**Progression of Diabetic Macular Edema (DME)**

**Major Sites of Diabetic Complications**

- **EYES**
  - Diabetic Retinopathy (DR)
  - Macular Edema
  - Retinal Angiogenesis
  - Diabetic Macular Edema (DME)
- **HEART**
  - Diabetic Cardiovascular Disease (CVD)
- **KIDNEYS**
  - Diabetic Nephropathy
- **PERIPHERAL CIRCULATION**
  - Diabetic Peripheral Neuropathy
  - Diabetic Peripheral Vascular Disease (PVD)
- **PERIPHERAL NERVES**
  - Diabetic Neuropathy

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**Diabetes**

- **Chronic Hyperglycemia**
  - Impaired Glucose Metabolism
  - Dyslipidemia
  - Hypertension

**Retinopathy**

- **Blood Retinal Barrier Damage**
  - Permeability
  - Inflammation
  - Endothelial Cell Loss
  - Hypoxia
  - VEGF Release

**Vascular Permeability**

- **Fluid Accumulation**
  - Retinal Thickening

**Diabetic Macular Edema (DME)**

1. **Normal Retina**
   - The retinal and choriocapillaris provide different retinal layers with oxygen and nutrients, 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.
   - VEGF release, which is within 1 disk diameter of the center of the macula.
   - Retinal thickening at or within 1 disk diameter of the center of the macula; an area or areas of retinal thickening at or within 500 microns from the center of the macula; hard exudates at or within 500 microns from the center of the macula.

3. **Clinically Significant DME**
   - High levels of VEGF increase vascular permeability.
   - As the vessels leak in the retina, the macula develops edema.
   - Seeding of the macula reduces visual acuity.

**Anti-VEGF Treatments for DME**

**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.

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Anti-VEGF therapy can result in:
1) Reduced vascular permeability
2) Decreased thickening of the macula and retina
3) Improved visual acuity
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**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.

**Ramipril** is an anti-VEGF monoclonal antibody fragment. It is typically 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).

**Ranibizumab** 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. **Before**
   - Reduced visual acuity
   - Hard exudates persist

2. **After**
   - Non-leaky vessel
   - Fluid reabsorbed

**Although responses vary, in clinical trials, many DME patients gain multiple letters in visual acuity.

Repeat injections are necessary to maintain benefit.**