Age related macular degeneration (AMD) is the most common cause of blindness among people over 60 years of age and represents a major worldwide public health crisis. Exactly why it develops is not known. The disease is frustrating because currently there are very few treatment options and no proven preventive therapy.

Demographics
AMD is a widespread condition in the elderly which is increasing. According to Framingham data: AMD may affect as many as 20% of people age 65 and over, compared with less than 2% of people aged 52 to 64.

Types
Two distinct types –

Nonexudative or dry
Exudative or wet

Each representing a different stage of the same disease process.

AMD dry type
Nonexudative macular degeneration also called "dry," atrophic, or non-neovascular macular degeneration. The dry type carries a better prognosis. The hallmark of dry macular degeneration is small, round, white-yellow lesions in the macula, called drusen.

AMD wet type
Exudative macular degeneration also called "wet" or neovascular degeneration. Causes severe visual deterioration faster than the dry form.

The pathogenesis of the wet form is formation of aberrant choroidal angiogenesis i.e. neovascularization. The exact mechanism for the formation of these new vessels is unknown but is believed to involve damage to Bruch's membrane, presumably by drusen. The drusen allow an angiogenic stimulant (such as vascular endothelial growth factor) to promote the growth of underlying choroidal blood vessels into the sub retinal space and retina. These tufts of neovascularization are fragile and have a propensity to leak and bleed, eventually forming a fibro vascular scar and resulting in irreversible vision loss.

Vision Loss
The cause of vision loss in patients with dry macular degeneration is atrophy of the retinal pigment epithelium and the overlying photoreceptor cells. In wet or exudative type the macula degenerates when capillaries proliferate under the RPE, sometimes growing into the sub retinal space. These capillaries leak leading to RPE detachment and they eventually bleed leading to scar formation in the macula destroying central vision.
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**Signs and Symptoms**
AMD are relatively few and should be immediately recognizable.

The classic symptoms are decreased central visual acuity, metamorphopsia and perhaps a central scotoma.

Dry AMD patients may have no symptoms

Ophthalmoscopy - Macular examination clinically is enough to come to a diagnosis. The use of slit lamp bio-microscopy with contact or non-contact lenses is the mainstay. Direct ophthalmoscopic examination is also valuable.

**Dry type**
- *Early signs* - yellow-white, round, macular drusen.
- *Late signs* - fibro vascular scarring, hemorrhage, atrophy.

**Wet type**
- *Early signs* - focal macular edema with underlying dirty grayish membrane at choroidal level which may have surrounding hemorrhages. May also present with a serous macular detachment.
- *Late signs* - established macular edema with sub retinal hemorrhage and exudation. Any of these findings should prompt an urgent referral to a retina specialist.

**Angiographic Diagnosis**

**Fluorescein Angiogram (FA)**
The hallmark of diagnosis and treatment of choroidal neovascularization.

- FA often pinpoints the location and extent of nonvascular membranes and can guide laser photocoagulation.
- Unfortunately, only about 13% of angiograms show a treatable localized lesion, or "classic" choroidal neovascularization. The other 87% show diffuse, poorly defined, hyperfluorescent lesions that are not amenable to laser photocoagulation. These images are called "occult" choroidal neovascularization

**Indocyanine Green Angiogram (ICGA)**
- Indocyanine green (ICG) dye has recently proved effective for demarcating poorly defined or occult fluorescein angiographic areas of neovascularization.
- ICG dye permits better visualization through overlying blood and serous sanguineous fluid which are substances often responsible for blocked visualization on fluorescein angiograms.
- ICG angiography offers potential for increasing early detection of macular degeneration amenable to laser photocoagulation.

**Proven Treatment**
- For dry AMD - Currently no treatments or preventive measures, other than low vision aids.
- For wet AMD - The clinically proven treatment for wet AMD is macular laser photocoagulation to the choroidal neovascular tissue and photo dynamic therapy. The guidelines for laser photocoagulation for choroidal neovascularization were outlined in a series of studies, "macular photocoagulation study group".

**Amsler Grid**
Single most important tool in detecting progress of AMD. It is an objective test to find out image distortion. All ophthalmologists must be familiar with its use and it must be recommended to all patients with AMD.
Laser Photocoagulation
Laser photocoagulation is a destructive treatment in which tissue is ablated by heat. Since subfoveal neovascularization lies directly below the fovea, laser treatment inevitably destroys this important tissue.

Photo-Dynamic Therapy (PDT)
The current form of treatment for WET AMD with classical choroidal neovascular membranes. This treatment has revolutionized AMD management in the last few years and so far offers the best available treatment modality. PDT is a dye and laser combination therapy. A Photosensitive dye and a non thermal laser

» Injected dye localizes in neovascular tissue then the tissue is subjected to laser. This activates the dye leading to development of singlet oxygen and other free radicals, which damage nearby cells including endothelial cells lining the neovascular tissue. A thrombus is produced that closes neovascular vessels.

» Theoretically, the underlying abnormal blood vessels can be selectively destroyed without damaging the overlying sensory retina, which always happens in thermal laser photocoagulation.

Surgery
Many AMD patients are offered the choice of surgery. There are basically two modalities - submacular surgery -performing a vitrectomy with retinotomy, entering the subretinal space, and excising the neovascular membranes. This does not allow central vision to return but prevents future hemorrhage and destruction of more macular tissue as the lesion is excised out of the eye. Retinal translocation - rotating the whole retina or shifting the macula a few degrees in an attempt to create a new fovea.

Alternative treatments
» Proton beam irradiation
» Drugs - still under investigation, oral zinc may be useful, but clinical data limited. Several drugs are in early stages of investigation, interferons, angiogenesis inhibitors, and nerve growth factors

Focusing on Prevention
» The outer retina is rich in polyunsaturated fatty acids, which are easily oxidized by free-radicals and singlet oxygen produced in the course of normal metabolism and also through the effects of light which may cause macular damage.

» Some vitamins function as anti-oxidants, chemicals that work against this activated oxygen, and perhaps protect the macula from damage.

Antioxidants and AMD
» It is claimed that anti-oxidant vitamins (vitamin A, C and E) can help slow down macular degeneration and other aging factors.

» The role of vitamins, minerals, and antioxidants in the prevention of macular degeneration has conflicting information.

» High serum levels of vitamins E, A, and C, as well as zinc, may be beneficial.

Carotenoids and AMD
» Because nutritional factors may play a role in AMD, Seddon et al. decided to correlate the disease with dietary antioxidant intake in subjects participating in the NIH eye disease case-control study.

» Enrolled were 356 case subjects with AMD (56% female; average age 71) and 520 control subjects with other eye diseases (55% female; average age 68).

Study Results
» Statistically significant and apparently linear trend for a reduction in risk for AMD (estimated 43% reduction) with increasing amounts of carotenoids in the diet.

» Of the carotenoids, lutein and zeaxanthin were the most strongly associated with reduced risk of AMD - obtained primarily from dark green, leafy vegetables. Eating spinach and collard greens five or more times a week markedly reduced the risk of AMD (odds ratio 0.14).
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Oxidation and Tissue Damage
» Some normal metabolic processes produce reactive by products which can do damage if not kept under control. Among these reactive by products are three forms of oxygen: molecular oxygen, peroxide and superoxide.
» These all react by taking electrons from other molecules, a type of reaction called oxidation.
» The body prevents damaging oxidations by providing compounds with which the oxidants can react harmlessly - antioxidants.

Aging and Antioxidants
Researchers have found that as we get older, our bodies’ systems for controlling potentially harmful oxidants by reacting them with antioxidants become less effective. The enzyme that catalyzes the reactions may not be as abundant.

Those with the highest levels of the antioxidants selenium, vitamin C, and vitamin E may have a 70% lower risk of developing macular degeneration³.

People who eat fruits and vegetables high in beta-carotene, another antioxidant, are also at low risk. Goldberg J, Flowerdew G, Smith E, et al. Factors associated with age-related macular degeneration¹.

Recommendations
Some doctors of natural medicine recommend antioxidant supplements to reduce the risk of macular degeneration; reasonable adult levels include 200 mcg of selenium, 1,000 mg vitamin C, 400 IU of vitamin E, and 25,000 IU of natural beta-carotene per day.

Recent Studies
» The potential effects of vitamins and age related macular degeneration.⁵
» Associations of antioxidant enzymes with cataract and AMD. The POLA study.⁶
» Antioxidant vitamins and age related eye disease⁷.

Conclusions
» Oxidative mechanisms may play an important role in the etiology in delaying the onset of cataract and AMD.
» Evidence from epidemiological studies support the role. But it has not yet been possible to conclude the assumption.
» Well designed randomized trials are required to evaluate definitely the benefit of the supplementations.
» A summary of the epidemiological evidence suggests that it is prudent to consume diets high in vitamins C and E and carotenoids, particularly the xanthophylls as an insurance against the development of cataract and AMD⁸.

References