

Science of **DME**

www.scienceofdme.org



LEARN, TRACK, SHARE A Patient Guide to **Diabetic Macular Edema**



This brochure will guide you, as a person with diabetes, in understanding your risk for developing DME and the treatment options available for DME patients.



The **Angiogenesis**
Foundation



INTRODUCTION: The Science of DME

Diabetic macular edema (DME) is a vision-threatening disease that can cause moderate to severe, and even permanent, vision loss. It was estimated in 2010 that 21 million people live with DME worldwide. With the growing prevalence of diabetes around the world, this number is likely increasing.

We believe everyone affected by DME can be empowered with knowledge of relevant treatments and the practical steps they can take to fight vision loss.

Use this resource to learn:

- ▶ How diabetes can lead to severe or even permanent vision loss
- ▶ Why annual comprehensive exams are critical for anyone living with diabetes
- ▶ The role VEGF plays in the development of DME
- ▶ What you can do to prevent vision loss
- ▶ Evidence on the benefit of anti-VEGF therapy for treating DME
- ▶ Future directions for treating DME



Diabetes is the leading cause of new cases of blindness among adults aged 20–74 years.

OUR MISSION

Our mission at the Angiogenesis Foundation is to improve health globally, through education and advocacy, and to empower patients to take an active role in fighting vision loss. We work with DME patients, their advocates and healthcare providers around the world to disseminate knowledge about anti-VEGF treatments for DME in order to improve patient outcomes.

TAKE ACTION

This Science of DME resource empowers you to take the necessary steps for understanding your condition and seeking the best treatment options:

1. **LEARN** how diabetes puts you at risk for developing DME and how you can prevent vision loss.
2. **TRACK** your condition with regular screenings and discuss available treatments with your eye care specialist.
3. **SHARE** information about DME and the importance of regular eye exams for people with diabetes.



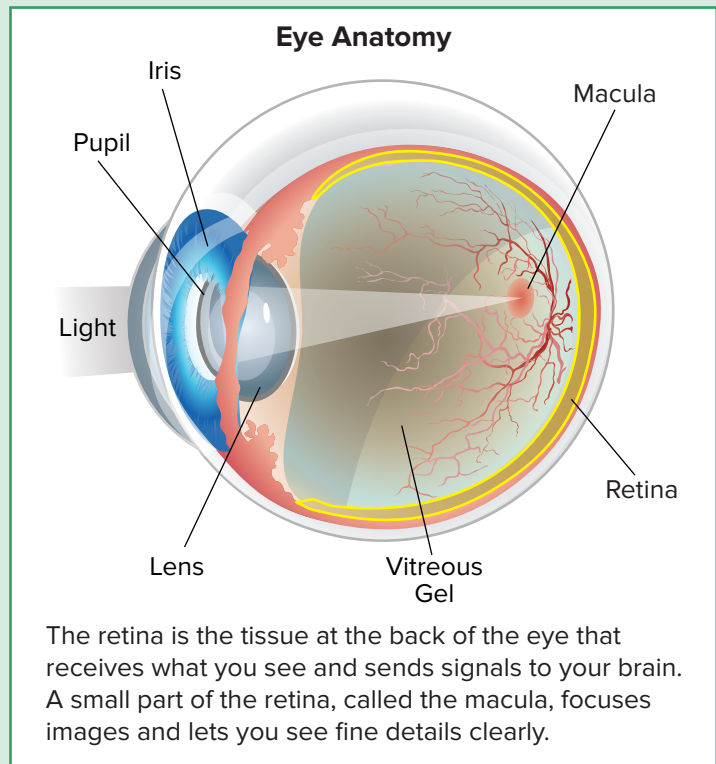
LEARN: The Science of DME

Diabetes, DR, and DME

Globally, the total number of people affected by diabetes was estimated to be 346 million in 2011. Diabetes is a chronic disease that needs consistent management. Currently, there is no cure but a number of treatments have been effective in maintaining patient quality of life.

DME develops from an eye condition called diabetic retinopathy, which is a complication of type 1 and type 2 diabetes. Diabetic retinopathy is a disorder of the retina that occurs when retinal blood vessels are damaged as a complication of diabetes. Diabetic retinopathy affects approximately 93 million people worldwide as of 2010. Global estimates in 2010 found that a third of people with diabetes have signs of diabetic retinopathy.

Over 20% of people living with type 1 diabetes and 14-25% of people with type 2 diabetes (depending on their use of insulin) will develop DME within ten years.

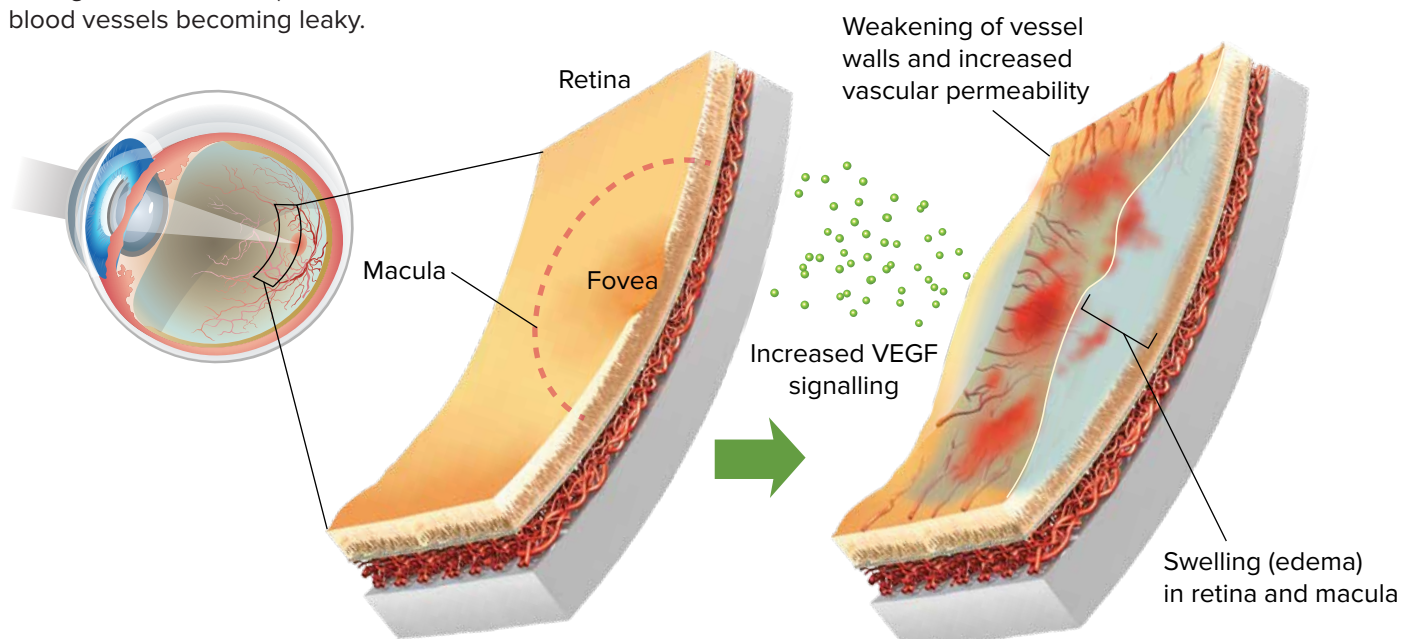


Development of DME

In people with diabetes, elevated blood glucose levels in the retina cause damage to the retinal blood vessels, starving the retina for oxygen and nutrients and leading to an increase, or upregulation, in the glycoprotein VEGF (vascular endothelial growth factor). High levels of VEGF weaken the vessel wall and increase vascular permeability (the ability of small molecules and whole cells to pass through the vessel wall). These mechanisms contribute to blood vessels becoming leaky.

As the vessels leak fluid and blood into the retina and, ultimately, the macula, the macula swells and thickens; this is the condition known as macular edema.

Swelling of the macula reduces visual acuity, blurs sight, and ultimately causes severe vision loss.



YOUR ROLE: Become Empowered

ARE YOU AT RISK FOR DR and DME?

A risk factor is anything that affects your chances of getting a disease.

Diabetic retinopathy and DME both develop as a complication of diabetes and have similar risk factors.

Duration of Diabetes	Everyone with type 1 or 2 of diabetes is at risk of getting DR. The longer you have lived with diabetes, the greater the chances of developing DR and, ultimately, DME.
Hyperglycemia	Chronic high levels in blood sugar increase the risk of developing DR and DME, and increase the rate of disease progression.
Dyslipidemia	Abnormal levels of blood lipids (cholesterol and triglycerides) in patients with diabetes increase the risk of developing DR and DME.
Hypertension	Elevated blood pressure increases the risk of developing DR and DME.
Other Diabetes Complications	Recent research suggests that the risk of developing DME tracks with the presence of other diabetes complications, such as diabetic neuropathy.
Other	Other risk factors include smoking, pregnancy, cardiovascular disease, kidney disease, anemia, sleep apnea, glitazone usage, obesity, genetics, frequent alcohol consumption, and sedentary lifestyle.



WHAT YOU CAN DO

There are steps that you can take to prevent or delay vision loss, and manage your condition and treatment:

- **Regular Screening:** Get a comprehensive dilated eye exam at least once a year. If you have diabetic retinopathy, you may need to have eye exams more often.
- **Control Blood Glucose:** Keep your blood glucose levels as close to normal as you can. Hyperglycemia initiates many other risk factors, so controlling blood glucose can prevent other diabetic complications and slows down or even prevents the development of retinopathy.
- **Control Blood Pressure:** Studies have demonstrated that keeping your blood pressure as close to normal as possible reduces the risk of complications in the microvascular system by roughly 33%.
- **Control Blood Lipids:** Keeping your cholesterol levels as close to normal as possible reduces the risk of complications. High levels of total cholesterol or triglycerides can increase the risk of developing DME by two- or three-fold.

YOUR ROLE: Become Empowered

MONITORING AND SYMPTOMS

Monitoring: Diabetic retinopathy develops without early symptoms or causing pain. Macular edema can develop at any stage of diabetic retinopathy without affecting vision. It is important not to wait for symptoms.

Symptoms: If blood vessels bleed into the eye, you may see spots in your vision. The spots may clear temporarily, but bleeding may reoccur and damage vision if the condition is left untreated. You may also experience blurry vision, or colors may look “washed out” or faded. Go see an eye care professional at the first sign of any of these symptoms.

Here are some **symptoms** of DME:

- ▶ Blurring of vision and difficulty seeing sharp details, both up close and from a distance
- ▶ Blind spots in vision
- ▶ Straight lines appear wavy or fractured in parts of the visual field
- ▶ Colors look “washed out” or faded
- ▶ Distortions of lines and shapes in everyday objects, such as crooked doorframes

When to Get Tested

Type 1 Diabetes

Patients with type 1 diabetes aged ten years or older should have their first comprehensive dilated eye exam within 5 years of developing diabetes.

Type 2 Diabetes

Patients with type 2 diabetes should have their first comprehensive dilated eye exam as soon as their diabetes is diagnosed.

Both type 1 and 2 diabetes patients should continue to receive subsequent eye exams on an annual basis. Exams will be more frequent if retinopathy is progressing. Work with your ophthalmologist or optometrist to identify the best frequency of testing for you.



Normal Vision



Vision with DME



TESTING

If you have type 1 or type 2 diabetes, you should get a comprehensive eye exam at least once a year to screen for diabetic retinopathy and diabetic macular edema. An ophthalmologist or optometrist who is experienced in diagnosing, managing and treating DR and DME is best suited to conduct these exams.

A comprehensive eye exam typically includes a dilated eye exam, visual acuity test and tonometry. These tests can detect early signs of DR or DME, such as:

- ▶ Retinal blood vessels that leak
- ▶ Damage or any change to the blood vessels
- ▶ Swelling or thickening of the retina

WARNING: Diabetic retinopathy & DME develop with **NO** symptoms! Up to 50% of diabetes patients do not get their eyes examined or are diagnosed when it is too late for treatment to be effective.

ANTI-VEGF THERAPY

ANTI-VEGF THERAPY

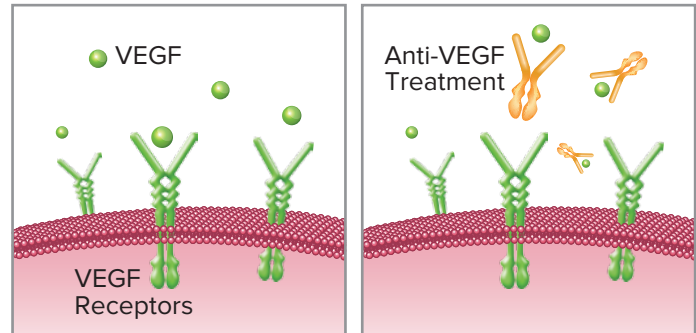
A major development in treating vision loss in people with DME has been the introduction of anti-VEGF drugs, which leverage recent advances in our understanding of the different mechanisms that cause DME. These drugs are designed to attack specific factors that contribute to DME development and are improving our ability to treat this condition.

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

Anti-VEGF drugs have been effective in treating DME for many patients, demonstrating prolonged improvement in vision without risk of developing other major eye conditions.



The advent of anti-VEGF therapy has revolutionized treatment of DME and offers patients new promise for maintaining a higher quality of life.



There are three major responses to anti-VEGF therapy:

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

Once over-expression of VEGF is halted, its effects subside and blood vessels stop leaking, reducing DME.

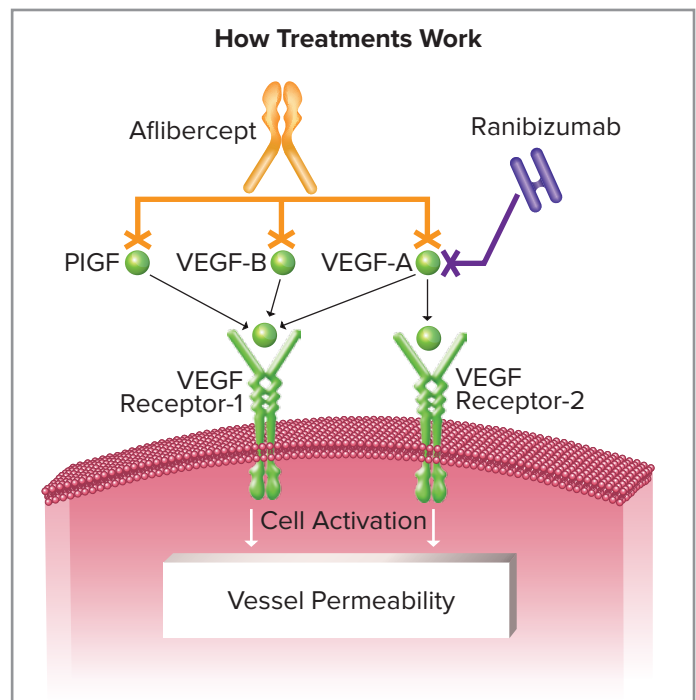
Approved Anti-VEGF Therapy:

Lucentis (ranibizumab) is a type of anti-VEGF drug called a monoclonal antibody fragment that was developed to treat retinal diseases. It is injected directly into the eye and can stabilize or even improve vision loss.

Anti-VEGF Therapy on the Horizon:

Eylea (aflibercept) is a type of anti-VEGF drug known as a fusion protein, which is approved for treatment of the eye diseases wet age-related macular degeneration (wet AMD) and central retinal vein occlusion (CRVO), and is currently in late stage clinical trials for treating DME. Eylea targets VEGF, as well as another protein called placental growth factor (PIGF).

Learn more about these treatments and find detailed clinical trial information on our website:
www.scienceofdme.org/treat



Anti-VEGF therapy is the preferred treatment 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 (see more info about these treatments on the following page). However, response is not always uniform among patients and combination therapy may be appropriate for some patients. A major study showed that combining anti-VEGF and laser therapies could have long-term benefits in reduced edema and require less frequent injections. Combining corticosteroid therapy with anti-VEGF treatment has not demonstrated additional benefit to anti-VEGF treatment alone.

ADDITIONAL TREATMENTS

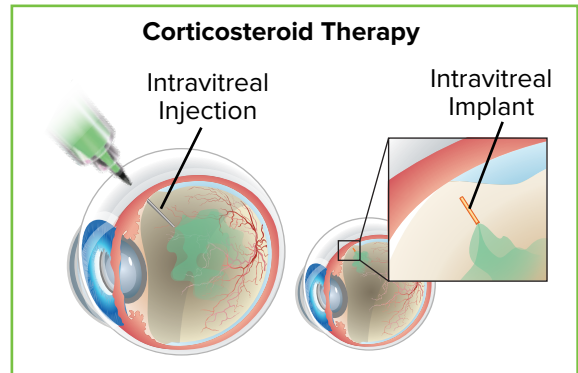
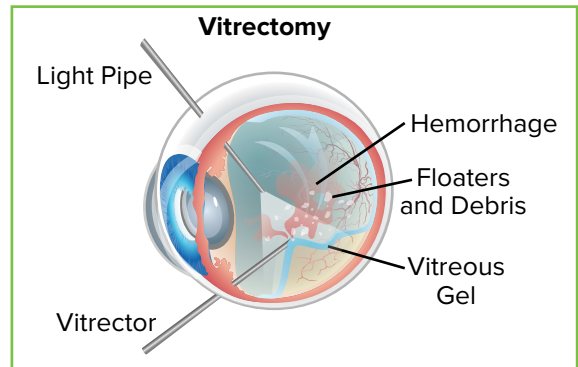
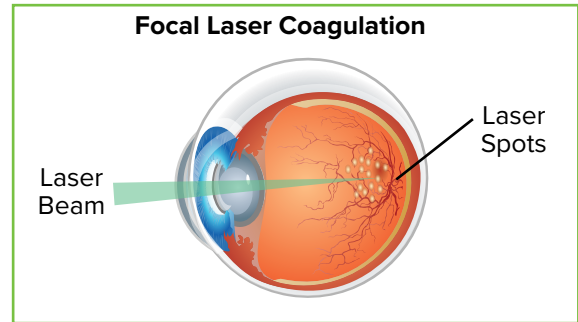
ADDITIONAL EXISTING TREATMENTS

Focal laser photocoagulation: This procedure has, until recently, been the standard treatment for DME. It stabilizes vision and can prevent vision loss caused by DME, but rarely improves visual acuity. Laser therapy has not been effective in most patients with diffuse DME.

During laser photocoagulation, areas of leakage in the retina are exposed to small laser burns that decrease the quantity of fluid and slow down leakage. This treatment is usually completed in one session but some cases require multiple procedures. If you have DME in both eyes, laser therapy will be applied to one eye at a time, with procedures typically separated by several weeks. Laser therapy can cause discomfort during the procedure and potential damage or scarring to the retina.

Vitrectomy: If too much blood has leaked into the vitreous or the retina has detached from the eye, your doctor may recommend getting a vitrectomy. Vitrectomy is a procedure in which the vitreous is replaced with a salt solution, improving visual acuity and maintaining the anatomy of the eye. Vitrectomy has been successful with restoring sight in the short term by removing blood, but it is not as effective for re-attaching the retina.

Corticosteroids: This therapy works by targeting two of the different mechanisms that cause the disease: inflammation (swelling) and VEGF expression. Corticosteroids can be delivered by intravitreal injection or by sustained release implants. Implants may have the benefit of less frequent dosing than injections. Corticosteroid therapy has been found to have greater short-term benefit than laser treatment, in terms of visual acuity gain. However, their benefit declines after several months and ultimately becomes inferior to laser by the second and third year. Corticosteroid therapy may cause other eye complications such as cataracts or an increase in intraocular pressure, which is a major risk factor for glaucoma.



FUTURE DIRECTIONS

Trials are ongoing and further data is needed to understand the role of anti-VEGF agents and the limitations of other agents. Strategies for managing DME will continue to evolve as more data is collected from these trials. Visit <http://clinicaltrials.gov/> to learn more about clinical trials.

There is a growing need for effective management of DME as the world population ages and the prevalence of DME increases. Further research is needed to understand better the role of other risk factors in DME development and to improve the ability to predict one's risk for developing DME, which would inform public health programs and help prevent new cases of DME.

Such developments hold significant promise for providing each patient with the most effective treatment and greatly improving patient quality of life. To learn more and get involved in our awareness program, visit www.scienceofdme.org.



As a DME patient, you can take control of your condition. Know your options and work with your eye care specialist to determine the best treatment plan for you.





The Angiogenesis Foundation is the world's first nonprofit organization dedicated to conquering disease using a groundbreaking approach based on angiogenesis, the growth of new capillary blood vessels in the body. Angiogenesis is the "common denominator" in health, including diseases such as diabetic retinopathy.

The Angiogenesis Foundation built this resource to provide accurate, easy to understand, and useful information about the evidence supporting anti-VEGF therapy for DME. We believe everyone affected by DME can be empowered with the knowledge of relevant treatments and the practical steps they can take to fight vision loss.



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