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 $\rightarrow \downarrow$ lumen diameter
3) Loss of endothelial barrier function
What are the three histological vascular derangements in DBR?

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Pericyte loss, and thickening of the BM with decreased lumen diameter, lead to what pathologic event?
What are the three histological vascular derangements in DBR?

1) **Pericyte loss**
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*Pericyte loss, and thickening of the BM with decreased lumen diameter, lead to what pathologic event?*
*Vascular occlusion*
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Vascular occlusion leads to what pathological event?
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Vascular occlusion

*Vascular occlusion leads to what pathological event?*
Retinal nonperfusion
What are the three histological vascular derangements in DBR?
1) Pericyte loss
2) BM thickening $\rightarrow$ ↓ lumen diameter
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*Loss of endothelial barrier function leads to what pathologic event?*
What are the three histological vascular derangements in DBR?

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

1) Pericyte loss
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Loss of endothelial barrier function leads to what pathologic event?
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
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*Loss of endothelial barrier function leads to what pathologic event?*
Leaching of serum into the retina

*Leaching of serum into the retina leads to what pathological state?*
Retinal edema
Diabetic Retinopathy: Classification

Classification of diabetic retinopathy

Two broad categories of DBR
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

- Nonproliferative diabetic retinopathy (NPDR)
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Classification of diabetic retinopathy

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What is the histological definition of proliferation in this context?
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Two broad categories of DBR

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

Classification of diabetic retinopathy

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- **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

15% chance of high-risk PDR within 1 year

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Pre-proliferative: Severe or very severe NPDR + CWS
Classification of diabetic retinopathy

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

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- 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
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Three basic levels of NPDR

- One more level (not universally used)

- **Proliferative diabetic retinopathy (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**

Three basic levels of NPDR

One more level (not universally used)

One level of concern
Classification of diabetic retinopathy

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

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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

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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**: definition
  - **Severe**: 
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- Proliferative diabetic retinopathy (PDR)
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Classification of diabetic retinopathy

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Classification of diabetic retinopathy

Nonproliferative diabetic retinopathy (NPDR)
- **Mild**: Any DBR < moderate
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- **Severe or very severe NPDR + CWS**

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

What is the 4:2:1 rule?
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- Proliferative diabetic retinopathy (PDR)

**What is the 4:2:1 rule?**
- 4 retinal quadrants of...
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What is the 4:2:1 rule?
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Proliferative diabetic retinopathy (PDR)
Classification of diabetic retinopathy

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Proliferative diabetic retinopathy (PDR)
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- Proliferative diabetic retinopathy (PDR)

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Diabetic Retinopathy: Classification

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    - 1 retinal quadrant of IRMA
  - 15% chance of high-risk PDR within 1 year

- Proliferative diabetic retinopathy (PDR)
  - **Pre-proliferative**: Severe
  - **Proliferative**: 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
  - Think of it as neovascularization that has not broken through the ILM
Classification of diabetic retinopathy

- Nonproliferative diabetic retinopathy (NPDR)
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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 venous beading
  - 1 retinal quadrant of IRMA
  - Presence of diabetes retinopathy minor abnormalities

- What does IRMA stand for?
  - Intraretinal microvascular anomalies
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What does IRMA stand for?
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What does that mean?
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What is the histological definition of proliferation in this context?
- Retinal neovascularization that hasn't broken through the internal limiting membrane (ILM)
Classification of diabetic retinopathy

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Very severe: definition

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

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Proliferative diabetic retinopathy (PDR)

- **High-risk PDR**

Per the DRS, what % of severe NPDR cases will progress to high-risk PDR in 1 year?
Diabetic Retinopathy: Classification

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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?
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Proliferative diabetic retinopathy (PDR)

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Classical classification of diabetic retinopathy

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- **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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Proliferative diabetic retinopathy (PDR)

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Pre-proliferative

Proliferative diabetic retinopathy (PDR)

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- **Proliferative diabetic retinopathy (PDR)**

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  - Blood glucose
  - Blood pressure
  - Lipid profile

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- Severe or very severe NPDR + CWS
Classification of diabetic retinopathy

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Proliferative diabetic retinopathy (PDR)

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

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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

**Definitions**

- **NVD** = Neovascularization of the disc
- **NVE** = Neovascularization of the retina
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  - Any NVD associated with vitreous heme (VH), **OR**
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\[ DD = \text{Disc diameter} \]

**definition 3**
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NVE = Neovascularization elsewhere (ie, anywhere but the disc)
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)**
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    - How big is a DD in microns?
Diabetic Retinopathy: Classification

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  - How big is a DD in microns?
    - 1500 (1.5 mm)
Diabetic Retinopathy: Classification

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- Pre-proliferative
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What landmark clinical trial provided this system of PDR classification?
The 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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What does PRP stand for in this context?
Panretinal photocoagulation
Diabetic Retinopathy: Classification

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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).

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**Proliferative diabetic retinopathy (PDR)**

*High-risk PDR*

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**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.
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Snellen acuity ≤ 5/200 (20/800)

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Q

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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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- **Mild?** Nope
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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?

It is for severe NPDR (but not mild or moderate).
Diabetic Retinopathy: Classification

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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.
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Where does DME fit into this classification scheme?
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DME is addressed in detail in its own slide-set

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