Age-related macular degeneration

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INTRODUCTION

Age-related macular degeneration (AMD) is a common cause of severe central vision loss and legal blindness in adults. The etiology, diagnosis, and treatment of AMD will be reviewed here.

DEFINITION AND CLASSIFICATION

AMD is a degenerative disease of the photoreceptors of the central portion of the retina (the macula) and the supporting retinal pigment epithelium [1-3]. It is characterized by loss of central vision.

For clinical purposes, AMD is classified as either "dry" or "wet". The more common form (affecting approximately 75 percent of patients) is dry AMD (also known as nonexudative or nonneovascular AMD). The less common form is wet AMD (also known as exudative or neovascular AMD).

Both forms of the disease are characterized by the presence of lipid-rich extracellular deposits under the retinal pigment epithelium called drusen, as well as retinal pigmentary and atrophic changes [4,5]. Wet AMD is characterized by new vessel formation in and under the retina [3,5]. These abnormal blood vessels have a tendency to leak, leading to collections of fluid and/or blood in and/or beneath the retina.

Dry AMD progresses to wet AMD in a minority of patients. The risk of developing wet AMD in people with bilateral, early, dry AMD (bilateral soft drusen) was estimated at approximately 3

per 100 person-years if both eyes have early- or intermediate-stage AMD [6].

Dry AMD can also progress to an advanced stage called geographic atrophy in approximately 15 percent of cases. Geographic atrophy and wet AMD are considered advanced forms of the disease and are responsible for most of the severe vision loss in AMD.

There is no consensus for classification and staging of AMD. Several classification schemes have been developed based on the appearance of the fundus. The most common one comes from the Age-Related Eye Disease Study (AREDS) [7], ranging from zero to four, with points assigned based on patient factors such as the presence of large drusen or pigment abnormalities [8,9]. Another classification scheme comes from the Beckman Initiative for Macular Research Classification Committee, with three stages of the disease and one for a normal, aging phenotype [10]. In clinical practice, the early/intermediate stage is clearly distinct from the universally accepted advanced wet AMD or geographic atrophy. However, the distinction between early and intermediate is less formal and could be based on patient symptoms and/or examination findings. (See 'Staging' below.)

EPIDEMIOLOGY

AMD is the most common cause of severe central vision loss and legal blindness among adults in the Western world [11]. The estimated worldwide prevalence of AMD is approximately 8 to 9 percent, affecting approximately 190 million people (18 million in the United States) [12-15]. It is predicted that worldwide, almost a quarter billion people will be affected by this disease by 2040 [12]. The incidence and prevalence increase with age. A study from 2004 of the United States population showed an overall prevalence of 1.5 percent that increases by tenfold (15 percent) for those over the age of 80 [16,17]. A study among European patients showed prevalence of early AMD increasing from 3.5 percent among people aged 55 to 59 to over 17 percent for those over the age of 85 [18].

PATHOGENESIS

The pathogenesis of AMD remains poorly understood. It is clearly a multifactorial, polygenic disease [1,2,19-23]. Aging remains the single most important risk factor [24-26]. Whole-genome sequencing has identified a set of 52 common variants mapped to 34 loci, with most notable changes in chromosome 1 (complement factor H locus) [27-31] and chromosome 10 (ARMS2/HTRA1 locus) [19]. Other factors identified to be involved in AMD pathogenesis include lipid dyshomeostasis [4,32], impaired autophagy [33-36], increased oxidative stress [37,38],

inflammation/para-inflammation [39-41], local iron overload/ferroptosis [42], and accumulation of toxic drusen-associated materials [43-46].

RISK FACTORS

Important nonmodifiable risk factors include older age and genetic risk, while modifiable risk factors include smoking and type of diet (low dietary intake of antioxidants) [47,48]. Epidemiologic studies have shown that current smokers are twice as likely to have AMD compared with nonsmokers, whereas ex-smokers had significantly less risk and people who quit smoking >20 years previously were not at increased risk [49]. A Mediterranean diet that includes fruits, vegetables, and fish is associated with a lower risk of AMD [50-57].

The data on the relationship between blood pressure and AMD are not strong or reproducible [58,59]. Similarly, the relationship between elevated lipid or other cardiovascular risk factors and AMD remains controversial [60].

CLINICAL PRESENTATION

AMD may be asymptomatic in early stages. Patients tend to present with problems in contrast sensitivity and adaptation to dark environments. They may complain that they need brighter lighting and more time to read and that their visual function is worse in situations with low contrast like rainy or overcast days. They will also be affected on bright days when they go from a bright to a dark environment (ie, when driving and entering a tunnel) or when they go from a brightly lit room to a darkened one. Eventually, as the disease progresses, their central visual acuity declines and they have trouble not only in reading but in recognizing faces and facial expressions of other people. In almost all patients, the peripheral visual function will remain very similar to that of unaffected individuals. Some patients may also notice distortion of straight edges such as doors or window blinds. Sudden onset of this later symptom requires urgent examination within few days to a week since it could herald progression to the advanced wet form.

It is estimated that approximately 15 percent of patients will become legally blind (central visual acuity less than 20/200), but complete blindness is not a typical outcome of this disease. The disease affects both eyes, but it can be asymmetric. If one eye converts to the advanced stage of the disease, the other eye has a 50 percent chance of advancing to that stage within five years [8,9].

EVALUATION

Primary care evaluation

History — In any patient presenting with symptoms of visual disturbance, the history should include age and the rate of vision loss; whether one or both eyes are involved; and whether the vision loss is for distance vision, near vision, or both. Patients with an acute distortion or loss of central vision may have an initial presentation of wet AMD. The evaluation of the patient with acute vision loss is discussed separately. (See "Amaurosis fugax (transient monocular or binocular visual loss)" and "Approach to the adult with acute persistent visual loss".)

Further questions should inquire about other symptoms suggestive of AMD:

- Is there a need for greater contrast sensitivity? (Does the patient require brighter sources of light to read?)
- Are there difficulties with dark adaptation? (Does the patient have issues going from a bright environment to a dark environment?)
- Is greater time needed to process visual information? (Patients will complain that they are not able to see the highway signs until they are very close to them or need more time to discern reading material.)

A family history of eye problems should be taken into account, including age of onset. Earlier onset in family members may suggest greater likelihood or progressive disease for the patient.

Eye examination — Eye examination by the primary care physician is limited to central visual acuity with either a near card or a distance chart, if available. Vision should always be checked by having the patient wear their glasses for the appropriate distance. Additional examination of distortion or scotomas with an Amsler grid can be useful. (figure 1) (see 'Amsler grid' below). An undilated funduscopic examination may reveal drusen or macula hemorrhage.

Primary care providers may be able to send photographs and rarely optical coherence tomography (OCT) images to a specialist. However, images are sometimes of limited quality and there may be little utility of such an approach if a patient will eventually be referred to an eye doctor.

Ophthalmologic evaluation and diagnosis — AMD is a clinical diagnosis based on the presence of characteristic findings on dilated eye examination using a slit-lamp instrument (biomicroscopy):

- In dry AMD, drusen are visible on dilated eye examination. Patches of geographic atrophy of the retina may be evident as areas of depigmentation; increased pigmentation may be seen with retinal pigment epithelium pigmentary mottling.

- In wet AMD, dilated examination may reveal subretinal fluid and/or hemorrhage. Wet AMD appears as a grayish-green discoloration in the macular area. The presence of subretinal hemorrhage or a gray subretinal membrane is strongly suggestive of wet AMD. These patients require an urgent assessment by an eye care specialist trained to treat wet AMD where a thorough evaluation and appropriate management can be instituted.

Additional specialized imaging of the retina includes color photograph of the retina, autofluorescence imaging of the retina, and an OCT. Depending on the suspected stage (intermediate to advanced wet AMD), a fluorescein angiogram or an indocyanine green angiogram, as well as OCT angiography may also be obtained to evaluate for the presence of wet AMD. Functional tests such as contrast sensitivity, dark adaptation, and microperimetry are not commonly available in a clinical setting.

Staging — Staging may be based on visual symptoms, as follows:

Early stage:

- Mild vague visual complaints
- Issues with low contrast
- Issues with adapting from bright to dark environments
- More light needed for reading

Intermediate stage:

- Distortion
- Blurriness
- Mild to moderate decreased visual acuity
- More significant loss of contrast sensitivity
- More prolonged dark adaptation times

Advanced stage:

- Loss of central visual acuity
- Significant distortion
- Significant central/paracentral scotomas
- Legal blindness

ADVICE FOR ALL PATIENTS

Smoking cessation — All patients should be encouraged to quit smoking or to avoid initiating smoking due to the increased risk of development or progression of AMD [49,58].

Diet/alcohol — Increasing evidence suggests that a Mediterranean diet may decrease the risk of developing advanced AMD [50-57]. In one of the largest studies, the association between adherence to a Mediterranean diet over the prior 12 months and prevalence of AMD (evaluated by eye examination and digital retinal color photography) was assessed among 4753 older adults in seven European countries [55]. Participants' diets were categorized according to the Mediterranean Diet Score, scored from zero to nine, with higher scores indicating greater adherence. Compared with those who scored four or less, participants with scores of six or greater had lower odds of wet AMD (odds ratio 0.53, 95% CI 0.27-1.04). The Mediterranean diet is described in detail separately. (See "Healthy diet in adults", section on 'Mediterranean diet'.)

Moderate consumption of alcohol lowers AMD progression risk; however, high alcohol intake may worsen advanced AMD [51,58,61].

Limited role for antioxidant vitamins — There is lack of conclusive evidence about the benefit of multivitamin supplements in AMD. Although multivitamin supplements are heavily marketed for people with AMD, evidence for effect on the progression of AMD is equivocal and they may have harmful effects [62-65].

Vitamin supplements are not appropriate for people with early stages of the disease or bilateral advanced disease.

We suggest daily vitamin supplements, consistent with the Age-Related Eye Disease Study 2 (AREDS2) formula, can be considered for patients with intermediate dry AMD or advanced AMD in one eye. However, it is also reasonable not to use these supplements based on limited benefit. Further, if a patient's disease progresses to the point of bilateral advanced disease with end-stage vision, we discontinue vitamin supplements due to lack of benefit.

In 2001, a formula containing high doses of vitamin C, vitamin E, beta-carotene, zinc oxide, and cupric oxide (also known as the AREDS formula) was shown in post hoc subgroup analysis of a phase 3 trial to reduce the risk of progression to wet AMD; however, there was controversy surrounding the results of this study and findings have not been replicated [7,62-64].

Further, the AREDS formula had some safety concerns due to the inclusion of high levels of vitamin A and zinc. High vitamin A is associated with increased risk of lung cancer in smokers [66-71], and the 100 mg/day of supplemental zinc is associated with advanced prostate cancer

in the Health Professionals Follow-up Study [72]. Thus, a new formula (AREDS2) was developed with reduced zinc content (25 mg) and no vitamin A (lutein + zeaxanthin as carotenoid replacement).

In the AREDS2 trial, 4203 participants at risk for progression to advanced AMD were randomized to a placebo control, lutein and zeaxanthin only, omega 3 fatty acids only, and lutein/zeaxanthin plus omega 3 fatty acids in addition to various modifications of the original AREDS formulation [73]. After a five-year follow-up, none of the treatment options resulted in a greater probability of reduction in progression to advanced AMD when compared with placebo (29, 31, 30, and 31 percent, respectively). However, in a further randomization, eliminating beta-carotene from the AREDS formulation resulted in fewer cases of lung cancer (11 [0.9 percent] versus 23 [2 percent]).

In a systematic review of trials, antioxidant vitamin and mineral supplementation did not prevent, but might delay, the onset of AMD and there was little effect from lutein and zeaxanthin alone [65].

WET AGE-RELATED MACULAR DEGENERATION TREATMENT

Early treatment of wet AMD is associated with better outcomes. In the early stage of the disease, the chance of conversion to wet AMD is less than 5 percent over five years. The chance of conversion to wet AMD increases to approximately 50 percent over five years when the disease is in the "advanced intermediate" stage [74-76].

Our approach — For most patients with wet AMD, we initiate treatment with vascular endothelial growth factor (VEGF) inhibitors or VEGF-angiopoietin-2 (VEGF-Ang2) inhibitors, for example intravitreal bevacizumab, ranibizumab, aflibercept, or faricimab. We do not routinely offer brolucizumab, due to the risk of occlusive vasculitis. In rare cases, we may use photodynamic therapy (PDT; polypoidal variety of wet AMD).

VEGF inhibitors — VEGF is a potent mitogen and vascular permeability factor that plays a pivotal role in wet AMD. Anti-VEGF treatments are the main therapies for wet AMD and have revolutionized management due to their ability to limit progression of wet AMD and stabilize, or reverse, visual loss [3,77].

Treatment with these agents should be initiated as soon after the diagnosis of wet AMD is made. Delay in the initiation of VEGF therapy (greater than 21 weeks compared with less than seven weeks) after first symptoms of wet AMD has been associated with poorer vision outcomes

[78]. In practice, most retina specialists would prefer to treat patients within a week of symptom initiation.

Several anti-VEGF molecules have been developed that can limit the destructive effects of neovascularization in patients with AMD. The best studied include intravitreal ranibizumab, aflibercept, faricimab, and bevacizumab [79-82].

In a meta-analysis of six trials (2667 patients), patients treated with anti-VEGF therapy (bevacizumab or ranibizumab) were more likely to have improvement in visual acuity (defined as a gain of ≥15 letters on the vision chart) after one year compared with those in the placebo or control group (18 versus 4 percent, respectively; risk ratio 4.19, 95% CI 2.3-7.6) [77]. Patients treated with anti-VEGF also had greater improvements in vision-related quality-of-life scores (mean difference 6.7 points on a 100-point scale). Rates of serious adverse ocular events in these trials were low, the most serious of them being an infection or retinal detachment, which occurred at a rate of 1/4000 injections or less. Systemic serious adverse events were closer to one to two percent and very similar to the control group.

Ranibizumab, aflibercept, and bevacizumab have similar efficacy. For example, ranibizumab and bevacizumab have similar visual and safety outcomes [77,83-86] and aflibercept has been found to be noninferior to ranibizumab [82]. Intravitreal injection of ranibizumab every four weeks, bevacizumab (off label) every four weeks, or aflibercept every eight weeks have similar efficacy [87]. Since bevacizumab is approved for treatment of patients with metastatic colon cancer, its ophthalmic use is off label and it is significantly cheaper than ranibizumab or aflibercept [88,89]. Faricimab (Vabysmo) is a bispecific anti-VEGF and anti-ANG2 molecule found to be noninferior in efficacy to aflibercept [90].

Another anti-VEGF agent to obtain US Food and Drug Administration (FDA) approval is a small single-chain antibody fragment called brolucizumab (Beovu), which was found not to be noninferior in efficacy to aflibercept, with up to one-third of the patients being able to be dosed at intervals of up to 12 weeks. Unfortunately, brolucizumab was found to cause in 2 percent of the people serious occlusive vasculitis and, thus, its adoption in real-world practice has been minimal [91-93].

Biosimilars — The cost of FDA-approved anti-VEGF medications for wet AMD is high (approximately $1000 to $2000 per injection in the United States). Biosimilar drugs promise to decrease cost, increase adherence, and potentially improve outcomes, especially in low-socioeconomic populations [94]. **It is important to know that biosimilars are not automatically interchangeable with the original product**. Interchangeable status can be

granted by the FDA after additional evidence from studies in patients evaluating multiple switches between biosimilar and original product.

As of December 2022 the following biosimilars are approved in the United States for use in the eye:

- Ranibizumab-nuna (Byooviz), a biosimilar product interchangeable with ranibizumab (Lucentis)
- Ranibizumab-eqrn (Cimerli), a biosimilar product interchangeable with ranibizumab (Lucentis)

The naming of biosimilars is governed by distinct and differing process in the European Union and United States. In Europe, the unique brand name of a biosimilar is paired with the standard international nonproprietary name (eg, ranibizumab [Byooviz]). In the United States, a meaningless, random distinguishing four-letter lowercase suffix by hyphen is added to the standard international nonproprietary name (eg, ranibizumab-nuna [Byooviz]).

Risks of anti-VEGF injections — Most risks of anti-VEGF therapy are transient and related to the injections itself. Serious risks include infection and retinal detachment. Risks per injection should be interpreted in light of the fact that patients receive multiple injections over long periods of time.

Systemic exposure to anti-VEGF is limited due to its local administration, although there is some concern of increased risk of vascular events. There appears to be a slight increased risk of stroke with ranibizumab, which is likely true with other agents as well. Further studies are needed, but clinicians should be aware of this potential risk when using VEGF inhibitors in patients who are at increased risk for hemorrhagic stroke or other serious bleeding or thrombotic events.

Significant risks of anti-VEGF injections:

- Endophthalmitis (1/2000 to 1/10,000) [95-98]
- Retinal detachment (1/2000 to 1/10,000) [99,100]
- Cerebrovascular events (1 to 2 percent versus 1 percent in the control) [85,101]
- Very rare but serious vasculitis with occlusion (reported with ranibizumab) [102]

Safety in patients taking anticoagulants or antiplatelet drugs — The bleeding risk of intravitreal injections in patients taking anticoagulants is minimal, and anticoagulation should not be discontinued prior to injection [103,104].

Treatment schedules for VEGF inhibitors — The optimal frequency for injections of VEGF inhibitors is not known. After initial treatment and disease stabilization, there are strategies designed to limit subsequent treatments.

One common approach is discontinuous treatment, with injections given on an as-needed basis, guided by results of optical coherence tomography (OCT). This approach has been evaluated with ranibizumab and bevacizumab and found to result in fewer injections and equivalent visual outcomes compared with monthly injections [105-109]. However, patients treated in this fashion should have indefinite close follow-up so as not to miss disease reoccurrence [110].

Another dosing approach is a "treat-and-extend" regimen in which, after initial treatment and stabilization, the intervals for patient follow-up and treatment are adjusted based on clinical findings. Intervals are extended if neovascular activity is not present and shortened if either fluid or hemorrhage is seen; anti-VEGF treatment is administered at every visit, regardless of disease activity, so there is no prolonged lapse in treatment. This approach can decrease the number of injections and clinic visits while maintaining comparable visual improvement compared with fixed-interval dosing [111-114].

Ranibizumab and bevacizumab are usually given monthly for three to six months and then on an as-needed basis after assessment of disease activity or on "treat and extend" [115]. The on-label schedule for aflibercept is three doses (2 mg) at four-week intervals, followed by 2 mg every eight weeks [116]. However, most physicians use the treat-and-extend paradigm or on an as-needed basis. Similar approaches are used for faricimab and brolucizumab.

Photodynamic therapy — The role for photodynamic therapy (PDT) has decreased with the increasing use of anti-VEGF therapy. We now rarely use PDT (with or without intravitreal anti-VEGF) only for unique situations involving wet AMD [117,118] or central serous chorioretinopathy [119-121].

PDT utilizes the photosensitizing dye verteporfin (Visudyne), and laser activation [122-126]. Treatment involves intravenous injection of verteporfin, which accumulates in the abnormal blood vessels of wet AMD and, when stimulated by a low-power nonthermal red laser (689 nm) in the presence of oxygen, produces highly reactive, short-lived singlet oxygen and other reactive oxygen radicals, resulting in local damage to the endothelium and blockage of the vessels. Not all patients with wet AMD are eligible for PDT therapy (mostly patients with a subtype called "classic wet AMD" are eligible). Furthermore, treatment with PDT usually does not lead to vision gains but it does reduce the rate of vision decline in wet AMD. Dosing can be repeated for up to four times a year. As it is a photosensitizer, patients must avoid sun exposure

for two to three days after the injection. Rare adverse reactions include severe vision loss from occlusion of normal vessels and reversible idiopathic low back pain.

Experimental and surgical treatments — Experimental submacular surgery with translocation of the retina [127] as well as radiation therapy for wet AMD [128,129] have also been tried, and some patients who have been recipients of these older approaches are still alive and may display late sequelae related to these interventions. Although these interventions have been mostly abandoned, submacular surgery for evacuation for large hemorrhages from wet AMD with or without tissue plasminogen activator and/or air are performed occasionally [130,131]. The optimal management of large, central submacular hemorrhages due to wet AMD is unknown, and outcomes remain mostly poor [131].

Geographic atrophy — Geographic atrophy is a form of advanced dry AMD, affecting 15 percent of AMD patients, characterized of loss of photoreceptors, retinal pigment epithelium, and choriocapillaris.

In 2023, the FDA approved the first two drugs aimed at this disease (intravitreal injection of pegcetacoplan and intravitreal injection of avacincaptad pegol) based on surrogate endpoint trial results that demonstrated a calculated reduction in lesion size [132-135]. However, approval of these drug has been controversial due to lack of demonstration of functional benefit and significant side effects [136]. Early after pegcetacoplan approval, reports of rare but serious vasculitis events with significant vision loss were reported by the American Society of Retina Specialists [137]. Due to lack of demonstration of functional benefit to any subgroup of patients, and the associated risks of vision loss, we do not endorse the use of these injections.

PREVENTION AND MONITORING

Adherence to a healthy lifestyle by quitting smoking and adopting a diet rich in plants, vegetables, and fish (eg, Mediterranean) is the best way to reduce risk of developing and progression of AMD. Regular annual visits to an eye doctor after the age of 55 may identify early AMD and become an opportunity for earlier counseling regarding the modifiable risk factors.

Amsler grid — Once AMD is detected, self-monitoring at home with an Amsler grid weekly is one of the best ways to detect, at the earliest phase, conversion from dry to wet AMD (figure 1).

Instructions for how to use an Amsler grid are as follows:

- The chart should measure 10 cm × 10 cm in size (approximately 4 × 4 inches), should be well illuminated, and is used to measure central 20° visual field when kept at a distance of 33 cm (13 inches) from the eye.
- Testing should be done with glasses if the patients need them.
- In a well-illuminated room, ask the patient to hold the grid approximately 13 inches away from the face and test one eye at a time. (Ask to cover one eye.)
- While looking directly at the center dot, the patient should observe the grid without redirecting the focus from the central point. Determine whether the patient can see all corners and sides of the grid. If any lines or areas look blurry, wavy, dark, or blank, mark that area in a chart note and schedule an urgent eye consult.

Home monitoring technology is improving and is becoming more common as both a way to detect the disease earlier and to manage the disease in a personalized fashion [138-146].

Retina specialists tend to monitor patients with dry AMD at least once a year. This periodic monitoring serves the dual purpose of identifying patients who progress from dry to wet AMD without having symptoms and to also educate the patient about the disease.

VISUAL AIDS

Being diagnosed with AMD can lead to significant central vision loss for approximately 15 to 30 percent of patients and can affect many more to a lesser degree. Having AMD and impaired vision does not need to mean losing control of one's life [147,148]. There is plenty of support available from several sources and professional services as well as a large array of equipment called "low-vision aids" including magnifiers [149], products that use color or contrast to make things easier to see and use, as well as merchandise designed for people with impaired vision. Many items such as reading stands, antiglare spectacles, and task lights can be found useful by individuals, though solid evidence is lacking for many of them [147].

Most electronic devices have special operating system modes made for the visually impaired, and these can have a significant impact on the quality of life of patients [150-154].

Low-vision devices for patients with AMD affecting their vision include:

- Reading handheld optical magnifiers.
- Portable electronic magnifiers.

- High-power reading glasses (affects reading distance; patient needs to be very close to the book).
- Video magnifiers (higher cost than handheld optical magnifiers).
- Telemicroscopic glasses (restricted visual field).
- Increase in contrast (increase lighting or darker print on brighter background). Certain computer monitors and electronic devices have special settings to accommodate need for higher contrast. White/black reverse modes for monitors.
- Increase lighting (especially coming from behind the patient to decrease glare such as with goose neck lamps).
- Large-print books.

Useful sites providing more information on visual aids and rehabilitation services available:

- Macular Society; low-vision aids
- National Library Service for the Blind and Print Disabled, Library of Congress
- American Foundation for the Blind; resources for adults new to vision loss
- American Academy of Ophthalmology; links and resources for people with low vision
- VisionAware; locate vision rehabilitation services
- United States Department of Veterans Affairs (844-698-2311); veterans can receive services and devices free of charge

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Age-related macular degeneration (The Basics)" and "Patient education: Age-related vision loss (The Basics)")

SUMMARY AND RECOMMENDATIONS

- **Definition and classification** – Age-related macular degeneration (AMD) is a degenerative disease of the photoreceptors of the central portion of the retina (the macula) and the supporting retinal pigment epithelium. AMD is classified as either dry or wet. The more common form is dry AMD (also known as nonexudative or nonneovascular AMD). The less common form is wet AMD (also known as exudative or neovascular AMD). (See 'Definition and classification' above.)

- **Epidemiology and risk factors** – AMD is the most common cause of severe central vision loss and legal blindness among adults in the Western world. Risk factors include older age, genetic risk, smoking, and low dietary intake of antioxidants. (See 'Epidemiology' above and 'Risk factors' above.)

- **Clinical presentation** – AMD may be asymptomatic in early stages. Patients tend to present with problems in contrast sensitivity and adaptation to dark environments. As the disease progresses, central visual acuity declines. (See 'Clinical presentation' above.)

- **Evaluation and diagnosis** – Primary care evaluation includes a history and evaluation of visual acuity. Diagnosis requires ophthalmologic evaluation and is based on the presence of characteristic findings on dilated eye examination using a slit-lamp instrument (biomicroscopy). (See 'Ophthalmologic evaluation and diagnosis' above.)

- **Advice for all patients** – We advise all patients quit smoking or avoid initiating smoking. We suggest that patients adhere to a Mediterranean diet (**Grade 2C**). (See 'Advice for all patients' above.)

- **Antioxidant vitamins** – For patients with intermediate dry AMD in both eyes or severe AMD in one eye, we suggest daily vitamin supplements consistent with the Age-Related Eye Disease Study 2 (AREDS2) formula (**Grade 2C**).

  However, it is also reasonable not to use these supplements based on demonstration of only modest benefit in these patients. Further, once disease has progressed beyond the stages described above, the supplements can be stopped due to lack of benefit.

  The AREDS2 formulation contains a daily dose of vitamin C 500 mg, vitamin E 400 international units, lutein 10 mg, zeaxanthin 2 mg, zinc 80 mg (as zinc oxide), and copper 2 mg (as cupric oxide). (See 'Limited role for antioxidant vitamins' above.)

- **Treatment for wet AMD** – For patients with AMD and neovascularization, we recommend as first-line treatment an intravitreal vascular endothelial growth factor (VEGF) inhibitor (eg, bevacizumab, ranibizumab, aflibercept) (**Grade 1B**). (See 'VEGF inhibitors' above.)

- **Monitoring** – Once AMD is detected, self-monitoring with an Amsler grid weekly is one of the best ways to detect, at the earliest phase, conversion to wet AMD. (See 'Amsler grid' above.)

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