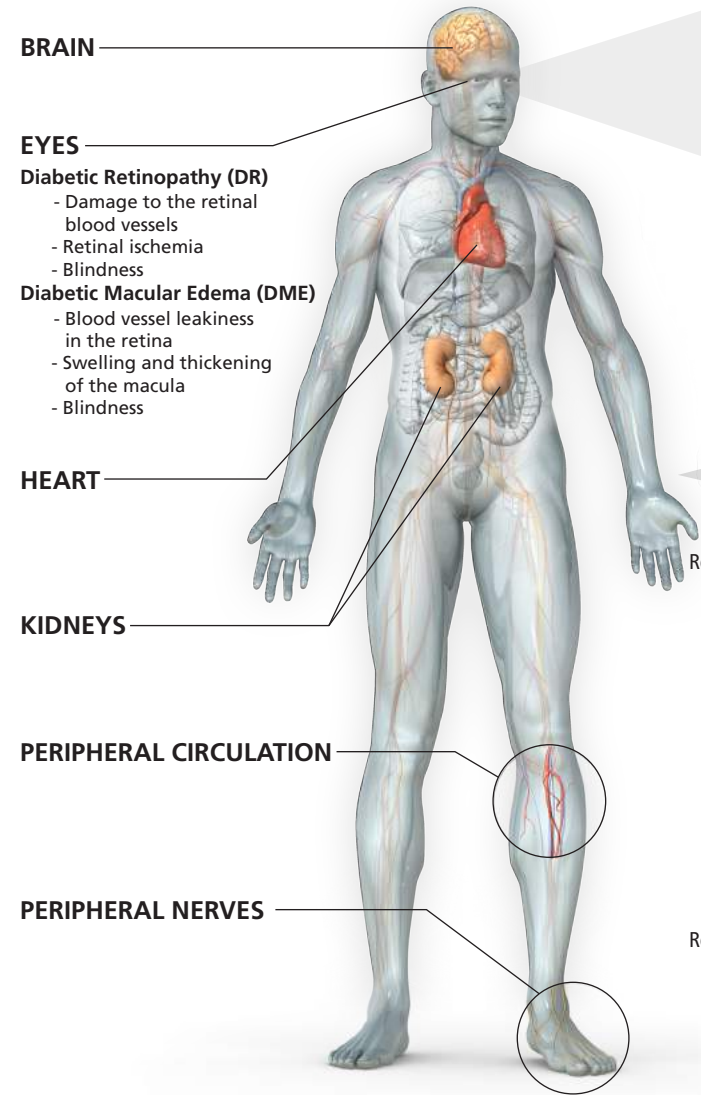


Progression of Diabetic Macular Edema (DME)

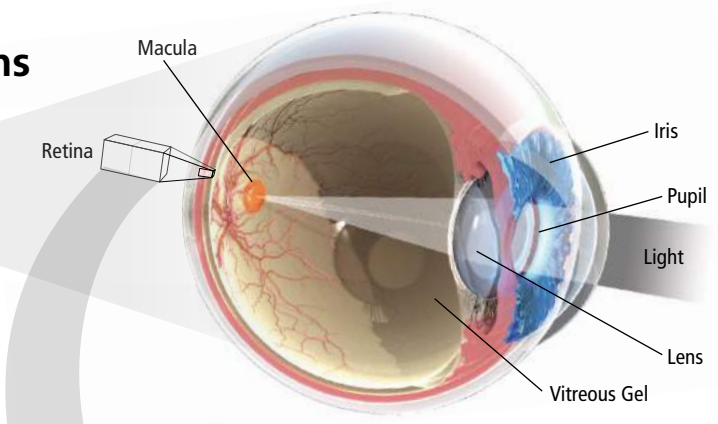
Major Sites of Diabetic Complications



Normal Vision vs Vision with DME

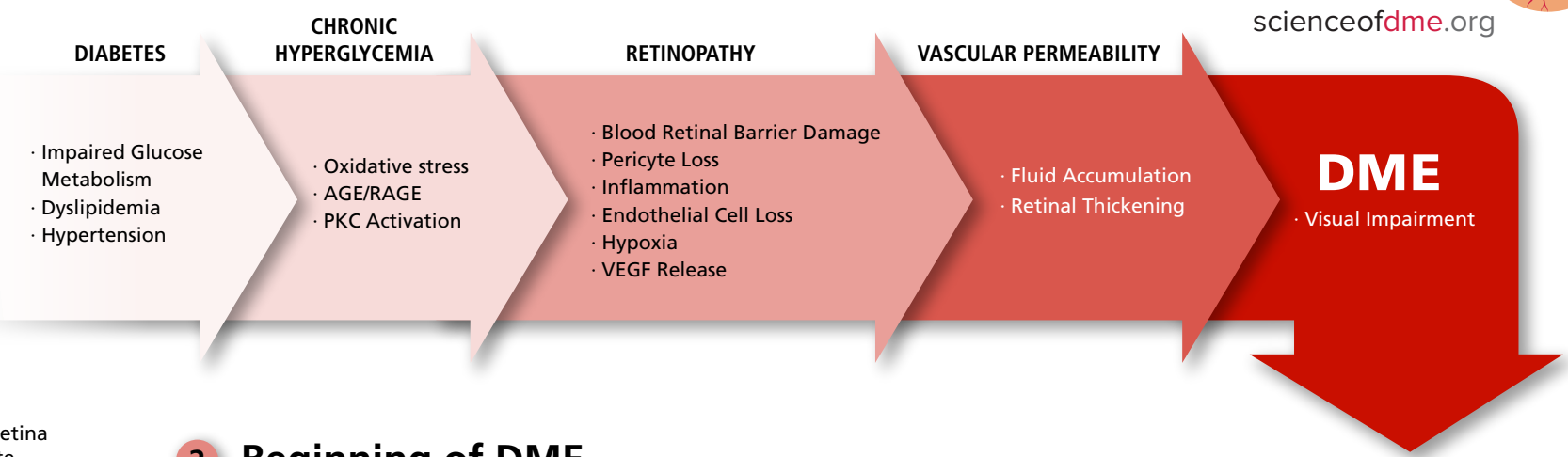
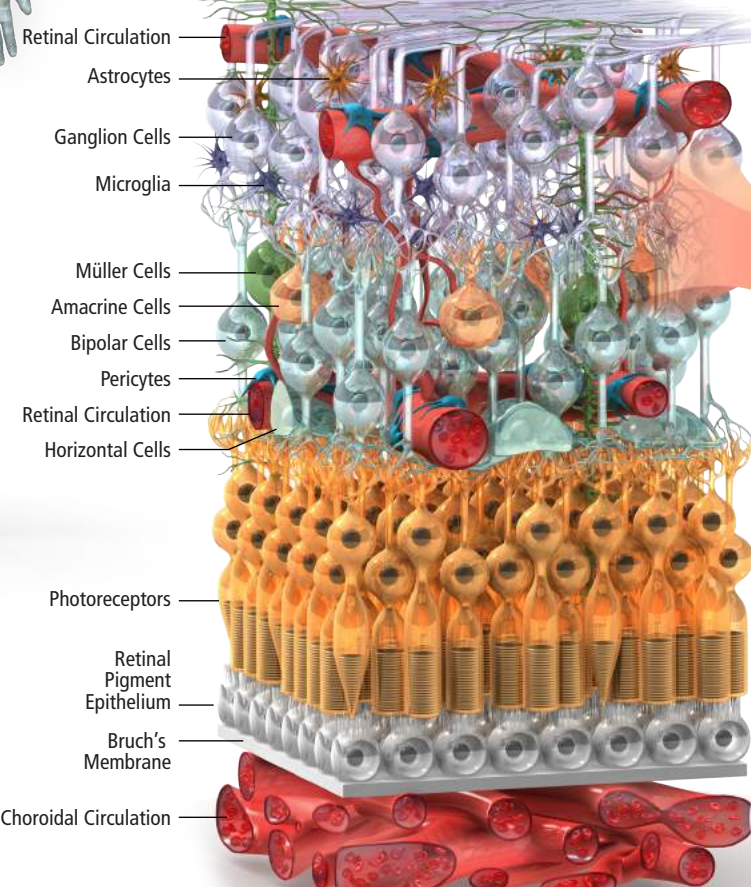


Retina Macula



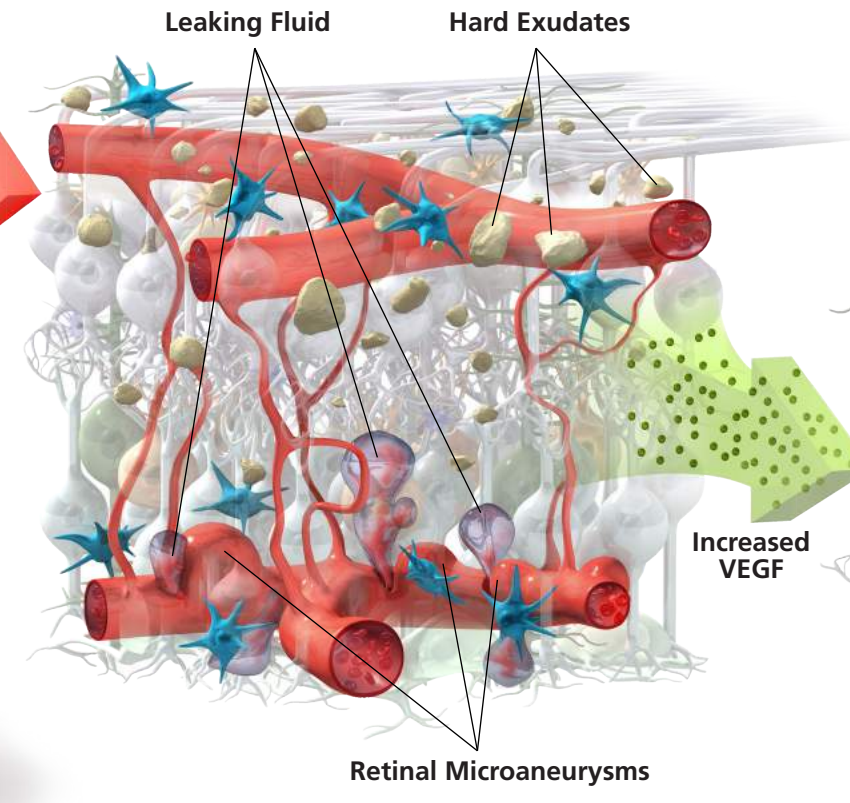
1 Normal Retina

The retinal and choroidal circulations provide different retina layers with oxygen and micronutrients, and remove waste products. The retina has a high metabolic demand, making it vulnerable to metabolic stress from diabetes.



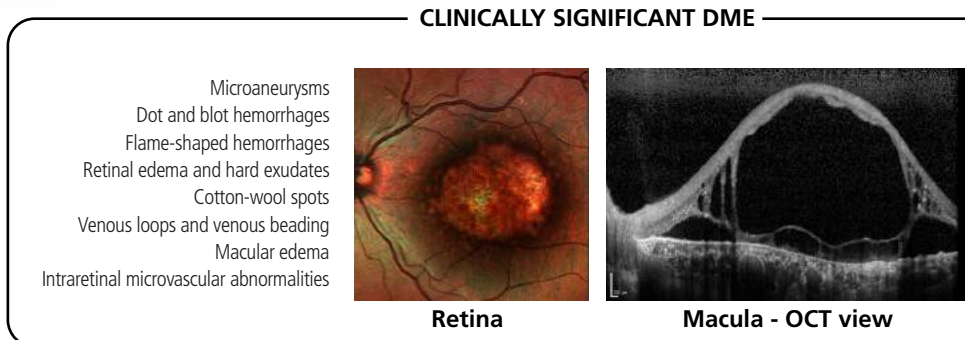
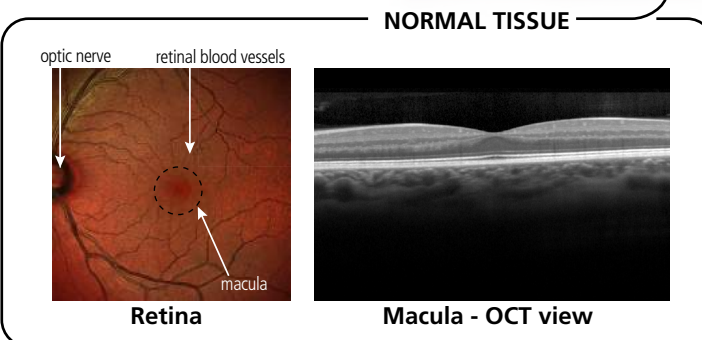
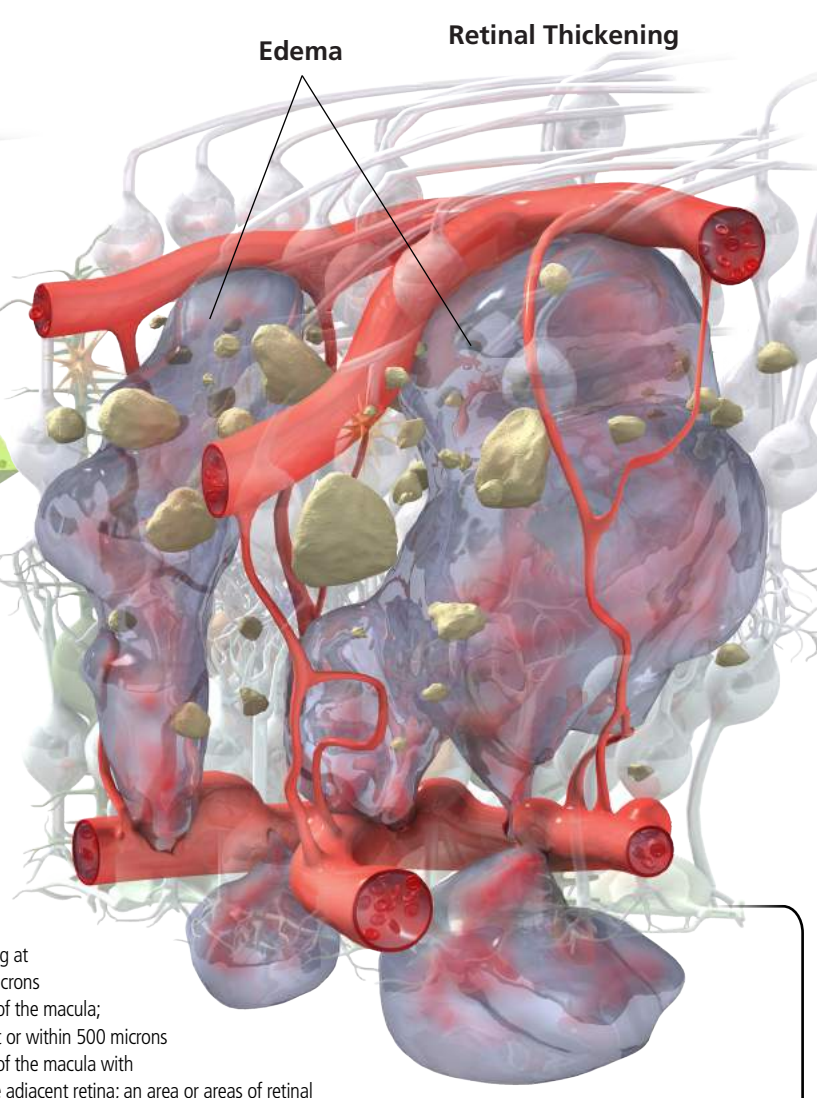
2 Beginning of DME

Elevated blood glucose levels damage retinal blood vessels, leading to a condition called Diabetic Retinopathy (DR). Retinal blood vessels swell and microaneurysms form. Retinal hypoxia develops, which stimulates production of VEGF.



3 Clinically Significant DME

High levels of VEGF increases vascular permeability. As the vessels leak in the retina, the macula develops edema. Swelling of the macula reduces visual acuity.



Anti-VEGF Treatments for DME

Anti-VEGF agents target and block VEGF (vascular endothelial growth factor). In DME, VEGF is produced at higher than normal amounts in the retina. Lowering levels of VEGF reduces its effects on retinal blood vessels and reverses macular edema.

Anti-VEGF Drugs

A major development in treating vision loss in people with DME has been the introduction of anti-VEGF drugs, which emerge from our understanding of different mechanisms that cause DME.

Anti-VEGF therapy can result in:

- 1) Reduced vascular permeability
- 2) Decreased thickening of the macula and retina
- 3) Improved visual acuity

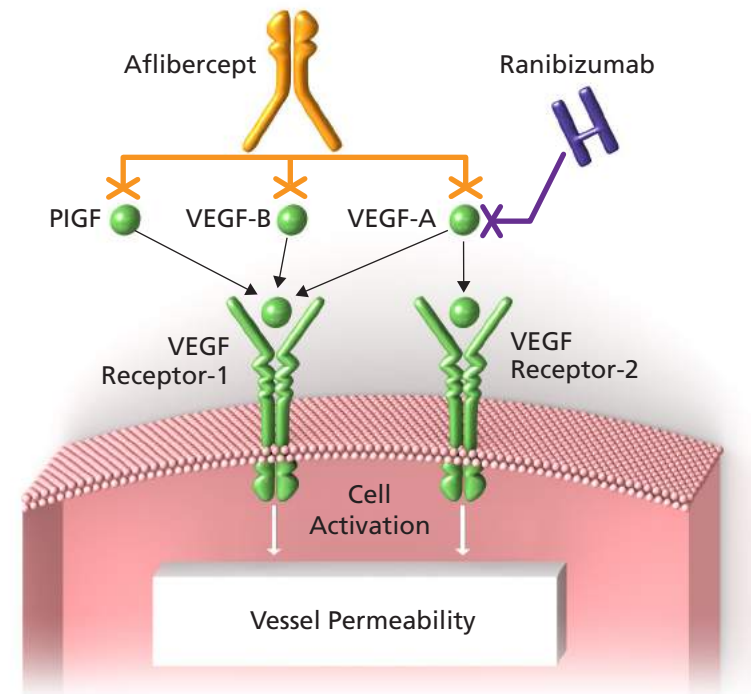
Once VEGF is halted, its effects subside and blood vessels stop leaking, reducing DME. Repeat injections are necessary to maintain benefit.

Anti-VEGF Treatments

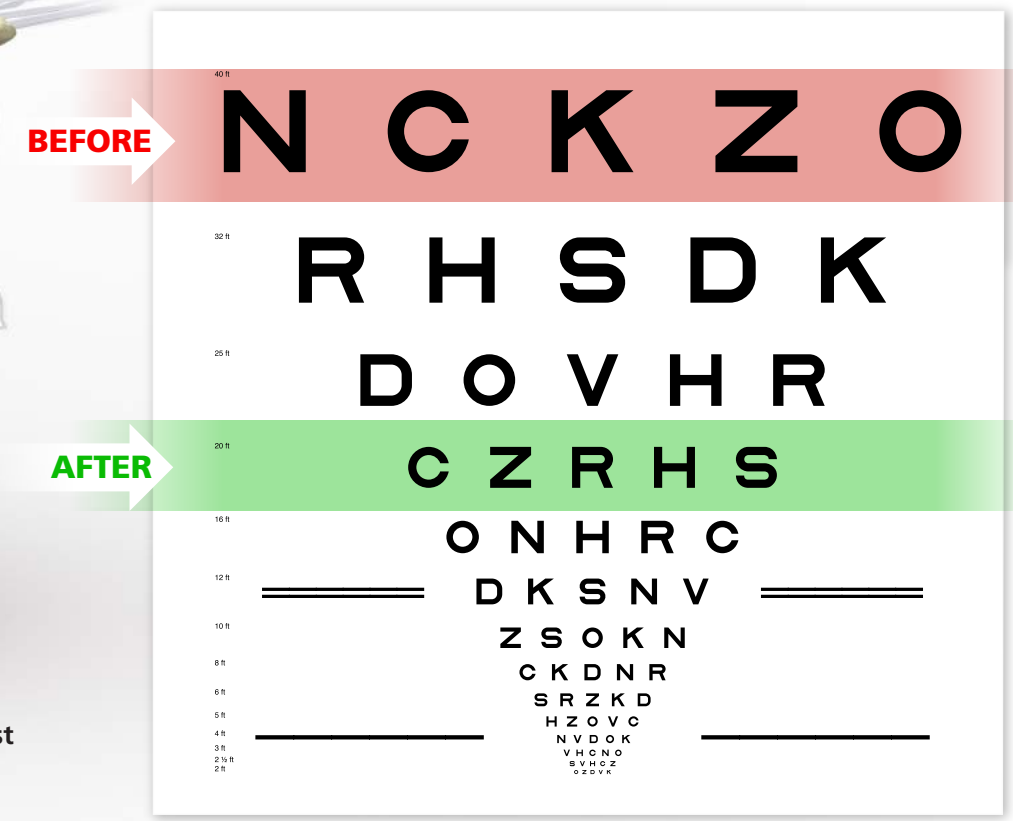
Anti-VEGF therapy is the preferred treatment for DME with visual impairment and clinical trials have demonstrated that it is more effective in reducing DME and improving vision than corticosteroid therapy or laser photocoagulation without causing complications associated with the former treatments. However, response is not always uniform among patients and combination therapy may be appropriate for some patients.

Ranibizumab is an anti-VEGF monoclonal antibody fragment. It is injected directly into the eye and can stabilize or even improve vision in DME. Ranibizumab is FDA approved for the treatment of multiple eye diseases, including diabetic macular edema (DME), wet age-related macular edema (wet AMD), and macular edema following retinal vein occlusion (RVO).

Aflibercept is an anti-VEGF fusion protein. It is injected directly into the eye and can stabilize or even improve vision in DME. Aflibercept is FDA approved for the treatment of multiple eye diseases, including DME, wet AMD, and macular edema following central retinal vein occlusion (CRVO).



ETDRS Visual Acuity Testing Chart



1 Anti-VEGF treatments are administered as intravitreal injections and suppress the levels of VEGF in the eye, leading to decreased vascular permeability and leakage.

2 Fluid is reabsorbed into the surrounding tissue, which decreases retinal thickening.

3 Although responses vary, in clinical trials, many DME patients gain multiple letters in visual acuity. Repeat injections are necessary to maintain benefit.