

About Genetics, Lifestyle and Age-Related Macular Degeneration

Michael Waisbourd MD and Anat Loewenstein MD

Department of Ophthalmology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
Affiliated to Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

Key words: age-related macular degeneration, ethnicity, genetics, environment

IMAJ 2007;9:674–675

Age-related macular degeneration is the leading cause of blindness and visual impairment in the developed world [1]. In their interesting work that appears in the current issue of IMAJ, Abu Asleh et al. [2] suggest that AMD is less common in Arabs compared with Jews in the city of Jerusalem. They compared the number of patients eligible for certification of blindness and the number of patients who underwent photodynamic therapy for neovascular AMD and provided additional convincing evidence that ethnic background plays an important role as a risk factor for advanced AMD. This finding coincides with other studies that describe wide variations in AMD prevalence among different ethnic groups, ranging from 1% in black Africans older than 65 years to 100% in 90 year olds in Finland [3]. The reasons for such huge differences may be both non-modifiable risk factors, such as genetic background, and modifiable ones such as differences in lifestyle.

Unfolding the genetics of AMD

Family history is a well-known risk factor for the development of AMD [4]. This fact motivated clinical and basic science research in order to uncover the underlying genetic factors influencing the disease. For instance, twin studies found that the concordance rate for AMD in monozygotic twins was almost double that of dizygotic twins [5]. Genetic studies identified the most important genetic factor to be the complement factor H (*CFH*) gene, a major inhibitor of the complement system [6]. A common coding variant of this gene significantly increases the risk for AMD and very likely explains approximately 43% of AMD in older adults [6,7]. Thus, the genetic factor alone may be the decisive factor in determining disease prevalence in any given ethnic group.

Diet and AMD

There is growing evidence that diet is a risk factor for AMD [8,9]. Several theories have suggested that the pathogenesis of AMD is multifactorial and may involve oxidative stress, angiogenesis, and inflammatory or immune responses, all of which may be influenced by diet.

A high dietary intake of anti-oxidative agents, such as beta carotene, vitamins C and E, and zinc, was associated with a substantially reduced risk of AMD in elderly persons living in a middle-class suburb of Rotterdam, The Netherlands [8]. An

Australian study noted that the consumption of fish, which is rich in omega-3 fatty acids, may protect against AMD as well [9]. Dietary habits are inevitably related to ethnicity, with different social groups having different dietary preferences. While some groups may be accustomed to and prefer a healthier "AMD-protective" diet, others may choose to consume, or have no choice but to consume, less nutritious substances. Yuzawa et al. [10] reported that the number of exudative AMD patients was estimated to have almost doubled over the 6 year period since the initial survey in 1987. It is well known that there have been drastic changes from traditional Japanese to westernized diets over the years, and it is tempting to draw a parallel between these two phenomena.

Cigarettes, alcohol and AMD

Both cigarette smoking and alcohol consumption are modifiable risk factors for developing AMD. Evans and collaborators [11] speculated that smoking alone may be attributing to approximately 28,000 cases of the disease in the United Kingdom. Some studies suggested that certain alcoholic beverages are associated with up to a threefold risk for developing advanced AMD, but the issue is controversial [12]. In terms of their relation to ethnicity, both habits cross borders and ethnic lines, and certain subgroups are at greater risk than their ethnic brethren. For instance, smoking has been universally associated with poorer high school educational achievement, lower graduation rates, and limited professional aspirations [13]. Thus, a genetic advantage could be challenged by a disadvantaged lifestyle.

Obesity and other modifiable risk factors for developing AMD

The growing epidemic of obesity may be related to more than cardiovascular, endocrine and psychological morbidity: some reports have suggested that there may be an increased risk for progression to advanced AMD in individuals with larger waist circumferences and higher waist-hip ratios [14]. Moreover, physical activity may have a beneficial effect on the progression to advanced AMD [14], and obesity has strong social and environmental origins that may well be affected by ethnicity. Other environmental insults, such as serum cholesterol, hypertension, sunlight exposure, and many others were associated with AMD pathogenesis as well [15] and they, too, are linked to ethnic influences.

AMD = age-related macular degeneration

Different characteristics of AMD according to ethnic background

Not only does the prevalence of the disease differ among various ethnic groups, but several studies have revealed new variants of AMD that characterize specific populations. The Inuit population in east Greenland was shown to have a "Greenlandic type" of AMD in the form of reticochoroidal atrophy, which is characterized by peripapillary and central retinochoroidal atrophy and sclerosis resembling a recumbent Russian matushka doll [16]. In a study conducted in Fukushima, Japan, neovascular AMD in Japanese patients had different demographic features than those reported for Caucasian patients: the Japanese had a preponderance of polypoidal choroidal vasculopathy, male gender, unilaterality, and absence of drusen in the second eye [17].

In conclusion, different ethnic groups can have significantly different genetic patterns and can vary considerably in their lifestyles in terms of diet, cigarette smoking, alcohol consumption, etc. All these may explain, in part, the differences in the prevalence of AMD between Jews and Arabs in Jerusalem, as presented by Abu Asleh et al. [2]. A population-based survey is required to further estimate the overall prevalence of AMD among these ethnic groups in Israel.

Acknowledgment. Esther Eshkol is thanked for editorial assistance

References

- Bressler NM. Age-related macular degeneration is the leading cause of blindness. *JAMA* 2004;291:1900–1.
- Abu Asleh S, Chowers I. Ethnic background as a risk factor for advanced age-related macular degeneration in Israel. *IMAJ* 2007;9: 656–8.
- Moeller SM, Mares JA. Ethnic differences in diet and age-related maculopathies. *Int Ophthalmol Clin* 2003;43:47–59.
- Klein R, Peto T, Bird A, Vannewkirk MR. The epidemiology of age-related macular degeneration. *Am J Ophthalmol* 2004;137:486–95.
- Hammond CJ, Webster AR, Snieder H, Bird AC, Gilbert CE, Spector TD. Genetic influence on early age-related maculopathy: a twin study. *Ophthalmology* 2002;109:730–6.
- Haines JL, Hauser MA, Schmidt S, et al. Complement factor H variant increases the risk of age-related macular degeneration. *Science* 2005;308:419–21.
- Patel N, Adewoyin T, Chong NV. Age-related macular degeneration: a perspective on genetic studies. *Eye* 2007 May 11 (Epub ahead of print).
- van Leeuwen R, Boekhoorn S, Vingerling JR, et al. Dietary intake of antioxidants and risk of age-related macular degeneration. *JAMA* 2005;294:3101–7.
- Smith W, Mitchell P, Leeder SR. Dietary fat and fish intake and age-related maculopathy. *Arch Ophthalmol* 2000;118:401–4.
- Yuzawa M, Tamakoshi A, Kawamura T, Ohno Y, Uyama M, Honda T. Report on the nationwide epidemiological survey of exudative age-related macular degeneration in Japan. *Int Ophthalmol* 1997;21:1–3.
- Evans JR, Fletcher AE, Wormald RP. 28,000 Cases of age related macular degeneration causing visual loss in people aged 75 years and above in the United Kingdom may be attributable to smoking. *Br J Ophthalmol* 2005;89:550–3.
- Fraser-Bell S, Wu J, Klein R, Azen SP, Varma R. Smoking, alcohol intake, estrogen use, and age-related macular degeneration in Latinos: the Los Angeles Latino Eye Study. *Am J Ophthalmol* 2006;141:79–87.
- Braun BL, Hannan P, Wolfson M, Jones-Webb R, Sidney S. Occupational attainment, smoking, alcohol intake, and marijuana use: ethnic-gender differences in the CARDIA study. *Addict Behav* 2000;25:399–414.
- Seddon JM, Cote J, Davis N, Rosner B. Progression of age-related macular degeneration: association with body mass index, waist circumference, and waist-hip ratio. *Arch Ophthalmol* 2003;121:785–92.
- Chamberlain M, Baird P, Dirani M, Guymer R. Unraveling a complex genetic disease: age-related macular degeneration. *Surv Ophthalmol* 2006;51:576–86.
- Ostenfeld-Akerblom A. Age-related macular degeneration in Inuit. *Acta Ophthalmol Scand* 1999;77:76–8.
- Maruko I, Iida T, Saito M, Nagayama D, Saito K. Clinical characteristics of exudative age-related macular degeneration in Japanese patients. *Am J Ophthalmol* 2007;144:15–22.

Correspondence: Dr. M. Waisbourd, Dept. of Ophthalmology, Tel Aviv Sourasky Medical Center, 6 Weizmann Street, Tel Aviv 64239, Israel.
Phone: (972-3) 697-3408
Fax: (972-3) 697-3870
email: mwaisbourd@hotmail.com