The first acute thrombosis should be treated according to standard guidelines with a course of low molecular-weight heparin (LMWH) or fondaparinux (a pentasaccharide). Low molecular-weight heparins and fondaparinux have largely replaced unfractionated heparin because of their many advantages.

Oral administration of warfarin is started concurrently with LMWH or fondaparinux (except during pregnancy) and monitored with the international-normalized ratio (INR). A target INR of 2.5 (therapeutic range: 2.0-3.0) provides effective anticoagulation, even in *F2* 20210G>A homozygotes.

Rivaroxaban, a direct factor Xa inhibitor, is also approved for the treatment of acute DVT and PE and secondary prevention of recurrent VTE.

Note: LMWH and warfarin are both safe in women who are breast-feeding. Rivaroxaban is contraindicated during pregnancy and breast-feeding because animal studies showed reproductive toxicity, and evidence that the drug crosses the placenta and is secreted in milk.

The duration of oral anticoagulation therapy should be based on an individualized assessment of the risks of VTE recurrence and anticoagulant-related bleeding. Approximately 30% of individuals with VTE experience recurrent thrombosis within the subsequent five years. Recurrence risk is determined by the clinical circumstances of the first event (provoked or unprovoked), adequacy of early treatment, and individual risk factors. Other clinical guidelines and expert opinion also conclude that identification of 20210G>A heterozygosity should not affect clinical decision making. See Published Guidelines / Consensus Statements.

Anticoagulation for at least three months is recommended for persons with DVT and/or PE associated with a transient (reversible) risk factor.

Long-term oral anticoagulation is recommended for individuals with a first or recurrent unprovoked (i.e., idiopathic) VTE and no risk factors for bleeding with good anticoagulation monitoring. The decision should be based on an assessment of potential risks and benefits regardless of 20210G>A status. Long-term anticoagulation is considered in selected individuals homozygous for the 20210G>A allele or with multiple inherited or acquired thrombophilic disorders. In these individuals at higher risk for recurrence, the potential benefits of long-term anticoagulation may outweigh the bleeding risks.

LMWH, fondaparinux, warfarin, and rivaroxaban are the primary antithrombotic agents used for the acute and long-term treatment of VTE. Several direct thrombin inhibitors (lepirudin, argatroban, and dabigatran), and apixaban, a direct factor Xa inhibitor, are approved for use in specific circumstances.

Graduated compression stockings should be worn for at least two years following an acute DVT.

Treatment of thrombosis in children. Treatment recommendations for children with VTE are largely adapted from studies in adults. There is no evidence that a 20210G>A allele should influence decisions about the intensity or duration of anticoagulation in children. British guidelines for antithrombotic therapy in children do not consider inherited thrombophilia as a determinant of either the intensity or duration of therapy.

Children with a first VTE should receive initial treatment with either unfractionated heparin (UFH) or LMWH for at least five days. LMWH is favored over warfarin for continued therapy, especially in very young children and those with complex medical problems. Recommendations on the duration of antithrombotic therapy are based on the nature of the thrombotic event (e.g., spontaneous or provoked).

Anticoagulation is recommended:

- For at least three months after a VTE provoked by a clinical risk factor that has resolved.
- Beyond three months until the risk factor has resolved in children with ongoing but potentially reversible risk factors.
- For six to 12 months after a first idiopathic (unprovoked) VTE.
- Indefinitely for those with recurrent idiopathic VTE

Expert opinion emphasizes the importance of a careful risk/benefit assessment in each individual.

Consensus guidelines are also available for management of stroke in infants and children.

Prevention of Primary Manifestations

In the absence of a history of thrombosis, long-term anticoagulation is not recommended for asymptomatic 20210G>A heterozygotes, since the 1%-3% yearly risk for major bleeding from warfarin is greater than the estimated (<1%) yearly risk for thrombosis.

Prophylactic anticoagulation may be considered in high-risk clinical settings such as surgery, pregnancy, or prolonged immobilization, although currently no evidence confirms the benefit of primary prophylaxis for asymptomatic 20210G>A heterozygotes. Factors that may influence decisions about the indication

for and duration of anticoagulation include age, family history, and other coexisting risk factors. Recommendations for prophylaxis at the time of surgery and other high-risk situations are available in the 2012 American College of Chest Physicians consensus guidelines.

Surveillance

Individuals receiving long-term anticoagulation require periodic reevaluation to confirm that the benefits of anticoagulation continue to outweigh the bleeding risk.

Selected 20210G>A heterozygotes who do not require long-term anticoagulation may benefit from evaluation prior to exposure to circumstantial risk factors such as surgery or pregnancy. (See Prevention of Primary Manifestations.)

Agents/Circumstances to Avoid

F2 20210G>A heterozygotes:

- With a history of VTE should avoid estrogen contraception and HRT; asymptomatic women should be counseled on the risks of estrogen-containing contraception and HRT and should consider alternative forms of contraception and strategies for control of menopausal symptoms.
- Who are asymptomatic and elect to use oral contraceptives should avoid formulations with third-generation and other progestins with a higher thrombotic risk;
- Who elect short-term hormone replacement therapy for severe menopausal symptoms should use low-dose transdermal preparations, which have a lower thrombotic risk than oral formulations.

F2 20210G>A homozygous women with or without prior VTE should avoid estrogen-containing contraception and HRT.

Evaluation of Relatives at Risk

The genetic status of asymptomatic at-risk family members can be established using molecular genetic testing. However, as there is no clinical evidence that early diagnosis reduces morbidity or mortality, the indications for family testing are unresolved and the decision to test at-risk family members should be made on an individual basis.

Clarification of 20210G>A allele status may be useful in:

- Asymptomatic adult family members of probands with one or two known 20210G>A alleles, especially those with a strong family history of VTE at a young age;
- Asymptomatic female family members of probands with known prothrombin-related thrombophilia who are pregnant or considering estrogen contraception or pregnancy.

There is no clinical evidence to support testing asymptomatic children with a family history of thrombosis and/or inherited thrombophilia. Guidelines suggest delaying testing until children are able to understand the implications of the results and (optimally) can give informed consent for testing.

Pregnancy Management

No consensus exists on the optimal management of prothrombin thrombophilia during pregnancy; guidelines are derived from studies in non-pregnant individuals; see Published Guidelines / Consensus Statements. LMWH is the preferred antithrombotic agent for prophylaxis during pregnancy. All women with inherited thrombophilia should undergo individualized risk assessment. Decisions about anticoagulation should be based on the number and type of thrombophilic defects, coexisting risk factors, and personal and family history of thrombosis.

Prophylactic anticoagulation during pregnancy:

- Is recommended for all women:
  - With a history of unprovoked VTE, including those heterozygous for 20210G>A. LMWH should be given during pregnancy followed by six weeks of postpartum anticoagulation.
  - Heterozygous for the 20210G>A allele with a prior pregnancy or estrogen-related thrombosis who are also at an increased risk for recurrence.
- Should be considered for:

- Asymptomatic women doubly heterozygous for 20210G>A and factor V Leiden, especially those with coexisting circumstantial risk factors (obesity, immobilization, multiple gestation);
- Asymptomatic homozygous women with a family history of thrombosis.

- Is not routinely recommended in asymptomatic heterozygous women with no history of thrombosis or other risk factors. These women should be counseled about potential thrombotic complications during pregnancy and the postpartum period.
  - In two large prospective studies, low-risk asymptomatic women with thrombophilia (including 20210G>A heterozygosity) did not receive LMWH during pregnancy in the absence of additional risk factors. All women received a course of postpartum anticoagulation. The low incidence of antepartum VTE in both studies (0% and 0.34%) suggested that anticoagulation may be safely withheld during pregnancy in low-risk 20210G>A heterozygotes who do not have other risk factors.

A six-week course of postpartum prophylactic anticoagulation is recommended for:

- Heterozygous women with a positive family history of VTE or other additional risk factors;
- All asymptomatic homozygous women;
- All women with a prior history of VTE.

Prevention of pregnancy loss. It is still unkown if prophylactic antithrombotic therapy improves pregnancy outcome in women with inherited thrombophilia and recurrent pregnancy loss. The available evidence consists of predominantly uncontrolled trials, observational studies, and a few randomized trials with important methodologic limitations. There are no prospective randomized trials that include an untreated control group that confirms the benefit of LMWH for preventing pregnancy loss in women with inherited thrombophilia. Of note, the ALIFE2 study, a multicenter randomized trial of LMWH versus standard surveillance in women with inherited thrombophilia and a history of recurrent miscarriage, began recruitment in December 2012 (www.trialregister.nl, NTR 3361).

Current consensus guidelines and expert opinion recommend against the use of antithrombotic therapy in women with inherited thrombophilia and unexplained recurrent pregnancy loss outside of clinical trials because of the absence of high quality evidence confirming benefit.

Studies suggesting that prophylactic anticoagulation improves pregnancy outcome:

- The results of several observational studies suggested that prophylactic antithrombotic therapy may improve pregnancy outcome in women with inherited thrombophilia and recurrent pregnancy loss.
- A recent study of women with a history of unexplained pregnancy loss compared the frequency of obstetric complications in women with factor V Leiden or 20210G>A alleles and women without thrombophilia. Women with a thrombophilic disorder with a prior fetal loss after ten weeks'gestation who received enoxaparin during their next pregnancy had a significantly lower rate of fetal loss and severe preeclampsia and a higher rate of live births compared to women without a thrombophilic disorder with the same obstetric history who did not receive prophylaxis.
- A prospective randomized trial compared prophylactic-dose enoxaparin and low-dose aspirin in women heterozygous for 20210G>A, factor V Leiden, or protein S deficiency, and a history of a single unexplained fetal loss after ten weeks'gestation. Enoxaparin prophylaxis was associated with a significantly higher live birth rate of 86% compared to 29% with aspirin. However, there were methodologic problems with this study and the results have not been confirmed in other trials.

Studies suggesting that prophylactic anticoagulation does not improve pregnancy outcome:

- Several studies found no benefit with LMWH on pregnancy outcome in women with inherited thrombophilia.
- Two recent randomized trials compared the efficacy of LMWH and aspirin to no antithrombotic therapy or placebo in women with unexplained recurrent pregnancy loss. Combined LMWH and low-dose aspirin did not increase the live birth rate in either study. Because only a small proportion of the study populations had inherited thrombophilia (3.5% and 15.7%), subgroup analyses were insufficiently powered to assess the effect of antithrombotic therapy.
- In the recent Thrombophilia in Pregnancy Prophylaxis Study (TIPPS) multinational randomized trial, antepartum prophylactic LMWH did not reduce the incidence of pregnancy loss or placenta-mediated complications in pregnant women with thrombophilia (22% with a 20210G>A allele) who are at high risk for these complications.

Other pregnancy complications. Data supporting the benefit of antithrombotic therapy in women with inherited thrombophilia and other pregnancy complications are considerably more limited and also conflicting. There is insufficient evidence that LMWH (with or without aspirin) reduces the risk for preeclampsia, placental abruption, or other obstetric complications in women with or without inherited thrombophilia. Current guidelines recommend against antithrombotic prophylaxis for women with inherited thrombophilia and a history of pregnancy complications.

Therapies Under Investigation

Several new oral anticoagulants (which have not been specifically studied in individuals with inherited thrombophilia) are alternatives to warfarin in specific clinical settings.

Dabigatran (a direct thrombin inhibitor) and rivaroxaban and apixaban (two new factor Xa inhibitors) are approved for the prevention of stroke and systemic embolism in patients with atrial fibrillation.

Search ClinicalTrials.gov in the US and www.ClinicalTrialsRegister.eu in Europe for access to information on clinical studies for a wide range of diseases and conditions.

AGE-RELATED MACULAR DEGENERATION

We have found a pathogenic variant in the CFH gene.

We have found a pathogenic variant in the ARMS2 gene.

You have an increased risk of developing Age-related macular degeneration

Description

Age-related macular degeneration is an eye disease that is a leading cause of vision loss in older people in developed countries. The vision loss usually becomes noticeable in a person's sixties or seventies and tends to worsen over time.

Age-related macular degenerationmainly affects central vision, which is needed for detailed tasks such as reading, driving, and recognizing faces. The vision loss in this condition results from a gradual deterioration of light-sensing cells in the tissue at the back of the eye that detects light and color (the retina). Specifically, age-related macular degeneration affects a small area near the center of the retina, called the macula, which is responsible for central vision. Side (peripheral) vision and night vision are generally not affected, but reduced dim light (scotopic) vision often occurs in the early stages of the disease.

Researchers have described two major types of age-related macular degeneration, known as the dry form and the wet form. The dry form is much more common, accounting for 85 to 90 percent of all cases of age-related macular degeneration. It is characterized by a buildup of yellowish deposits called drusen beneath the retina and vision loss that worsens slowly over time. The condition typically affects vision in both eyes, although vision loss often occurs in one eye before the other.

The wet form of age-related macular degeneration is associated with severe vision loss that can worsen rapidly. This form of the condition is characterized by the growth of abnormal, fragile blood vessels underneath the macula. These vessels leak blood and fluid, which damages the macula and makes central vision appear blurry and distorted.

Frequency

Age-related macular degeneration has an estimated prevalence of 1 in 2,000 people in the United States and other developed countries. The condition currently affects several million Americans, and the prevalence is expected to increase over the coming decades as the proportion of older people in the population increases.

For reasons that are unclear, age-related macular degeneration affects individuals of European descent more frequently than African Americans in the United States.

Causes

Age-related macular degeneration results from a combination of genetic and environmental factors. Many of these factors have been identified, but some remain unknown.

Researchers have considered changes in many genes as possible risk factors for age-related macular degeneration. The best-studied of these genes are involved in a part of the body's immune response known as the complement system. This system is a group of proteins that work together to destroy foreign invaders (such as bacteria and viruses), trigger inflammation, and remove debris from cells and tissues. Genetic changes in and around several complement system genes, including the CFH gene, contribute to a person's risk of developing age-related macular degeneration. It is unclear how these genetic changes are related to the retinal damage and vision loss characteristic of this condition.

Changes on the long (q) arm of chromosome 10 in a region known as 10q26 are also associated with an increased risk of age-related macular degeneration. The 10q26 region contains two genes of interest, ARMS2 and HTRA1. Changes in both genes have been studied as possible risk factors for the disease. However, because the two genes are so close together, it is difficult to tell which gene is associated with age-related macular degeneration risk, or whether increased risk results from variations in both genes.

Other genes that are associated with age-related macular degeneration include genes involved in transporting and processing high-density lipoprotein (HDL, also known as "good" cholesterol) and genes that have been associated with other forms of macular disease.

Researchers have also examined nongenetic factors that contribute to the risk of age-related macular degeneration. Age appears to be the most important risk factor; the chance of developing the condition increases significantly as a person gets older. Smoking is another established risk factor for age-related macular degeneration. Other factors that may increase the risk of this condition include high blood pressure, heart disease, a high-fat diet or one that is low in certain nutrients (such as antioxidants and zinc), obesity, and exposure to ultraviolet (UV) rays from sunlight. However, studies of these factors in age-related macular degeneration have had conflicting results

Actions and Advice

Who is at risk?

Age is a major risk factor for AMD. The disease is most likely to occur after age 60, but it can occur earlier. Other risk factors for AMD include:

- **Smoking**. Research shows that smoking doubles the risk of AMD.
- **Race**. AMD is more common among Caucasians than among African-Americans or Hispanics/Latinos.
- **Family history and Genetics**. People with a family history of AMD are at higher risk. At last count, researchers had identified nearly 20 genes that can affect the risk of developing AMD. Many more genetic risk factors are suspected. You may see offers for genetic testing for AMD. Because AMD is influenced by so many genes plus environmental factors such as smoking and nutrition, there are currently no genetic tests that can diagnose AMD, or predict with certainty who will develop it. The American Academy of Ophthalmology currently recommends against routine genetic testing for AMD, and insurance generally does not cover such testing.

Does lifestyle make a difference?

Researchers have found links between AMD and some lifestyle choices, such as smoking. You might be able to reduce your risk of AMD or slow its progression by making these healthy choices:

- Avoid smoking
- Exercise regularly
- Maintain normal blood pressure and cholesterol levels
- Eat a healthy diet rich in green, leafy vegetables and fish

How is AMD detected?

The early and intermediate stages of AMD usually start without symptoms. Only a comprehensive dilated eye exam can detect AMD. The eye exam may include the following:

- **Visual acuity test.** This eye chart measures how well you see at distances.

- **Dilated eye exam.** Your eye care professional places drops in your eyes to widen or dilate the pupils. This provides a better view of the back of your eye. Using a special magnifying lens, he or she then looks at your retina and optic nerve for signs of AMD and other eye problems.
- **Amsler grid.** Your eye care professional also may ask you to look at an Amsler grid. Changes in your central vision may cause the lines in the grid to disappear or appear wavy, a sign of AMD.
- **Fluorescein angiogram.** In this test, which is performed by an ophthalmologist, a fluorescent dye is injected into your arm. Pictures are taken as the dye passes through the blood vessels in your eye. This makes it possible to see leaking blood vessels, which occur in a severe, rapidly progressive type of AMD (see below). In rare cases, complications to the injection can arise, from nausea to more severe allergic reactions.
- **Optical coherence tomography.** You have probably heard of ultrasound, which uses sound waves to capture images of living tissues. OCT is similar except that it uses light waves, and can achieve very high-resolution images of any tissues that can be penetrated by light—such as the eyes. After your eyes are dilated, youll be asked to place your head on a chin rest and hold still for several seconds while the images are obtained. The light beam is painless.

During the exam, your eye care professional will look for *drusen*, which are yellow deposits beneath the retina. Most people develop some very small drusen as a normal part of aging. The presence of medium-to-large drusen may indicate that you have AMD.

Another sign of AMD is the appearance of pigmentary changes under the retina. In addition to the pigmented cells in the iris (the colored part of the eye), there are pigmented cells beneath the retina. As these cells break down and release their pigment, your eye care professional may see dark clumps of released pigment and later, areas that are less pigmented. These changes will not affect your eye color.

Questions to ask your eye care Professional

Below are a few questions you may want to ask your eye care professional to help you understand your diagnosis and treatment. If you do not understand your eye care professional's responses, ask questions until you do understand.

- What is my diagnosis and how do you spell the name of the condition?
- Can my AMD be treated?
- How will this condition affect my vision now and in the future?
- What symptoms should I watch for and how should I notify you if they occur?
- Should I make lifestyle changes?

What are the stages of AMD?

There are three stages of AMD defined in part by the size and number of drusen under the retina. It is possible to have AMD in one eye only, or to have one eye with a later stage of AMD than the other.

- **Early AMD.** Early AMD is diagnosed by the presence of medium-sized drusen, which are about the width of an average human hair. People with early AMD typically do not have vision loss.
- **Intermediate AMD.** People with intermediate AMD typically have large drusen, pigment changes in the retina, or both. Again, these changes can only be detected during an eye exam. Intermediate AMD may cause some vision loss, but most people will not experience any symptoms.
- **Late AMD.** In addition to drusen, people with late AMD have vision loss from damage to the macula. There are two types of late AMD:
  - In geographic atrophy (also called dry AMD), there is a gradual breakdown of the light-sensitive cells in the macula that convey visual information to the brain, and of the supporting tissue beneath the macula. These changes cause vision loss.
  - In neovascular AMD (also called wet AMD), abnormal blood vessels grow underneath the retina. ("Neovascular" literally means "new vessels.") These vessels can leak fluid and blood, which may lead to swelling and damage of the macula. The damage may be rapid and severe, unlike the more gradual course of geographic atrophy. It is possible to have both geographic atrophy and neovascular AMD in the same eye, and either condition can appear first.

AMD has few symptoms in the early stages, so it is important to have your eyes examined regularly. If you are at risk for AMD because of age, family history, lifestyle, or some combination of these factors, you should not wait to experience changes in vision before getting checked for AMD.

Not everyone with early AMD will develop late AMD. For people who have early AMD in one eye and no signs of AMD in the other eye, about five percent will develop advanced AMD after 10 years. For people who have early AMD in both eyes, about 14 percent will develop late AMD in at least one eye after 10 years. With prompt detection of AMD, there are steps you can take to further reduce your risk of vision loss from late AMD.

If you have late AMD in one eye only, you may not notice any changes in your overall vision. With the other eye seeing clearly, you may still be able to drive, read, and see fine details. However, having late AMD in one eye means you are at increased risk for late AMD in your other eye. If you notice distortion or

blurred vision, even if it doesnt have much effect on your daily life, consult an eye care professional.

Questions to ask your eye care professional about treatment

- What is the treatment for advanced neovascular AMD?
- When will treatment start and how long will it last?
- What are the benefits of this treatment and how successful is it?
- What are the risks and side effects associated with this treatment and how has this information been gathered?
- Should I avoid certain foods, drugs, or activities while I am undergoing treatment?
- Are other treatments available?
- When should I follow up after treatment?

Loss of Vision

Coping with AMD and vision loss can be a traumatic experience. This is especially true if you have just begun to lose your vision or have low vision. Having low vision means that even with regular glasses, contact lenses, medicine, or surgery, you find everyday tasks difficult to do. Reading the mail, shopping, cooking, and writing can all seem challenging.

However, help is available. You may not be able to restore your vision, but low vision services can help you make the most of what is remaining. You can continue enjoying friends, family, hobbies, and other interests just as you always have. The key is to not delay use of these services.

What is vision rehabilitation?

To cope with vision loss, you must first have an excellent support team. This team should include you, your primary eye care professional, and an optometrist or ophthalmologist specializing in low vision. Occupational therapists, orientation and mobility specialists, certified low vision therapists, counselors, and social workers are also available to help. Together, the low vision team can help you make the most of your remaining vision and maintain your independence.

Second, talk with your eye care professional about your vision problems. Ask about vision rehabilitation, even if your eye care professional says that “nothing more can be done for your vision.” Vision rehabilitation programs offer a wide range of services, including training for magnifying and adaptive devices, ways to complete daily living skills safely and independently, guidance on modifying your home, and information on where to locate resources and support to help you cope with your vision loss.

Where to go for services

Low vision services can take place in different locations, including:

- Ophthalmology or optometry offices that specialize in low vision
- Hospital clinics
- State, nonprofit, or for-profit vision rehabilitation organizations
- Independent-living centers

What are some low vision devices?

Because low vision varies from person to person, specialists have different tools to help patients deal with vision loss. They include:

- Reading glasses with high-powered lenses
- Handheld magnifiers
- Video magnifiers
- Computers with large-print and speech-output systems
- Large-print reading materials
- Talking watches, clocks, and calculators
- Computer aids and other technologies, such as a closed-circuit television, which uses a camera and television to enlarge printed text

For some patients with end-stage AMD, an Implantable Miniature Telescope (IMT) may be an option. This FDA-approved device can help restore some lost vision by refocusing images onto a healthier part of the retina. After the surgery to implant the IMT, patients participate in an extensive vision rehabilitation program.

Keep in mind that low vision aids without proper diagnosis, evaluation, and training may not work for you. It is important that you work closely with your low vision team to get the best device or combination of aids to help improve your ability to see.

Questions to ask your eye care professional about low vision

- How can I continue my normal, routine activities?
- Are there resources to help me?
- Will any special devices help me with reading, cooking, or fixing things around the house?
- What training is available to me?
- Where can I find individual or group support to cope with my vision loss?

Coping with AMD

AMD and vision loss can profoundly affect your life. This is especially true if you lose your vision rapidly.

Even if you experience gradual vision loss, you may not be able to live your life the way you used to. You may need to cut back on working, volunteering, and recreational activities. Your relationships may change, and you may need more help from family and friends than you are used to. These changes can lead to feelings of loss, lowered self-esteem, isolation, and depression.

In addition to getting medical treatment for AMD, there are things you can do to cope:

- Learn more about your vision loss.
- Visit a specialist in low vision and get devices and learning skills to help you with the tasks of everyday living.
- Try to stay positive. People who remain hopeful say they are better able to cope with AMD and vision loss.
- Stay engaged with family and friends.
- Seek a professional counselor or support group. Your doctor or eye care professional may be able to refer you to one.

Information for family members

Shock, disbelief, depression, and anger are common reactions among people who are diagnosed with AMD. These feelings can subside after a few days or weeks, or they may last longer. This can be upsetting to family members and caregivers who are trying to be as caring and supportive as possible.

Following are some ideas family members might consider:

- Obtain as much information as possible about AMD and how it affects sight. Share the information with the person who has AMD.
- Find support groups and other resources within the community.
- Encourage family and friends to visit and support the person with AMD.
- Allow for grieving. This is a natural process.
- Lend support by “being there.”

What research is being done?

NEI conducts and supports research in labs and clinical centers across the country to better prevent, detect, and treat AMD.

NEI-funded research over the past decade has revealed new insight into the genetics of AMD. By screening the DNA of thousands of people with and without AMD, scientists have identified differences in genes that affect AMD risk. Armed with this knowledge, researchers are identifying key biochemical pathways involved in the disease and are exploring therapies that could interrupt these pathways. It might also be possible to develop drug therapies for AMD that are targeted specifically to a person's unique genetic risk factors.

Scientists are also exploring ways to regenerate tissues destroyed by AMD. One approach is to make stem cells from a patient's own skin or blood. In a lab, these stem cells can be specially treated to form sheets of retinal pigment epithelium (RPE)—the pigmented layer of tissue that supports the light-sensitive

cells of the retina. The goal is to generate layers of RPE that can be implanted into the patient's eye to preserve vision.

The NEI Audacious Goals Initiative (AGI) is taking on one of the biggest challenges in medicine: the regeneration of nerve cells in the retina and brain. In humans, once brain and retinal neurons are gone—due to injury or diseases like AMD—they are typically gone for good. However, lessons from nature suggest that it may possible to overcome this limitation. For example, in some fish and amphibians, if the retina is damaged, it can grow back. Through targeted research, the NEI AGI aims to unlock these secrets and utilize them in humans—to develop new therapies to regenerate neurons and neural connections in the eye and visual system.

GLOSSARY

ALLELE	An allele is a variant form of a gene that is located at a specific position, or genetic locus, on a specific chromosome. Humans have two alleles at each genetic locus, with one allele inherited from each parent.
CHROMOSOME	Chromosome is a thread-like structure of DNA that carries hereditary information, or genes. Human cells have 22 chromosome pairs plus two sex chromosomes, giving a total of 46 per cell.
GENOME	A genome is an organism's complete set of DNA, including all of its genes. Each genome contains all of the information needed to build and maintain that organism. In 2018 humans, a copy of the entire genome—more than 3 billion DNA base pairs—is contained in all cells that have a nucleus.
GENOTYPE	The genetic makeup of an individual organism. It may also refer to just a particular gene or set of genes carried by an individual. The genotype determines the phenotype, or observable traits of the organism.
ODDS RATIO	The odds ratio is a way of comparing whether the odds of a certain outcome is the same for two different groups. In this report, the odds ratio estimates the probability of a condition occurring in a group of people with a certain genetic variant compared to a group of people without that variant. An odds ratio of 1 means that the two groups are equally likely to develop the condition. An odds ratio higher than 1 means that the people with the genetic variant are more likely to develop the condition, while an odds ratio of less than 1 means that the the people with the variant are less likely to develop the condition.
PHENOTYPE	A description of an individual's physical characteristics, including appearance, development and behaviour. The phenotype is determined by the individual's genotype as well as environmental factors.
POPULATION ALLELE FREQUENCY	The allele frequency represents the incidence of a variant in a population. Alleles are variant forms of a gene that are located at the same position, or genetic locus, on a chromosome.
SNP	Single nucleotide polymorphisms, frequently called SNPs, are the most common type of genetic variation among people. A SNP is a variation in a single nucleotide that occurs at a specific position in the genome.

dante labs

www.dantelabs.com

DANTE LABS™ TEST RESULTS

KIT ID: Sample