diabetic retinopathy (PDR)**

- High-risk PDR
  - Any NVD associated with vitreous heme (VH), **OR**
  - Large (at least ¼ DD) area of NVD with or without VH, **OR**
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What does the term high-risk PDR mean? High risk of what?

In the DRS, patients with this level of neovascularization were found to be at high risk of severe vision loss (SVL).

An important aside: The ETDRS looked at whether PRP reduced the risk of SVL in pts with mild, moderate and/or severe NPDR. It found a modest reduction in the risk among pts with severe NPDR, but not for those with mild or moderate dz. Thus, PRP is justified in severe NPDR, but not in mild or moderate dz.

To answer an earlier question: Per the DRS, is PRP effective at preventing SVL? Indeed it is — it reduces the risk by 50% at 5 years post-treatment.

High-risk PDR

- Any NVD associated with vitreous heme (VH), OR
- Large (at least ¼ DD) area of NVD with or without VH, OR
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Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)
- **Mild?** Any DBR < moderate
- **Moderate?** DBR > mild but < severe
- **Severe?** Presence of any 1 of the 4:2:1 rule

Proliferative diabetic retinopathy (PDR)
- **High-risk PDR**
  - Any NVD associated with vitreous heme (VH), OR
  - Large (at least ¼ DD) area of NVD with or without VH, OR
  - Large (at least ½ DD) area of NVE with VH

To answer an earlier question: Per the DRS, is PRP effective at preventing SVL? It is for severe NPDR (but not mild or moderate)

The ETDRS looked at whether PRP for mild, moderate and/or severe NPDR reduced the risk of SVL. What did it find in this regard?

It found that PRP resulted in a modest reduction of SVL in severe NPDR (especially in pts with Type 2 DM), but not in mild or moderate dz

Per the DRS, is PRP effective at preventing SVL?
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)

- **Mild?** Nope
- **Moderate?** Nope
- **Severe?** Yes!

The ETDRS looked at whether PRP for mild, moderate and/or severe NPDR reduced the risk of SVL. What did it find in this regard? It found that PRP resulted in a modest reduction of SVL in severe NPDR (especially in pts with Type 2 DM), but not in mild or moderate dz.

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Classification of diabetic retinopathy

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- **Mild? Nope**
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Proliferative diabetic retinopathy (PDR)

To answer an earlier question: Per the DRS, is PRP effective at preventing SVL?
It is for severe NPDR (but not mild or moderate)
Take note: DBR is a **progressive** condition, one that passes through a well-defined series of stages on its way to blinding a pt. If DBR is identified at an early stage, the pt has a chance to enact lifestyle modifications that will lead to its resolution. If it is recognized at a later (but pre-SVL) stage, treatment can be performed that may prevent it from blinding the pt. *This is why we screen DM pts on the reg.*
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
  - Mild: Any DBR < moderate
  - Moderate: DBR > mild but < severe
  - Severe: Presence of any 1 of the 4:2:1 rule
    - 15% chance of high-risk PDR within 1 year
  - Very severe: Any 2 of the 4:2:1 rule
    - 45% chance of high-risk PDR within 1 year

- Proliferative diabetic retinopathy (PDR)
  - High-risk PDR
    - Any NVD associated with vitreous heme (VH), OR
    - Large (at least ¼ DD) area of NVD with or without VH, OR
    - Large (at least ½ DD) area of NVE with VH

And finally: With respect to DBR, what does DME stand for?

Diabetic macular edema (DME) can occur at any level of NPDR or PDR.
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)
- **Mild**: Any DBR < moderate
- **Moderate**: DBR > mild but < severe
- **Severe**: Presence of any 1 of the 4:2:1 rule: 15% chance of high-risk PDR within 1 year
- **Very severe**: Any 2 of the 4:2:1 rule: 45% chance of high-risk PDR within 1 year

Pre-proliferative: Severe or very severe NPDR + CWS

Proliferative diabetic retinopathy (PDR)
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And finally: With respect to DBR, what does DME stand for?
Diabetic macular edema

Diabetic Retinopathy: The Basics
**Classification of diabetic retinopathy**

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  - **Very severe:** Any 2 of the 4:2:1 rule
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*And finally: With respect to DBR, what does DME stand for?*
Diabetic macular edema

*Where does DME fit into this classification scheme?*
Classification of diabetic retinopathy

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- **Very severe**: Presence of any 2 of the 4:2:1 rule
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Pre-proliferative: Severe or very severe NPDR + CWS

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And finally: With respect to DBR, what does DME stand for? 
Diabetic macular edema

Where does DME fit into this classification scheme? 
DME can occur at any level of NPDR or PDR

Diabetic Retinopathy: The Basics
**Classification of diabetic retinopathy**

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**And finally:** With respect to DBR, what does DME stand for?

Where does DME fit into this classification scheme?

DME can occur at any level of NPDR or PDR

**Diabetic Retinopathy: The Basics**

DME is addressed in detail in its own slide-set