# A Current Understanding of Age-related Macular Degeneration

Susan K. Keil

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It is a well known fact that age-related macular degeneration (ARMD) is the leading cause of blindness in the Western world in individuals over fifty years of age.[1-4] As a result of increasing mean age, the incidence of ARMD is increasing.[5] In light of this, as a primary eyecare practitioner, one needs to have a current understanding of ARMD, how to diagnose, treat, and manage this ocular disease. The purpose of this review is to discuss age-related macular degeneration in the form of a generalized review with the emphasis on current treatment and management including surgical intervention, prophylactic treatment and the prescription of low vision devices. Patient education and counseling will also be discussed.

The definition of age-related macular degeneration has not, as of yet, achieved universal acceptance. This is primarily due to the fact that many patients develop degenerative changes without ever exhibiting a decrease in visual acuity. For the purposes of this review, the following clinical features will be considered as age-related macular degeneration; drusen and geographic atrophy of the retinal pigment epithelium (RPE) as well as retinal alterations associated with subretinal neovascular membranes (SRNVM's) in patients over fifty years of age. However, since more than half of the geriatric population greater than seventy-years-old exhibit drusen, [2,6] some clinicians elect to save the term ARMD for individuals with the clinical features noted above and some degree of visual loss. Generally, central visual field loss develops with ARMD when the following

occur; serous and hemorrhagic detachment of the retina and RPE due to SRNVM development (80-90%), serous detachment of the RPE without an associated neovascular membrane (5-10%), and a progressive geographic atrophy of the RPE not associated with hemorrhage or exudation (5% or less).[7]

Despite the prominent occurrence of ARMD in the geriatric population, relatively little is known as to its etiology. However, it is believed that the original disease process begins within the RPE/Bruch's membrane complex. The tissue changes which ensue are most severe in the outer retinal layer of the foveal avascular zone (FAZ). Several theories have evolved concerning the factors implicated in producing the pathological changes within the retina. All reported theories center their hypotheses around the development of drusen, the consequences of vascular insufficiency, and the deposition of abnormal cellular material within the RPE/Bruch's membrane complex.[8]

There are two major classifications to be distinguished concerning ARMD: Non-exudative (dry) and exudative (wet) ARMD. The dry form of the disease process is characterized by observable alterations within the RPE at or near the macular region. These alterations may present in the form of RPE clumping, mottling, hyperplasia, or atrophy. As the degenerative changes progress, the underlying choroid and choriocapillaris become involved. It is at this level of degeneration that vision is compromised as a consequence of photoreceptor dysfunction.

Wet age-related macular degeneration possesses a more concise definition. The distinction of wet ARMD is associated

with the fundus signs of an RPE detachment and/or the developmental signs of choroidal neovascularization. These characteristics include the appearance of a sensory retinal detachment, a RPE detachment, and the presence of a Coat's response (hard exudates in the absence of clinically evident retinal vascular disease). In addition to these features one may also observe the appearance of intraretinal hemorrhages (in the absence of clinically evident retinal vascular disease), subretinal hemorrhages temporal or near to the optic nerve head, RPE tears, or disciform scarification in the macular region. Geographic ARMD (a subclassification of dry ARMD) clinically presents itself as well circumscribed areas of atrophy varying in size from 200-500+ microns. Neovascularization may occur at the peripheral edges of these atrophic areas, however it is rare for new blood vessel growth to occur within the choroid or choriocapillaris.[9] The disciform lesion represents a response of the fundus tissues to pre-existing disease affecting the subretinal structures.

Drusen are the hallmark finding and earliest clinical feature of ARMD. Drusen form as a result of compromised RPE cells. When the function of the RPE cells falters, an extracellular material, lipofuscin, is formed which is then deposited onto Bruch's membrane. Lipofuscin is comprised of a combination of mucopolysaccharides and lipids, however the true composition of drusen is controversial and varies throughout the retina.[10]

Five different types of drusen have been described according

to their appearance within the retina. These types are hard, soft, basal laminar, calcified, and mixed variety drusen.

Hard drusen appear as tiny, well-circumscribed yellow deposits located in the inner and outer collagenous layers of Bruch's membrane. These drusen are sometimes referred to as hyaline drusen.

Soft drusen differ from hard drusen in that they are larger and have more ill-defined borders. They possess diameters of greater than 63 microns. As these drusen coalesce, they resemble serous detachments of the RPE.[11-13] Often this type is associated with hypopigmentation or hypertrophy of the overlying RPE.[7,14] These drusen are located between the basement membrane of the RPE and the inner collagenous layer of Bruch's membrane. Over 25% of patients between 70 and 80 years-old exhibit this type of drusen.[15]

Basil laminar drusen are commonly found in younger patients. They present as multiple, fine yellow spots. Also known as diffuse drusen by some researchers, they are considered to be hyaline thickenings of the RPE. Diffuse drusen act to weaken the inner aspect of Bruch's membrane and may occasionally predispose the retina to small, yellow exudative detachments due to the extreme thickening they cause there.

Calcified drusen are those which have aged and hardened with time. They often appear as glistening deposits composed of cholesterol.[13]

Mixed variety drusen are described by Sarks [11] "as drusen that have the characteristics of both hard and soft drusen. They

appear as flat drusen with smudgy, ill-defined borders. They are associated with thickening of the basement membrane of the RPE, the inner portion of which is narrowly distanced from the remainder of Bruch's membrane."

Drusen indicate that the metabolism of the normal healthy retina has been altered. Irregardless of the drusen type, all varieties indicate a breakdown at the level of the RPE/Bruch's membrane complex. If there are multiple drusen present in or around the macular region, it is a known fact that there is a greater than 80% chance of degenerative macular changes occurring. This is in comparison to an only 2% chance in the population of individuals without drusen.[16]

Rarely, blood breaks through the neurosensory retina into the vitreous cavity, more commonly known as a vitreous hemorrhage. Vitreous hemorrhages can be differentiated from those beneath the RPE in that they obscure fundus blood vessels, especially the inferior and superior arcades. Vitreous hemorrhages are known to be a complication which is more common in patients on anticoagulants.

The development of drusen predisposes the choroid to neovascular growth and RPE detachment. In greater than 90% of RPE detachments, a sensory detachment occurs concurrently. In patients older than 55 years, RPE detachment is a poor prognosis sign. The vision loss which occurs may be due to choroidal neovascularization, atrophy, or an RPE tear. Up to thirty percent of patients older than 55 with RPE detachments will develop choroidal neovascularization and approximately ten

percent of this same age group will develop associated RPE tears.[17-18]

Fluorescein angiography (FANG) combined with stereoscopic biomicroscopy is necessary for the proper diagnosis of an RPE detachment. FANG will exhibit a lesion which grows early and evenly and remains stained late into the angiogram. The presence of an RPE detachment does not necessarily guarantee the presence of a choroidal neovascular membrane.

Initially, a choroidal neovascular membrane (CNVM) appears as a gray-green area that is a result of decompensation of the associated vessels. As fibrosis occurs, this area yellows with leakage of the affected vessels and an RPE or sensory detachment results creating metamorphopsia and decreased visual acuity.

The end result of CNVM development may initiallly limit the size of retinal destruction and the size of the central scotoma. However, the scar may reactivate and lead to a more severe hemorrhagic scar.

The clinical presentation of dry ARMD is characteristically described and will be referred to as all observable age-related macular alterations of the RPE that can produce visual compromise up to but not including the development of choroidal neovascular growth and/or and RPE detachment. These alterations may include some or all of the following: drusen, granularity of the RPE, RPE hypo/hyperpigmentation, or RPE clumping. With advancement, RPE atrophy coalesces further producing signs of an underlying choroidal and choriocapillaris atrophy. With these degenerative changes vision loss occurs secondary to the disruption of

photoreceptor function.

As mentioned previously, when these non-exudative changes exhibit a well-defined pattern which varies in size from 200-500+ microns, this is often referred to as geographic atrophy. Prognosis for the severity of vision loss which follows is not predictable or constant.

Wet ARMD may be differentiated from the dry ARMD in that it is associated with the signs of an RPE detachment and/or the appearance of a gray-green neovascular net near the macula (with an associated metamorphopsia). Additional characteristics include a RPE detachment, a sensory retinal detachment, Coat's response, or intraretinal hemorrhages near the macular region (and in the absence of other retinal vascular disease), or a subretinal hemorrhage near the macula or temporal to the optic nerve head. The fundus of a patient with exudative ARMD may also exhibit scarring or atrophy in the macular area or a RPE tear.

There are several risk factors which predispose an individual to ARMD, however by far the greatest risk is increasing age, hence its inclusion in the name; age-related macular degeneration. Individuals at greatest risk to the development of ARMD are between the ages of 75 and 85 years of age. In an epidemiological study completed by Vinding et al of 1000 aged individuals, three factors were significantly associated with the development of ARMD: Age, smoking (with inhalation), and the use of hypnotic medications. [19] However, the only universally accepted risk factor is age. Among individuals 75-85 years of age the risk of ARMD was found to be 30 times

greater than in individuals aged 60-64 years. This was true for both the atrophic and exudative form of the disease. Smoking was significantly associated with the presence of ARMD. Compared to nonsmokers, smokers who inhaled possessed a much greater risk of macular degeneration. The corresponding increase for the geographic form was statistically significant versus the increase for the wet form which was insignificant. Smokers who did not inhale had a higher (although not statistically significant) risk than for nonsmokers for all ARMD forms.

Among individuals on daily hypnotics, the risk of ARMD was two times greater than individuals who were not on this medication type. Only the exudative form was found to be statistically significant with this risk factor. As some hypnotics are used as both sedatives and hypnotics, Vinding et al[19] analyzed the effect of the use of either drug. This combined variable was only significantly associated with the risk of the exudative form, although on a lower level than the hypnotics alone.

Other risk factors include a positive family history of the disease, weakness of hand grip, hyperopia, [20] light colored irides and hair, caucasians, [21] exposure to solar radiation, [22] low total serum cholesterol in females and increased amounts of HDL's in males with associated low total/HDL ratios, and high hematocrit and leukocyte values.[20-23]

The patient at greatest risk would then perhaps be a "caucasian of blue-eyed Scandinavian ancestry, older hyperopic female, pre-1984 pseudophake, smoker, cardiac patient not on

estrogen replacement but on a photosensitizing drug who exhibits retinal drusen and who eats a poor diet devoid of fruits and vegetables and high in fats, goes outdoors frequently without sun protection or with inadequate sunglasses, lives in the Southern United States, and has a positive family history of ARMD."[8]

At first glance several pathological processes may mimic the appearance of non-exudative ARMD. Some of the differentials which should be considered are idiopathic central serous choroidopathy (ICSC), central areolar choroidal dystrophy (CACD), macular holes, macular colobomas, Stargardt's hereditary dystrophy, and trauma.

Dry ARMD may be differentiated from ICSC in that the latter process usually presents itself unilaterally and affects younger males with Type A personalities.

Central areolar choroidal dystrophy is inherited as autosomal dominant and autosomal recessive with variable penetrance. The distinguishing features of CACD are an absence of drusen, a single large area of atrophy centered over the macula, and an acuity loss which is 10-20 years earlier than that seen with dry ARMD. Only rarely is there an associated pigment clumping with CACD unlike with the dry form of macular degeneration.

Macular holes are often difficult to differentiate from dry ARMD as well as are macular colobomas. Colobomas can be distinguished from dry ARMD by the fact that they are often detected at a younger age and possess a vision loss that is often long-standing and unilateral. Macular holes are idiopathic in

individuals older than 60 years. They are often bilateral and appear as a punched out round or slightly ovoid lesions at the macula. A gray halo of marginal retinal elevation usually surrounds the lesion. Yellow deposits at the base, known as pathological drusen, can confuse a clinician with the differential diagnosis.

Stargardt's hereditary dystrophy has a clinical appearance which can appear similar to ARMD. However, this is a bilateral and genetically determined condition (autosomal recessive) which often presents itself in younger individuals. Key distinguishing features of Stargardt's are a "bull's eye" appearance of the macula with fluorescein angiography and a "beaten bronze appearance" of the macula upon ophthalmoscopic examination. Characteristically, the Stargardt patient is myopic in refractive error in contrast to the typical hyperopic ARMD patient.

Trauma is yet another differential one should consider in relation to dry ARMD. A thorough case history should aid in making the correct differential diagnosis.

There are numerous retinal diseases which may clinically appear much like exudative ARMD. Presumed Ocular Histoplasmosis Syndrome (POHS)and angiomatosis retinae (Von-Hippel Lindau disease) are a few of these conditions. Additionally, angioid streaks, choroidal ruptures, and toxoplasmosis may also assume an appearance similar to wet ARMD when in association with choroidal neovascularization.

With POHS, again, a thorough case history will help with the differential diagnosis. Presumed Ocular Histoplasmosis Syndrome

ususally presents in younger individuals and is endemic to the Ohio and Mississippi River Valley. It has a characteristic triad of peripapillary atrophy, peripheral "punched out" histo spots, and an exudative maculopathy secondary to choroidal neovascular membranes. Angiomatosis retinae is characterized by retinal angiomas which are fed by adjacent collateral vessels and is genetically transmitted as an autosomal dominant trait with incomplete penetrance and no sex predilection. It occurs most frequently in individuals who are in their 20-40's. This condition is most remarkable in the temporal periphery.

Choroidal ruptures with choroidal neovascular membranes reveal a history of blunt trauma with contrecoup shock waves. The ruptures appear crescent shaped, following the contours of the optic nerve head. An active rupture usually has an associated bleed that makes the choroidal rupture difficult to visualize.

With toxoplasmosis, the key clinical diagnostic sign is the presence of an active vitritis. This condition usually manifests itself at a younger age than that of the ARMD patient.

Angioid streaks may be clinically differentiated from the clinical signs of exudative macular degeneration by the characteristic circumpapillary degenerative streaks which radiate outward from the posterior pole. A classic "orange peel" appearance is often observed temporal to the macula.

There are several tests which may be administered to aid in the diagnosis of ARMD. These tests examine the integrity of photoreceptor function, the anatomical intactness of the macular region, and the tissues immediately adjacent to the macula.

The Amsler Grid is one such test. It is a test that is qualitative in nature and which makes it possible to analyze an early neovascular net and its progression as well as to detect any scotomas encroaching onto the central ten degrees of vision.[24]

Figure 1 illustrates the Amsler Grid. Pre-testing information follows along with a sequence of questions which should be asked (in the office setting) and the purpose of each question.

The Amsler Grid is helpful in signaling when new complications may be arising with ARMD. "Patients with focal areas of hyperpigmentation or drusen that have progressed to the point of coalescence should be especially mindful of grid appearance since they are more likely to develop neovascular maculopathy. Because they may notice more distortions (metamorphopsia) on the grid before a choroidal neovascular membrane forms, however, these patients should carefully watch for new disturbances of sudden onset."[25]

The value of fluorescein angiography (FANG) in the diagnosis if ARMD cannot be overemphasized, especially in the case of exudative ARMD. Fluorescein angiography is based on the fact that fluorescein dye leaks freely from the normal choriocapillaris but does not penetrate healthy RPE and normal retinal capillaries because of the tight endothelial junctions present in the latter. Under optimum conditions, the smallest retinal capillary (5-10 microns in diameter) can be seen with this technique.

With FANG, hard drusen appear as transmission or window defects of the RPE during the "early transit" phases. This is

because the hypopigmentation of the overlying RPE enhances the transmission of the choroidal (background) fluorescence. In general, more drusen can be isolated and identified using angiography than ophthalmoscopy alone.

Soft drusen will show dye accumulation beneath the thickened inner aspect of Bruch's membrane and may pool in that region several minutes after injection of the fluorescein. The dye, however, will not leak beyond the margins of soft drusen. In contrast to soft drusen, mixed drusen will not stain as brilliantly although they may reveal some late staining.

Basal laminar drusen fluoresce discretely during the arterial or arteriovenous phase and then fade during the later stages of the angiogram. Due to the large numbers of these drusen, the FANG appearance of this type has been described as a "stars in the sky or Milky Way picture."[26]

The differentiation between dry or wet ARMD is not always an easy diagnosis to make. A good examination should incorporate one or more of the following instruments and lenses; direct ophthalmoscope, binocular indirect ophthalmoscope, and the 78D, 90D, gonioscopic, or contact lens.

For inital examination, one may use the direct ophthalmoscope to view the macular region. Many details may be seen magnified with this instrument. "Moving the poroprism up as high into the peephole without blocking the view, and stopping the viewing field down to a little larger than the optic nerve diameter, makes it easier to look through the pupil, and enhances the contrast."[27] With the red free filter on the direct

ophthalmoscope, subtle, leaky vessels and hemorrhages may be observed. Any leakage will appear black in coloration.

Viewing binocularly offers the advantage of stereopsis and allows the examiner to determine if the lesions are flat and within the same plane of the retina, or if they are raised, as with neovascular nets.

With biomicroscopy, increased magnification and the effect of stereopsis are extremely helpful with the examining the integrity of the macular area and the surrounding fundus. Several lens types can produce these effects. These are the contact, Hruby, and high plus aspheric lenses (78D and 90D). Each lens possesses advantages and disadvantages. Table 1 located at the end of this review lists these pros and cons.

The use of monocular color matching to help estimate increased risk is also very beneficial. An abnormal color-match-area effect was found to be very specific for increased risk of fundus appearance. [28] Acquired color vision defects may be present when macular function is impaired. It has been proposed that eyes with sluggish foveal dark adaptation rates and low blue-cone mediated sensitivity have a greater chance of developing exudatve ARMD. Foveal flicker sensitivity may also be of value in predicting the onset of exudative ARMD.[29-31]

Two additional tests are dependent on the arrangement of the yellow pigment in the inner layers of the macula lutea, those being Haidinger's brushes and Maxwell's spot. The visualization

of Haidinger's brushes, "propellor-like" rotating brushes (which appear extending from the fixation point when a patient views a brightly illuminated background through a polaroid filter) is impeded when macular disease is present. Maxwell's spot is an entoptic phenomenon which cannot be seen in a patient with maculopathy. Therefore, a clinician may use this phenomenon as a screening procedure in patients for whom exudative ARMD is suspected. However, when visualized, the spot appears as a 3 degree dark ring surrounded by a fixation target when viewing a bright white surface through a blue filter.

Three other tests should be considered when exudation is suspected at or near the macular region; the electroretinogram (ERG), the electro-oculogram (EOG), and the VEP.[24]

The ERG is a test of the electrical potential generated by the preganglionic retinal receptors to a diffuse light stimulus. For clinical purposes, the human response is a biphasic wave that has an early negative **a** wave which represents input generated from the photoreceptors followed by a larger, positive **b** wave, which represents input from the bipolar cells. The ERG is very useful in detecting early macular dysfunction before changes are evident with ophthalmoscopy.

The EOG measures the slow changes in the resting potential . It represents the presynaptic function of the retina. Any disease process which interferes with the functional interactions of the RPE and the photoreceptors will produce an abnormal or absent rise in the electro-oculogram. It is important to note, however, that this test may be lacking in that only very small

vessels of the retina are involved.

The Visual Evoked Potential measures the electrical potential generated to a visual stimulus at the occipital region of the brain. This is a test of great value in the study of macular disease as its role in ARMD is that of detecting subclinical lesions in the macular area.

Macular photostress testing may also be implemented to aid in the definitive diagnosis of ARMD. Any recovery greater than 55 seconds indicates macular dysfunction, although the macular region may clinically appear anatomically intact.

Laser photocoagulation is indicated with well-circumscribed neovascular nets with no overlying RPE detachment. Krypton laser photocoagulation is recommended for juxtafoveal choroidal neovascular membranes in nonhypertensive patients with ARMD. The theory behind the use of the Krypton Red laser is that it allows treatment closer to the fovea than Argon because of Krypton's specificity for the choroidal layers. Krypton is very useful in situations where the neovascular net is associated with melanin pigmentation and overlying hemorrhages. Argon laser photocoagulation has been proven effective in the treatment of extrafoveal neovascular nets.[32]

Several studies of patients with neovascular nets within the foveal avascular zone who were treated the Krypton Red laser demonstrated that improvement or visual stabilization may occur. Additionally, strong arguments have been made that the scar created by this laser will produce a smaller scotoma than the original neovascular net with its natural progression.[32-35]

Numerous attempts have been made to find a functional cure (or at least visual improvement) for the ARMD patient particularly with the exudative, more severe form of the disease. The application of various types of lasers have been used in an attempt to "seal off" or even decrease the size of the new blood vessel growth. Although several clinical trials have been completed concerning laser photocoagulation and the treatment of ARMD, probably the most reknown studies were completed by the Macular Photocoagulation Study Group (MPS). One randomized clinical trial studied the effects of Argon laser treatment on subfoveal recurrent neovascularization and compared the results to eyes receiving no laser therapy. Fifty-two percent of the treated eyes exhibited recurrent neovascularization by 24 months post-treatment.

In yet another study completed by the MPS group, which performed Krypton Red photocoagulation on parafoveal neovascular lesions, 66% of eyes with ARMD had persistent or recurrent neovascularization by 25 months post-treatment.[33-35] Sorenson et al[36] reported that in 59% of eyes with ARMD that received Krypton Red laser treatment, recurrent neovascularization or some other type of new blood vessel growth developed during follow-up. Although these statistics seem disheartening, the MPS group has since demonstrated that carefully placed laser photocoagulation, applied in a timely manner, decreases the risk of severe vision loss for patients with extrafoveal ARMD.[32-34,36]

In the original MPS group (1982), it was approximated that about 5% of subretinal neovascular membranes were treatable with

Argon laser photocoagulation. The laser treatment in this study was confined to the defined areas of neovascularization (via FANG) at least 200 microns from the foveal center. It was determined that the eyes of patients with indistinct neovascular margins have a poorer visual outcome. In the December 1993 issue of the Journal of the American Optometric Association, it was stated that approximately 75% of patients with exudative ARMD secondary to choroidal neovascularization pass through a potentially treatable stage. "Up to 80% of patients with visual symptoms for less than two weeks and over 50% with symptoms for less than four weeks will be treatable. The window for success is limited, therefore early detection and rapid intervention are critical if there is to be any hope for retention of visual function."[32-35]

As a treatment alternative to laser therapy, the surgical removal of choroidal neovascular membranes has been employed recently in an attempt to achieve maximum sparing of vision. The surgical procedure involves performing a posterior vitrectomy followed by a small retinotomy (see Figures 2-3). One group of researchers reported that seven of ten subfoveal CNVM's which were surgically removed showed visual improvement by six months post-op, however, long term prognosis has yet to be determined.[36]

Currently, no specific treatment has been shown to alter the natural progression of dry ARMD. In general, dry ARMD patients with drusen **only** in each eye do not need fluorescein angiography performed in their management. However, FANG should be performed on a patient with drusen that has recently experienced sudden

decreased visual acuity and/or metamorphopsia. FANG should be promptly performed if there is any suspicion of subretinal blood, fluid, or lipid present to determine if there is a treatable neovascular net present. This is especially true in following an eye with drusen only, in which the fellow eye has already experienced an exudative complication, since these eyes are at higher risk than eyes of patients with bilateral drusen only.[38,39]

The primary goal of the management of exudative ARMD is more complex than that of the non-exudative form. All geriatric patients with macular drusen should be placed on home monitoring systems (i.e. the Amsler Grid) and should be followed, minimally, on an annual basis. Until proven otherwise, all patients with unexplained metamorphopsia or decreased visual acuity should be suspected of having a subretinal neovascular membrane, a RPE detachment, or a retinal pigment epithelial tear. All gray-green areas in the macular area should be considered as a SRNVM until proven otherwise. The appearance of soft drusen or a Coat's response should also heighten the clinician's suspicion of a neovascular net.

If a neovascular net is suspected or other signs of wet ARMD are present, a FANG should be performed promptly, within 72 hours. One cannot delay in attempting preventative treatment as up to 73% of untreated foveal lesions can become subfoveal within one year.[39] Improper treatment of a SRNVM is a major cause of treatment failure or regrowth. A number of SRNVM's recur within one year of treatment and are not susceptible for retreatment. The majority of these recurrences are at the foveal side of the

treated scar due to the increased hemodynamic activity in this region. Risk of recurrence is associated with cigarette smoking, females, and a younger age present in up to 60% of eyes treated over time.[40] Figure 2 represents the rate of recurrence as determined by the Macular Photocoagulation Study.

As a result of the high recurrence rate, the post-operative management of the ARMD patient is critical. Color fundus photos should be taken immediately after surgery and at least 48 hours after application of laser treatment. Reapplication of laser therapy may be indicated if the first application failed. Until SRNVM regression has been proven, the use of aspirin and other such platelet inhibitors should be avoided. In addition, heavy lifting or situations of potential trauma should also be avoided. Once documentation of regression of the SRNVM has been completed, the patient should then be followed with fluorescein angiography at regular intervals after laser treatment, approximately 3-6 months depending on the state of the patients maculopathy. If recurrence is suspected fluorescein angiography is a must. The patient should also continue with Amsler Grid home monitoring on a daily basis.

Several different studies have been completed concerning investigational forms of treatment for ARMD. One relatively new concept is the efficacy of interferon alpha-2a. Interferon alpha-2a is a recombinant glycoprotein with antiviral and antiproliferative actions. The mechanism of action is believed to be an interference with the transcription of RNA and RNA directed protein synthesis. Interferon alpha-2a has been found

to inhibit angiogenesis and endothelial cell migration as well as to block endothelial cell receptors for growth factors.

Poliner et al [42] completed a randomized clinical trial to determine the efficacy of interferon alpha-2a for subfoveal neovascularization in patients with ARMD. Twenty eyes of 19 patients with subfoveal neovascularization secondary to ARMD were evaluated and ten were randomly selected to have 3 million units/m2 of interferon alpha-2a subcutaneously administered every other day for eight weeks. Ten eyes were used as controls. All eyes were followed for a minimum of six months. The researchers concluded that although the rate of neovascularization slowed during the first two months of initial treatment, the effect was not long-standing once treatment was discontinued. No long term benefit was noted. Unfortunately, if the researchers were to have lengthened the administration time, increased the frequency of administration, or increased the dosage of interferon alpha-2a, doing so would likely have produced unwanted and possibly even toxic side effects, as a significant number of adverse reactions were already noted in this study (67%).

The U.S. Census Bureau projects that by the year 2030, there will be 65 million Americans age 65 or older, and that by the year 2050 16 million Americans will be age 85 or older. As a result of the increasing mean age in our country, the incidence of age related macular degeneration is also increasing. Today ARMD represents 1/3 of the visually impaired or the legally blind population in the U.S. Therefore, the importance of possessing a knowledge of low vision devices for the ARMD patient cannot be

overemphasized.

Visual loss results from either an atrophic process involving the RPE, neurosensory retina, and choriocapillaris or from a subretinal fibrovascular scar associated with disciform degeneration. The visual disability of the ARMD patient primarily centers around reading and other near vision tasks. However, when attempting to decide upon the appropriate low vision device, probably the most critical question to ask the patient is what he/she wants to be able to do with his/her remaining vision? Other considerations which need to be taken into account are the convenience of the aid, other ongoing disease processes, and the patients motivation and attitude. Once these considerations have been made, the appropriate low vision devices may be prescribed.

Handheld magnifiers prove very useful to the ARMD patient as they permit variation of the patient's working distance from the eyes to the task at hand. Many low vision patients like to use these for aid in reading the newspaper or scanning the food labels in the grocery store. Some handheld magnifiers are illuminated and can be very helpful in darkly lit restaurants with reading menus. The disadvantages of these aids however are a limited field-of-view as well as the coordination difficulties some patients have with aligning the head and eyes with the aid and the material.

Stand magnifiers aid a low vision patient by allowing them to free their hands for better control of the task at hand. For example, one might prescribe these devices to patients who have

short to moderate reading tasks, i.e. personal bills. The drawback of the stand magnifier is the necessity of frequently moving the device. When a greater viewing distance is required, telemicroscopes should be considered, however, a considerable loss of peripheral field-of-view occurs with the utilization of these aids.

Microscopic spectacles are the most accepted devices by the ARMD patient. These are prescribed as single vision full lenses, half-eyes, or as microscopic bifocal additions. The advantage of these aids is the positive effect on the relationship of the size of the central scotoma to the size of the total field-of-view. Hence, the closer the object is viewed relative to the eye, the smaller the central scotoma becomes relative to the total field. These aids prove very useful with the geographic form of the disease.

The Closed Circuit Television (CCTV) has proven to be a very helpful low vision device for the ARMD patient. A recent study demonstrated that the most efficient near performance can be achieved with CCTV devices in patients who have experienced vision loss secondary to wet ARMD.[43] The CCTV allows patients to perform a great many tasks by allowing print size to be magnified or minified. It also allows contrast and background illumination to be altered as necessary. Many ARMD patients use this device to read their mail, to write out checks, and to view enlarged photos of family and friends. Unfortunately, the disadvantages of this device is its cost and its lack of portability.

Telescopes may be prescribed as distance aids. They are often used as hand-held spotting devices to view house numbers, street names, bus numbers, etc. The drawback of this particular device is a limited field-of-view.

For driving, binocular telescopes may be prescribed (depending on whether or not the patients home state legally allows this). The telescope should be mounted near the top of the spectacle lens. The patient drives using the lower spectacle lens to provide the unlimited field-of-view. The patient should also be educated to tip his or her head down to spot a directional sign, traffic light, or the orientation of another driver. When a larger field-of-view is needed, the patient should return to the use of the lower spectacle lens.

If a longer reading distance is required a telescope may be converted into a telemicroscope by utilizing a different objective lens focused for the appropriate reading distance. This device allows the patient to read at near and to look up to see at distance through the upper portion of the lens.[43]

Other considerations when dealing with low vision devices are magnification, color filters, contrast, illumination, and the position and direction of the light source.

As a clinician, one needs to remember that with high magnification lenses, an increased convergence demand is placed on the patient. Educating this fact to the patient is critical to the acceptance of the low vision device by the patient.

The optometrist has an important role to play in ascertaining that patients receive protection from damaging

ultraviolet radiation, since it is thought to play a detrimental role in the pathogenesis of ARMD.[44] The high wavelength end of the electromagnetic spectrum has been proven to be more hazardous than longer wavelengths of light in producing photochemical destruction. This damaging region has also been referred to as the "blue light hazard" or retinal hazard region. The photochemical damage is thought to be additive in nature.

The retina is protected from most ultraviolet radiation via the ocular anatomy, i.e. the cornea and the crystalline lens. The cornea absorbs 100% of UVC (290-100nm) light and the crystalline lens absorbs a large amount of UVB (320-290nm). With age, however, the crystalline lens absorption increases to include most wavelengths of 370nm and below. Unfortunately, much of the short wavelength is allowed to penetrate to the retina, with subsequent destruction of the photoreceptors.

Current re-analysis of the Cheasapeake Bay Waterman Study determined that increasing the duration of exposure to blue and visible light revealed an associated increase in the more severe grades of age-related macular degeneration. The conclusion was that there existed a "strong association between exposure to blue and visible light during the later years of life, suggesting that exposure in early life was not as significant as exposure later in life."[45] Therefore, optometrists have an important role to play in ascertaining that at risk patients (as well as diagnosed ARMD patients) receive protection from damaging UV light. Proper filters or sunglasses should be provided. Since as much as 40% of sunlight reaches the inner eye from around the top and the

sides of standard glasses frames, the best protection is provided by wrap-around sunglasses. Sunglasses are especially appropriate for aphakic or blue eyes. In the aphakic patient there exists no crystalline lens to protectively filter out destructive ultraviolet radiation. Blue colored irides have also been reported to suffer more damage from exposure to ultraviolet light than brown or heavily pigmented irides.[46]

The primary eyecare professional can do much to prevent damage to the macular region by prescribing near violet absorbing filters. Color filters such as NOIR may be worn by the ARMD patient to decrease light scatter of various wavelengths. The best method for determining the appropriate filter is by asking the patient through which filter does glare appear to be decreased the most?

Another important variable which should be controlled is illumination. With a diseased eye, as with the ARMD patient, the quality, type, and intensity of light becomes even more critical. Sloan et al[47] found that as illumination levels increased, acuity at near increased. In a study completed by Kia B. Eldred, which was designed to determine the optimum reading levels for patients with ARMD, it was suggested that "illumination levels higher than previously recommended will improve reading speed in most patients with ARMD."[48]

Position and direction also influence performance. To avoid glare, positioning the light source slightly behind the patient will help. Introducing a diffusor and altering the angle of incidence will reduce the amount of reflections coming off of the

reading material and therefore enhances reading performance.

The development of free radicals within the eye lead to the subsequent development of drusen and photoreceptor dysfunction through a series of complex, biochemical reactions. Because thesse free radicals produce such damaging effects to the retinal tissues, several protective mechanisms have evolved including the use of antioxidative compounds such as zinc, vitamins A and E, and beta-carotene.

The development of free radicals with the subsequent development of drusen leads to the destruction of photoreceptors. Therefore, antioxidant supplementation (i.e. zinc) should also be recommended to the ARMD patient, especially considering the fact that approximately 1/2 to 1/3 of geriatric patients between the years of 65-85 possess a dietary deficiency for zinc.

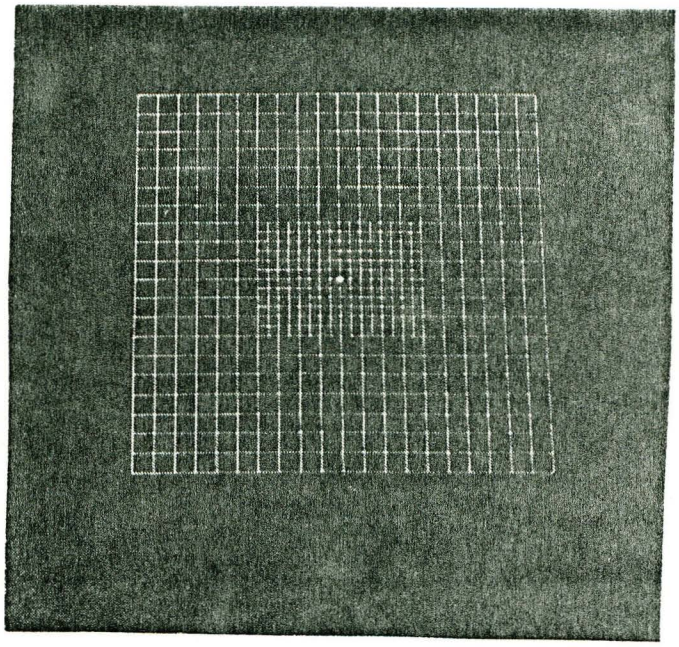
David Newsome, MD, in a 1988 article, reported that large dose zinc supplementation slowed down the progression of ARMD and resulted in fewer neovascular events. Large doses of zinc, however, may prove more harmful than helpful. Excessive doses of zinc can interfere with the functioning of important metalloenzymes such as superoxide dismutase. Large doses of zinc exceeding 25mg per day may also lead to abnormally high cholesterol levels and cholesterol imbalance. Zinc levels of above 50mg or more have been shown to decrease HDL cholesterol (the "good" form of cholesterol). Therefore, only moderate doses of zinc should be taken in an attempt to delay or prevent the clinical signs of ARMD. (Note: A large scale efficacy study evaluating the individual antioxidant nutrients for the ability

to halt the progression of ARMD is currently underway).[49]

Age-related macular degeneration is an ocular disease which will only increase in incidence with an increase in mean age. Therefore, it is important that as a primary eyecare practitioner one has a sound understanding of age-related macular degeneration; its diagnosis, treatment, and management. Hopefully, with the current trend towards investigational forms of therapy, one day soon the etiology behind this disease will be thoroughly understood and a cure may be found (or at least a definitve method for halting its progression). However, until a cure is found, one needs to have a good understanding of low vision devices that may be beneficial to the ARMD patient as well as an understanding of the psychological ramifications of this disease on the patient's psyche.

Testing for the Amsler Grid: Adapted from Clinical Procedures in Optometry. Eskridge, Amos, Bartlett, 1991.

Figure 1

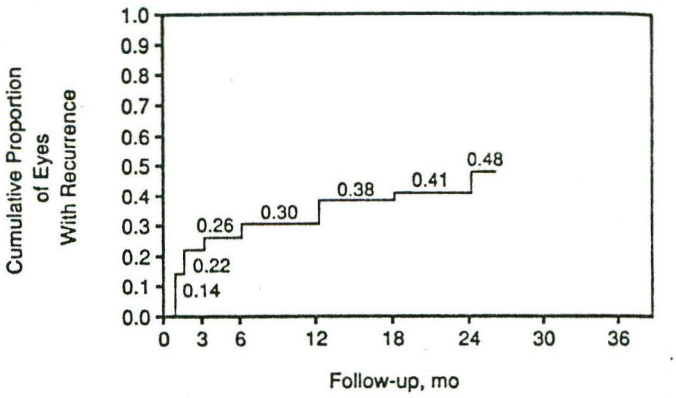


*NOT TO SCALE
(large square corresponds to 1° of visual field)

Questions to be asked:

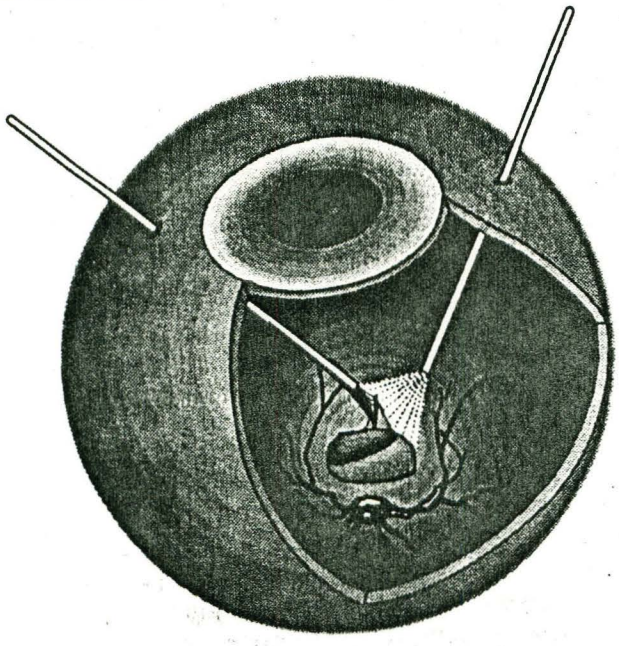
1. Can you see the central small dot?
2. Can you see all four sides and all four corners of both the larger and smaller squares?
3. Are any of the small squares blurry or missing on any part of the grid?
4. Do any of the left-to-right or up-and-down lines that make up the squares appear wavy or bent?
5. Is any part of the grid shimmering, flickering, or colored?

Figure 2



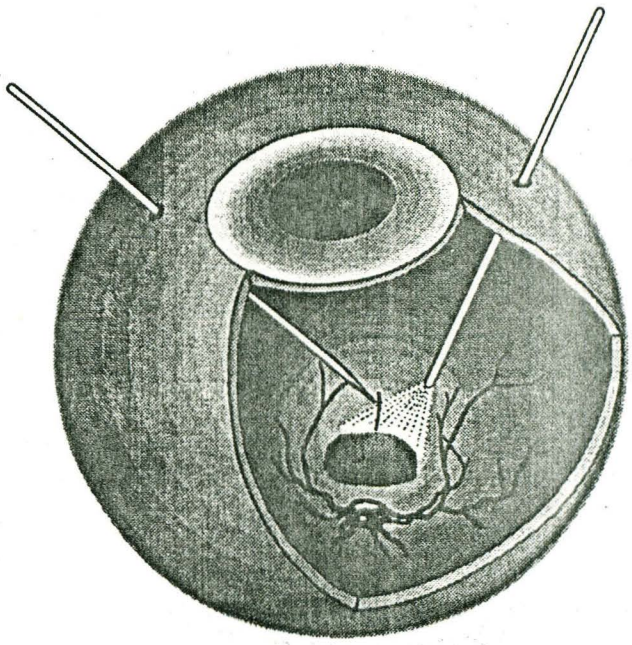

—Proportion of eyes in which recurrent neovascularization had developed by each specified time.

Figure 3



**Diagramatic representation of removal of subretinal CNVM with surgical forceps.**

Figure 4



**Diagramatic representation of retinotomy. The incision should attempt to follow the horizontal raphe to limit damage to the nerve fiber layer. Care must also be taken to protect the perifoveal capillary net.**

At-home testing procedures:

1. Hold the grid 12 inches away from your eyes while wearing your reading glasses.

2. Cover your noninvolved eye (right or left or one at a time if both eyes have the aging changes).

3. Look directly at the central small dot at all times.

4. If you notice any (new or recent) missing or distorted areas, mark them with a pencil.

5. Call the doctor's office as soon as possible to report the new changes. Bring the marked grid with you when you come to the office.

Note: Instructions should be in large print for the visually impaired patient.

Table 1: Source: Journal of the American Optometric Association, volume 59, number 5, May 1988, p.388.

**Table 1: Comparison of fundus lenses**

| | Hruby | Volk 90 | Goldmann 3-mirror lens | Krieger |
|---|---|---|---|---|
| Field of view | Small | Largest | Large | Larger |
| Image | Virtual erect | Real inverted reversed | Virtual erect | Virtual erect |
| Surface reflections | Many | Variable | Variable | Variable |
| Patient tolerance | Good | Good | Variable | Variable |
| Stereopsis | Good | Excellent | Excellent | Excellent |
| Approximate cost | $100–250 | $180 | $196 | $150 |
| Photodocument | Poor | Excellent | Very good | Very good |

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