MACULAR DEGENERATION **MEDICAL APPENDIX**

DEFINITION

1. Macular degeneration refers to progressive deterioration of the central neurosensory retina and underlying retinal pigment epithelial cells, causing central vision loss. As understanding of other causes of macular disease has grown the term has largely become confined to the disorder known as age-related macular degeneration (AMD). However, a number of other conditions may still be included under this classification, including macular holes, epiretinal membrane, central serous chorioretinopathy, cystoid macular oedema, toxic maculopathies and some hereditary diseases of the macula.

2. **Age-related macular degeneration (AMD)** This is the leading cause of severe vision loss in developed countries. Its prevalence gradually increases after the age of 50, being just over 1 per cent in those of 65 or less, 6 per cent in the 65-74 age group, and almost 20 per cent in people of 75 and over. It is usually bilateral.

3. There are very few studies evaluating the incidence of the condition but it is thought to be in the region of 2-4 per cent in the fourth and fifth decade of life, increasing to 5-10 per cent in those over 75 years.

4. The condition is categorised by non-neovascular and neovascular forms. Both are preceded by the formation of macular drusen (degenerative deposits of lipofuscin under the retina).

5. Non-neovascular AMD (the so-called non-exudative or dry form) is characterised by abnormalities of the retinal pigment epithelial layer including hyperpigmentation and atrophy.

6. Neovascular or exudative AMD (the wet form) may be accompanied by any or all of the features of the non-neovascular form, but its hallmark is the growth of new blood vessels (neovascularisation) in the choroid layer. This is often accompanied by intraretinal haemorrhage and other related manifestations, including detachment of the retinal pigment epithelial layer and subretinal scarring.

7. **Macular hole** In this condition, a full-thickness depletion of the retinal tissue occurs in the centre of the macular. The condition is usually unilateral, and occurs in otherwise healthy individuals in the sixth or seventh decade of life, although it may occur as early as the third decade. Women are affected more frequently than men in a ratio of 2:1.

8. **Epiretinal membrane** In this condition, a fibrocellular membrane proliferates on the inner surface of the retina. It causes traction on the macula and macular oedema.

9. **Central serous chorioretinopathy** This disorder is characterised by a retinal detachment in the macular area which is underlain by a collection of serous fluid. Typically it affects men in the age range 20-50. It does occur in older individuals but may then be difficult to distinguish from age-related macular degeneration.

10. **Cystoid macular oedema** This condition is a response of the retina to a number of possible insults, including ocular inflammation, infections and surgery. Fluid accumulates in a cystic pattern in the outer layer of the central macula.

11. **Toxic retinopathies** This is a diverse group of conditions caused by systemically administered drugs. They are often accompanied by retinal atrophy, crystal deposition and a 'bull's-eye' appearance of the macula itself.

12. **Hereditary macular dystrophies** Some less common forms of macular degeneration have a clear hereditary basis and many occur in a younger age group. They include Stargardt disease, Best disease and Sorsby fundus dystrophy. They possess important histopathological similarities to AMD.

CLINICAL MANIFESTATION

13. **Age-related macular degeneration** Patients usually present with blurred or distorted vision (metamorphopsia) in one or both eyes, but the condition may at first be asymptomatic. The onset may be slow or sudden, and is painless. Decreased reading ability, especially in dim light, and impaired dark adaptation are common complaints. Reduced contrast sensitivity also occurs and carries important functional implications.

14. Treatment is only occasionally of value in temporarily arresting the condition. It is not preventable and is generally progressive.

15. **Macular hole** This condition causes a painless central visual distortion or blurring. Typically it goes unnoticed by the patient until the contralateral eye is covered. Vision deteriorates over a period of months, then usually becomes stable. 50% of early macular holes improved spontaneously.

16. **Epiretinal membrane** Symptoms depend on the thickness of the abnormal membrane and the degree of retinal distortion. Blurring and distortion of vision are usual. Conservative treatment is recommended for mild cases; surgery is usually successful in more advanced cases, especially if performed early.

17. **Central serous chorioretinopathy** This condition usually presents with blurred or distorted vision and sometimes impaired dark adaptation. It is managed by laser photocoagulation, which reduces the duration of the serous detachment. Since most episodes resolve spontaneously laser treatment is reserved for patients who fail to improve after 4-6 months.

18. **Cystoid macular oedema** This condition causes reduced central visual acuity. Topical anti-inflammatory drugs are usually employed, or topical corticosteroids. In unrelenting cases, surgery may be required.

19. **Toxic retinopathies** In general, patients who are suffering from drug-related and other toxic retinal damage will complain of reduced and/or blurred vision. Early withdrawal of the causative agent is essential, and close screening of patients being treated with substances known to cause the condition.

20. **Hereditary macular dystrophies** In these conditions there is retinal cell aging and cell death. Symptoms of visual loss usually begin in childhood or the teens, although in some conditions such as fundus flavimaculatus, Best's disease and adult vitelliform degeneration the onset of visual symptoms occurs at a later age. Central loss of vision is the usual presentation.

AETIOLOGY

21. **Age-related macular degeneration**

21.1. Sociodemographic risk factors

21.1.1. **Age** All studies show that the prevalence, incidence and progression of AMD rise steeply with increasing age. The prevalence of moderate to advanced AMD doubles with each decade after the age of 60.

21.1.2. **Sex** Men have a slightly lower prevalence of AMD than women.

21.1.3. **Race and ethnic origin** Caucasians are more frequently affected. Age-related macular changes are also seen in people of Afro-Caribbean and Asian origin, however advanced age-related macular changes and AMD itself are much less frequent in these groups. These observations provide support for a possible genetic component to the disease.

21.1.4. **Socioeconomic status** No association has been found between socioeconomic status and AMD.

21.2. Ocular risk factors

21.2.1. **Iris colour** Some investigators have suggested that greater quantities of melanin in the eye may protect against postulated light-induced retinal damage. To date the evidence for an association between iris colour and AMD is inconclusive.

21.2.2. **Refractive error** Several case-controlled studies have identified an association between long-sightedness (hyperopia) and AMD, although other research has not confirmed the link. It has been found that eyes with a larger cup:disk ratio i.e. short sighted (myopic) eyes had a reduced risk of exudative AMD.

21.2.3. **Lens opacities** No consistent relationship has emerged between the presence of cataract and AMD. However there is some evidence that surgical cataract removal may increase the likelihood of subsequent AMD.

21.2.4. **Sunlight** A number of large studies have investigated this complex subject, with conflicting results. The difficulties include the measurement of lifetime exposure, and potential confounding variables such as sun sensitivity and sun avoidance behaviour. Inconsistencies also arise in the consideration of different populations, varying intensity of exposure and different definitions of the stages of AMD.

21.2.5. So far, the evidence does not support a link between exposure to ultraviolet radiation and the risk of AMD.

21.3. **Nutritional factors**

21.3.1. **Oxidative damage** The retinal tissues are exposed to light and to high levels of oxygen, and the membranous layers contain high concentrations of polyunsaturated fatty acids: all three are considered to be factors potentially leading to oxidative damage. The action of antioxidant substances in preventing AMD has therefore been investigated but as yet it is still unclear what the precise linkage is between oxidation-induced events and the onset and progression of AMD.

21.3.2. **Cholesterol levels and dietary fat intake** There is some evidence relating cholesterol level to exudative AMD and a possible association between AMD and dietary fat intake may indicate a relationship with atherosclerosis.

21.4. **Cardiovascular-related factors**

21.4.1. **Hypertension** Some workers have postulated a relationship between hypertension (especially if prolonged) and AMD but no definite association has yet been confirmed.

21.4.2. **Cardiovascular disease** There is some evidence of an association between atherosclerosis and AMD. Age-related lipid infiltration of the walls of choroidal blood vessels may cause decreased compliance and reduced choroidal perfusion.

21.5. **Hormonal factors** Although evidence is sparse, a protective effect of oestrogen on AMD cannot be ruled out. Some studies have shown a marked decrease in the risk of neovascular AMD among post-menopausal women who used hormone replacement therapy (HRT).

21.6. **Hereditary factors** There is increasing evidence that AMD may be a complex genetic disorder in which one or more genes contribute to an individual's susceptibility to the development of the condition. Twin and family studies as well as population-based genetic epidemiological methods have convincingly demonstrated the importance of genetic factors in AMD although the mechanisms remain unresolved.

21.7. **Smoking** There is a strong positive association between smoking and both wet and dry AMD. The risk appears to increase as pack years increase (1 pack year = 20 cigarettes a day for 1 year). The risk of AMD remains elevated for many years after smoking cessation. Many studies suggest that smoking is an important, independent, avoidable cause of AMD and the only known modifiable risk factor.

22. **Macular hole** The majority of these cases occur in eyes that have no previous ocular pathology and the aetiology in most cases is unknown. However a macular hole can occur after blunt trauma and the condition may be associated with other retinal disorders such as retinal detachment. It may also be due to hypertensive retinopathy and proliferative diabetic retinopathy.

23. **Epiretinal membrane** The condition is frequently primary, i.e. idiopathic. Secondary causes include:

    23.1. Retinal procedures, e.g. detachment surgery, photocoagulation therapy, cryotherapy.

    23.2. Retinal vascular disease.

    23.3. Long-standing vitreous haemorrhage.

    23.4. Intraocular inflammation.

    23.5. **Blunt or penetrating ocular trauma**.

24. **Central serous chorioretinopathy** Increasing evidence implicates impaired circulation in the choroid layer as the cause of this condition. However the underlying aetiology is as yet unexplained.

25. **Toxic retinopathies** A variety of drugs may be responsible for retinal damage.

    25.1. **Chloroquine, hydroxychloroquine** Chloroquine was used first for the prophylaxis and treatment of malaria and the closely related hydroxychloroquine may be used in the treatment of certain connective tissue diseases such as rheumatoid arthritis and systemic lupus erythematosus. Both drugs may cause pigmentary changes and circulatory abnormalities in the eye. If the dose of these drugs is kept below a recommended level, ocular complications are rare.

    25.2. **Thioridazine** This antipsychotic drug was found to cause retinal pigmentary changes of rapid onset. At the dosage now recommended this toxic effect rarely occurs.

    25.3. **Tamoxifen** This non-steroidal oestrogen antagonist is used in the treatment of breast cancer. Macular changes are very rare at the advised dosage.

    25.4. Other drugs which may cause retinal injury include niacin (vitamin B6) used at one time in high dosage to lower serum cholesterol; canthaxanthine, an artificial tanning agent and didanosine, an antiretroviral drug.

26. **Hereditary Macular Dystrophies** Continuing research has helped to identify some of the genetic defects implicated in the various inherited macular dystrophies. However many of these conditions are extremely rare and much work remains to be done to develop an accurate system of classification.

CONCLUSION

27. Macular degeneration is a term which is used to embrace a number of conditions in which there is a process of chronic degenerative change in the macular region of the retina. In most there is impairment of central vision.

28. Age-related macular degeneration is the commonest variety, mainly affecting older individuals. The aetiology of the condition remains to be fully clarified, but it is likely that a genetic basis underlies the degenerative process. Smoking is the only known modifiable risk factor. There is currently no effective treatment.

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