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?
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Does diabetes prevalence vary with age?
How many American adults are diabetic or pre-diabetic?
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Does diabetes prevalence vary with age?
Yes, it increases with advancing age
Diabetic Retinopathy: The Basics

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Diabetic Retinopathy: The Basics

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Does diabetes prevalence vary with ethnicity?
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Over 100M!

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Does diabetes prevalence vary with education level?
How many American adults are diabetic or pre-diabetic?  
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Yes, rates are twice as high among individuals with less than a high-school education
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What proportion of diabetics receive screening eye exams at recommended intervals?
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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
**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?*
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%
**Diabetic Retinopathy: The Basics**

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

Of those diabetics with retinopathy, what proportion have vision-threatening retinopathy?
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99%! 
**Diabetic Retinopathy: The Basics**

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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

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Of those diabetics with retinopathy, what proportion have vision-threatening retinopathy?
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25%

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50%!
Diabetic Retinopathy: The Basics

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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?
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(If you’re not sure what proliferative retinopathy is, no worries—it’ll be covered in this slide-set)

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%!
What are the three histological vascular derangements in DBR?
1) Pericyte loss
2) BM thickening
3) ↓ lumen diameter
What are the three histological vascular derangements in DBR?

1) Pericyte loss

2) BM thickening → ↓ lumen diameter

3) Loss of endothelial barrier function

\(BM = \text{Basement membrane}\)
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 $\rightarrow$ 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 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 → ↓ 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
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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 fenestrated or non-fenestrated.
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?

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?

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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.
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What are the three histological vascular derangements in DBR?

1) **Pericyte** loss

2) BM thickening $\rightarrow$ $\downarrow$ lumen diameter

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---

**Do retinal vessels have an intimal lining?**

Yes

**Do retinal vessels have a muscular wall?**

No

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**Do retinal vessels have an intimal lining?**
No

**Do they possess a muscular wall?**
No

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

inner blood-retina barrier

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

An **outer** blood-retina barrier

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

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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**?

**inner blood-retina barrier**
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

*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 **three words** cells

**inner blood-retina barrier**
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.

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

Which occurs first?
What are the three histological vascular derangements in DBR?

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

Which occurs first? Pericyte loss
Trypsin mount of normal retina--low and high mag

The dark nuclei belong to pericytes; the lighter, to endothelial cells. *Note that the ratio between them is roughly 1:1.*
Trypsin mount of DBR retina--low and high mag

But in a retina 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

2) BM thickening $\rightarrow$ ↓ lumen diameter

3) Loss of endothelial barrier function

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

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

Vessel occlusion leads to what pathological event?
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

*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
What are the three histological vascular derangements in DBR?

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3) Loss of endothelial barrier function

*What pathological state is the endpoint of decreasing lumen diameter?*
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*Vessel occlusion leads to what pathological event?*
Ischemia of the retinal area serviced by the vessel

*Retinal ischemia leads to what pathological state?*
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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
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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?

Diabetic Retinopathy: The Basics
What are the three histological vascular derangements in DBR?

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

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

1) Pericyte loss
2) BM thickening ➔ ↓ 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

- 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
- 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
Classification of diabetic retinopathy

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

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  - Moderate
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    - 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?
Classical retinopathy

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

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

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)

Three basic levels of NPDR
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 more level (not universally used)

One level of concern
Classification of diabetic retinopathy

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

  Three basic levels of NPDR

  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.
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
- Moderate
- Severe
- Very severe

Proliferative diabetic retinopathy (PDR)
- High-risk PDR

How are mild and moderate NPDR defined?
With respect to the standard photographs employed in the DRS
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
Diabetic Retinopathy: The Basics

Mild nonproliferative diabetic retinopathy
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:** 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 4:2:1 rule
    - 45% chance of high-risk PDR within 1 year

- **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 (4 retinal quadrants of extensive retinal hemorrhages, 2 retinal quadrants of venous beading, 1 retinal quadrant of IRMA)
- **Very severe**: Any 2 of the 4:2:1 rule (45% chance of high-risk PDR within 1 year)

Proliferative diabetic retinopathy (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...
- 2 retinal quadrants of...
- 1 retinal quadrant of...
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
    - 4 retinal quadrants of…extensive retinal hemorrhages
    - 2 retinal quadrants of…
    - 1 retinal quadrant of…
  - Very severe

- Proliferative diabetic retinopathy (PDR)

4:2:1 rule
Severe nonproliferative diabetic retinopathy:
Extensive hemorrhages
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...
- 1 retinal quadrant of...
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)**
Severe nonproliferative diabetic retinopathy: Venous beading
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...
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
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

- Very severe: Any 2 of the 4:2:1 rule

What does IRMA stand for?

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

Proliferative diabetic retinopathy (PDR)
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
  - 4 retinal quadrants of extensive retinal hemorrhages
  - 2 retinal quadrants of venous beading
  - 1 retinal quadrant of IRMA
  - 15% chance of high-risk PDR within 1 year

Proliferative diabetic retinopathy (PDR)

What does IRMA stand for?
- Intraretinal microvascular anomalies

4:2:1 rule
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

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

  4:2:1 rule

  - 15% chance of high-risk PDR within 1 year

- Proliferative diabetic retinopathy (PDR)

  - **Very severe:** Any 2 of the 4:2:1 rule

  - 45% chance of high-risk PDR within 1 year

- **What does IRMA stand for?** Intraretinal microvascular anomalies

- **What does that mean?**

  - Think of it as neovascularization that has not broken through the ILM
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 histological definition of proliferation in this context?**
Retinal neovascularization that breaks through the internal limiting membrane (ILM)

**What does IRMA stand for?**
Intraretinal microvascular anomalies

**What does that mean?**
Think of it as neovascularization that has not broken through the ILM
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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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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  - 15% chance of high-risk PDR within 1 year
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Proliferative diabetic retinopathy (PDR)
- *High-risk PDR*
Classification of diabetic retinopathy

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

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

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

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Pre-proliferative:

- Severe or very severe NPDR + CWS

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:

Proliferative diabetic retinopathy (PDR)

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

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- ...
- ...
- ...

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Pre-proliferative

Proliferative diabetic retinopathy (PDR)

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Pre-proliferative

Proliferative diabetic retinopathy (PDR)

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There is a clear role for controlling three systemic risk factors:
- Blood glucose
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- 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
-- Intravitreal steroids
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

- **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

- **Nonproliferative diabetic retinopathy (NPDR)**
  - **Mild:** Any DBR < moderate
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  - **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**
    - definition 1
    - definition 2
    - definition 3
    - OR
    - OR
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

\[ NVD = \text{Neovascularization of the disc} \]
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*
Diabetic Retinopathy: The Basics

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)*
Diabetic Retinopathy: The Basics

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
- **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

*How big is a DD in microns?*  
1500 (1.5 mm)
Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)
- **Mild:** Any DBR < moderate
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- **Very severe:** Any 2 of the 4:2:1 rule
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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 with or without VH, OR
  - Large (at least ½ DD) area of NVE with VH

**How big is a DD in microns?**
- 1500 (1.5 mm)
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
    - 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

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

What is the histological definition of proliferation in this context?

Retinal neovascularization
Diabetic Retinopathy: The Basics

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 that breaks through the internal limiting membrane (ILM)
  - Large (at least \( \frac{1}{2} \) DD) area of NVE with VH
  - Any NVD associated with VH
  - Large (at least \( \frac{1}{4} \) DD) area of NVD
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
  - 15% chance of high-risk PDR within 1 year

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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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What is the histological definition of proliferation in this context?

Retinal neovascularization (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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  - 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)

To summarize: Occlusive vasculopathy secondary to diabetic derangements produces retinal ischemia.

RETINOGENESIS OR DBR: WHAT IS THAT SIGNALING MOLECULE?

VEGF

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 that breaks through the internal limiting membrane (ILM)
  - OR
  - 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.

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
• Any NVD associated with vitreous heme (VH), OR
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Provisional classification of diabetic retinopathy (PDR)

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

VEGF (we will have much more to say about VEGF shortly)

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

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- Pre-proliferative: 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,
    - Large (at least ½ DD) area of NVE with VH

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

VEGF (we will have much more to say about VEGF shortly)
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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Retinal neovascularization that breaks through the internal limiting membrane (ILM)

Proliferative diabetic retinopathy (PDR)

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Diabetic Retinopathy: The Basics

What is the histological definition of proliferation in this context?

Retinal neovascularization that breaks through the internal limiting membrane (ILM)

What pathological state is the endpoint of decreasing lumen diameter?

Occlusion of the retinal vessel

Vessel occlusion leads to what pathological event?

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.

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?

Retinal neovascularization
What does VEGF stand for?
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

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?

VEGF-A

165
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)

VEGF-A165
What does VEGF stand for?
Vascular endothelial growth factor

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How potent?

VEGF-A165
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How potent?
About 10,000x more potent than histamine!

VEGF-A$_{165}$
What does **VEGF** stand for?
Vascular endothelial growth factor

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

Does **VEGF** do anything besides grow new blood vessels?
Yes, it also is a potent vasodilator (it was known originally as *vascular permeability factor*).

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

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?
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.
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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 is not a single entity—a number of similar-but-different proteins comprise the ‘VEGF family.’ These are differentiated as VEGF-A through VEGF-F. (One family member, placental growth factor [PIGF], is the exception to the naming rule.) When the term VEGF is used in the ophthalmology literature without a sub-family designation, it is understood to mean VEGF-A.
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VEGF-A

What does 165 signify?
What does VEGF stand for?
Vascular endothelial growth factor

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

**Broadly speaking, what is it?**
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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?
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Vascular endothelial growth factor

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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 of the 4:2:1 rule
    - 15% chance of high-risk PDR within 1 year
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- Pre-proliferative
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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 with or without VH, OR
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What landmark clinical trial provided this system of PDR classification?

Diabetic Retinopathy Study (DRS)

What question did the DRS seek to answer?

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

And the answer was...

We'll get to that in a few slides.
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Diabetic Retinopathy: The Basics

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Diabetic Retinopathy: The Basics

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What question did the DRS seek to answer?
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- We'll get to that in a few slides

What does PRP stand for in this context?
- Panretinal photocoagulation
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Diabetic Retinopathy: The Basics

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

Let’s drill down on PRP for a minute…
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?

<table>
<thead>
<tr>
<th>Mode</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Photo-chemical</td>
<td>aka photoactivation</td>
</tr>
<tr>
<td>Thermal</td>
<td></td>
</tr>
<tr>
<td>Photo-ablation</td>
<td></td>
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<tr>
<td>Plasma-induced ablation</td>
<td></td>
</tr>
<tr>
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Diabetic Retinopathy: The Basics

The five modes of laser-tissue interaction

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

- **Photo-thermal**
- **Photo-ablation**
- **Plasma-induced ablation**
- **Photo-disruption**

_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?

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Which thermal effect is employed most frequently?
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Which thermal effect 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?

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The five modes of laser-tissue interaction

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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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The five modes of laser-tissue interaction

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For more info on lasers, see slide-set FELT26
Which laser is used to perform PRP?
Diabetic Retinopathy: The Basics

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

How many shots constitute a full compliment of 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
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 \( \mu \text{m} \)

How much power?
Q/A

Diabetic Retinopathy: The Basics

- 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 \( \mu \text{m} \)
- How much power? Enough to produce a light-colored burn
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
Q

- 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?
● 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 vision
- Reduced vision
- Loss of # to # lines BCVA
What are known complications of PRP?

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

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

- Reduced **peripheral** vision
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- Reduced **contrast sensitivity**
- Loss of **1-2 lines BCVA**
- Decreased **accommodation**
- Decreased **corneal sensitivity**
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- Inadvertent **foveal** burn
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- Iatrogenic break in Bruch’s membrane
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- Decreased accommodation
- Decreased corneal sensitivity
- Macular edema
- Inadvertent foveal burn
- Choroidal detachment
- Iatrogenic break in Bruch’s \( \rightarrow \) 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
    - Large (at least ½ DD) area of NVE with VH

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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).**

**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).

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Indeed it is— it reduces the risk by 50% at 5 years post-treatment.
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Proliferative diabetic retinopathy (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 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
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**Q&A**

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

High-risk PDR

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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.
There is another ‘informal’ justification for PRP that has yet to be mentioned—what is it? The presence of extensive

four different words

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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

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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)

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

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Diabetic Retinopathy: The Basics

Extensive NVI
Nonproliferative diabetic retinopathy (NPDR)

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- **Moderate**: DBR > mild but < severe
- **Severe**: Presence of any of the 4:2:1 rule
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Pre-proliferative:
- Severe or very severe NPDR + CWS

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What was the definition of SVL in the DRS?

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Why was this level of vision chosen as the benchmark?

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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).

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

The presence of extensive neovascularization of the iris (NVI), or any neovascularization of the angle (NVA)

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.
Diabetic Retinopathy: The Basics

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Diabetic Retinopathy: The Basics

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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

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
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Diabetic Retinopathy: The Basics

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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)

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)

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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

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).
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 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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*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.

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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Pupillary vascular tufts
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LPI?

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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.)
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 need for LPI? No!

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

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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.

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

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--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

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

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

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

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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

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?

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

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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 # DM), but not in mild or moderate dz.

Per the DRS, is PRP effective at preventing SVL?

It is for severe NPDR (but not mild or moderate).
Classification of diabetic retinopathy

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- **Mild?** Nope
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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?
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Per the ETDRS, 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

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- **Moderate:** DBR > mild but < severe
- **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
- 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 (DME) can occur at any level of NPDR or PDR.
Classification of diabetic retinopathy

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Diabetic macular edema

Where does DME fit into this classification scheme?

Diabetic Retinopathy: The Basics
Classification of diabetic retinopathy

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

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- **High-risk PDR**
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  - Large (at least \( \frac{1}{2} \) DD) area of NVE with VH

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

DME is addressed in detail in its own slide-set

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

Diabetic Retinopathy: The Basics

Diabetic macular edema (DME)
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