MACULAR DEGENERATION: HOW BIG IS THE PROBLEM?

E. Cheraskin, MD, DMD
Birmingham, Alabama

Almost every report on macular degeneration begins with a somber reminder that macular degeneration is the single most common cause of blindness in the elderly in the United States and Europe. Almost every report also confirms that there is no known successful approach to slowing, stopping, reversing, or preventing this syndrome. In the light of these devastating statements, it is difficult to explain the paucity of information about the disease process in general and its epidemiologic implications in particular. What little is known deals with prevalence rates; no figures are available regarding the incidence. Additionally, almost without exception, the prevalence numbers are based on the assumption that macular degeneration is a binomial (black and white) problem. However, macular degeneration, like all chronic diseases, exists in a potentially infinite number of shades of gray. Hence, when viewed as an achromatic continuum, macular degeneration is more prevalent than generally believed. Recognizing this disorder earlier invites the greater possibility of a cure or primary prevention. (*J Natl Med Assoc.* 1992;84:873-876.)

Key words • macular degeneration • blindness

Most of us have heard the time-honored and oft-cited saying, "Those who have not read history are destined to repeat it." In this regard, past events have emphasized that unsolved medical issues are, in fact, puzzles made up of many shapes and sizes. Part of the puzzle deals with the scope of the problem. In the case of

macular degeneration, the public cry is, "How many people suffer with macular degeneration, and is it getting worse, better, or staying the same?" These very same questions are being directed at the scientific experts in different terminology: What are the prevalence and incidence rates?

Prevalence may be defined as the number of persons at a given time and in a stated place who suffer with the affliction. In other words, the prevalence rate simply provides the percentage of individuals afflicted in terms of the total population. Incidence represents the number of persons afflicted or expected to be affected at a given place and time. This same number given as a percentage of the total sample in that area and time is referred to as the incidence rate.

INCIDENCE AND PREVALENCE OF MACULAR DEGENERATION

In 1978, the World Health Organization's (WHO) Advisory Meeting on Program Development for the Prevention of Blindness emphasized the need to collect information on the number of blind people and their geographical distribution, as well as on the main causes of blindness.[1] Following a Task Force on Data on Blindness meeting in November 1978, a compilation of information available to WHO on the prevalence and causes of blindness throughout the world was prepared. A Blindness Data Bank was subsequently set up in the WHO Programme for the Prevention of Blindness in Geneva.

Since the outset, one difficulty in managing the Blindness Data Bank has been the multiplicity of definitions used by different countries... The Task Force on Data on Blindness considered it impossible to reach an accurate total number of blind in the world... More than 150 references have been analyzed for a total of 90 countries (or territories) as a basic source of information on the worldwide prevalence of blindness.[1]

Unfortuntately, the report contributes very little to the definition of blindness. It is therefore not surprising that it also does not enrich the definition of blindness as it relates to macular degeneration.

A subsequent literature search of publications purporting to deal with the problem of epidemiology revealed only one article published in the last 10 years. A more extensive search revealed the following studies, which are discussed in chronological order.

THE FRAMINGHAM STUDY

In 1948, the National Heart Institute initiated a survey of a representative sample of the adult population, ages 30 to 59, in Framingham, Massachusetts. About 6500 persons participated in what became known as the Framingham Heart Study.[2]

In 1973, the approximate 4000 remaining heart study participants were now close to 52 to 85 years of age. Incidentally, this is the age range of rapidly increasing prevalence of the four most common ocular disorders, including macular degeneration. This subset of the original group constitutes the Framingham Eye Study. The data discussed here were collected between February 1973 and February 1975.

There are a number of points that warrant special attention. First, 5.7% of the Framingham subjects had macular degeneration in one or both eyes. There was a sixteenfold increase (from 1.2% to 19.7%) in the prevalence of macular degeneration from the youngest age group to the oldest. Second, as far as it is possible to ascertain, there has been no follow-up on the prevalence of this disorder since 1973. Third, no incidence figures are cited. Finally, in this study, macular degeneration was defined as macular or posterior pole changes, not congenital or secondary to other causes, accompanied by visual acuity of 20/30 or worse in the same eye. This should be emphasized because these criteria are now generally viewed as the gold standard. Therefore, two characteristics of macular degeneration are specific macular findings and significant, albeit arbitrary, visual loss.

THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

Continuing in this chronological vein, the National Health and Nutrition Examination Survey[3] (NHANES I) was intended to measure the health and nutritional status of a cross-sectional sample of the US population. As part of this project, a detailed ophthalmologic examination was included and conducted between April 1971 and October 1972.

A comparison of the Framingham Eye Study and NHANES I discloses two major differences. First, NHANES I is a much larger ophthalmologic survey with 10 000 subjects compared with 4000 for the Framingham Eye Study. Second, whereas the Framingham Eye Study originally began as a heart study, NHANES I was designed to look at a representative sample of the entire population from its inception.

On the other hand, these two projects exhibit some common characteristics. The NHANES I and the Framingham studies remain the two largest international surveys, and their ophthalmologic aspects have only been publicized on one occasion. Both studies were government sponsored and actually were conducted at about the same time. Both studies provided only prevalence (no incidence) numbers. Both studies indicate that macular degeneration is time-related because in both studies, the prevalence figures increased with age. Also, it will come as no surprise that the findings are similar since the definitions for macular degeneration were essentially the same. Finally, it was discovered that the prevalence ranged from 0.3% in the youngest subset (25 to 34 years old) to 8.5% in the oldest group (65 to 74 years old).

THE COPENHAGEN CITY HEART PROGRAM

In one sense of the word, the Copenhagen Study[4-6] resembles the Framingham project as both were originally designed to ascertain the prevalence of heart disease and simply took on the additional responsibility for a visual analysis. The Copenhagen Heart Study was conducted from 1976 to 1978 and again from 1981 to 1983. It was designed to consider a random sample of 20 000 individuals out of a total population of 90 000 citizens from the Osterbro district of Copenhagen. Twenty-four percent of the sample were 60 to 80 years of age. One thousand of these subjects received an ophthalmologic examination from a random population according to an age and sex stratification that comprised four different age groups of 250 persons within each category and a male:female ratio of 1:1.

There are several unique features of this survey. First, of the 924 individuals with both maculae examined, 12.2% demonstrated macular pathology causing visual impairment in at least one eye. Second, redefining macular degeneration as being possible without visual loss, the prevalence rose to 28.5% of the population. In other words, recognizing the possible shades of gray of macular degeneration doubles the potential prevalence.

THE NEW ZEALAND PROJECT

Clear around the globe, a study was conducted in New Zealand as part of a medical/nutritional/social investigation of the elderly in Gisborne, New Zealand.[7] A total of 409 randomly selected participants were stratified by age (all study participants who were 80 years and older, one in six participants who were 75 to 79 years, and one in 20 participants who were between 65 and 74 years). These participants were examined in a hospital eye clinic. The estimated prevalence rate of senile macular degeneration was 6.4% ($\pm 1.5\%$) for those 65 years of age and older.

According to the authors, the prevalence in New Zealand under these conditions were lower than the values obtained in the Framingham and therefore also in the NHANES I survey. However, it is postulated that this discrepancy may well be the result of a difference in the definitions of macular degeneration.

THE CHINESE OBSERVATIONS

During the years 1985 and 1986, 1019 persons in different regions of China underwent ophthalmological examinations.[8] The study was intended to determine the possible effects of various racial origins in different geographic environments on macular degeneration. The subjects included 312 inhabitants of Guangzhou, a city in south China; 521 residents of Urumbi, a community in Xingjiang Uighur Autonomous Region, which is located in northwestern China; and 186 inhabitants of Lhasa, which is located on the famous Xirang Plateau (Tibet) in southwestern China.

The subjects were over 50 years of age, with the oldest being 98. It is appropriate to point out that the criteria for diagnosing macular degeneration were closely based on the Framingham Eye Study. Among the 1019 subjects examined, 108 were diagnosed as having macular degeneration for a prevalence of 10.59%. It also was discovered that the prevalence rate was different in the three areas. In the Xirang Plateau (Tibet), the prevalence rate was the highest (15.59%), and in Guangzhou, the rate was the lowest (6.41%) with Urumbi showing an intermediate rate of 11.32%.

Of the epidemiologic projects described thus far, this one shows the most unusual findings differing in the three regions by an order of approximately threefold. It is suggested in this report that the diversity of environmental factors such as sunshine, direct radiation level, oxygen density, and diet, may well explain the different prevalence rates. These potential risk factors will not be enlarged on here.

OTHER REPORTS

There are other less available epidemiologic studies. For example, macular degeneration has been surveyed in India.[9] At the time this article was written, the specifics had not yet been identified.

Also, Hakkinen[10] reported a survey of 546 residents from Turku, Finland. The conclusions, as far as we can determine, suggest the well-known observation of increasing macular degeneration with age. What appears to be most significant is that by the age of 85, 60% of these subjects exhibited symptoms.

WHAT IS THE EPIDEMIOLOGY OF MACULAR DEGENERATION?

There are two concluding points that emerge from these seven epidemiologic studies. First, it is noteworthy that, at least in surveys in industrialized societies, the prevalence rate seems to be remarkably constant. This consistency is even more obvious in the two American studies. Overall, for subjects over 50 years of age, the prevalence is approximately 6% to 8%. Second, there is no question from all of the reported observations that macular degeneration increases with age.

Naturally, the general assumption prevails that constancy implies accuracy. In other words, if everybody cites the same numbers, it is easy to assume that the figures are correct. Interestingly, Leibowitz et al note that "In any epidemiologic study, the observed prevalence is a function of the definitions and procedures used."[2] Consequently, the question arises as to what happens to the prevalence figures when new or different definitions are applied? The simple fact of the matter is that all chronic diseases can be plotted as a continuum—for example, no one goes to sleep nondiabetic and awakens the next morning diabetic. There is no evidence that one is nonarthritic on a given day and suddenly becomes arthritic a matter of hours later. It is likely that this is equally true of macular degeneration. Hence, the immediate questions are: How does one describe the shades of gray of macular degeneration? How many gradations are there between black and white? What happens to the prevalence figures when this continuum is recognized?

Brief mention is made of this type of analysis of the Framingham data by Sperduto and Seigel.[11] From a study of gradations of macular degeneration, they concluded that 50% of 52 + -year-old people show early evidence of this affliction.

In a relatively unsophisticated approach, Vinding[4-6] reexamined the prevalence of macular degeneration with and without significant visual loss. He reported figures of 12.2% for macular degeneration with visual

impairment and 28.5% for macular degeneration without visual impairment. He concluded, ". . . blindness caused by AMD (age-related macular degeneration) only represents the top of an iceberg depicting visual deterioration from AMD."[6]

The most sophisticated approach to the shades of gray of macular degeneration was reported by Neil Bressler and his colleagues at the Wilmer Eye Institute at the Johns Hopkins Hospital in Baltimore.[12] First, their study was designed to devise a grading scheme that would include the earliest fundus changes associated with macular degeneration as well as the drusen characteristics felt to be associated with an increased risk of developing the exudative, more severe vision-impairing forms of this disease. Second, to use this system to determine the prevalence of fundus changes associated with age-related macular degeneration in a population-based study, it was conducted on residents of the eastern shore of Maryland.

A four-point system was developed. Grade one represents minimal drusen increasing to grade four, which represents the most severe category (fundus changes that almost always leads to visual loss).

CONCLUSIONS

There are three conclusions to be drawn from this discussion. First, when one grants that there are shades of gray for macular degeneration, then one must admit that approximately three out of four persons under the age of 50 demonstrate this disorder. Second, it is clear that with advancing age, the prevalence rates are even higher. Finally, this suggests the possibility of prevalence figures of an order of 80% or more of specific populations—a number possibly tenfold greater than generally held.

Literature Cited
1. World Health Organization (WHO). *Available Data on Blindness: Update 1987.* Geneva, Switzerland: World Health Organization; 1987. WHO publication 87.14.
2. Leibowitz H, Krueger DE, Maunder LR, Kahn HA, Ganley JP, Milton RC. The Framingham Eye Study Monograph: an ophthalmological and epidemiological study of cataract, glaucoma, diabetic retinopathy, macular degeneration and visual acuity in a general population of 2631 adults, 1973-1975. *Surv Ophthalmol.* 1980;24(suppl):335-610.
3. Klein BE, Klein R. Cataracts and macular degeneration in older Americans. *Arch Ophthalmol.* 1982;100:571-573.
4. Vinding T. Age-related macular degeneration: macular changes, prevalence, and sex ratio: an epidemiological study of 1000 aged individuals. *Acta Ophthalmol (Copenh).* 1989;67:609-616.
5. Vinding T. Visual impairment of age-related macular degeneration: an epidemiological study of 1000 aged individuals. *Acta Ophthalmol (Copenh).* 1990;68:162-167.
6. Vinding T. Occurrence of drusen, pigmentary changes and exudative changes in the macula with reference to age-related macular degeneration: an epidemiological study of 1000 aged individuals. *Acta Ophthalmol (Copenh).* 1990;68:410-414.
7. Martinez GD, Campbell AJ, Reinken J, Allan BC. Prevalence of ocular disease in a population study of subjects 65 years old and older. *Am J Ophthalmol.* 1982;94:181-189.
8. Wu L. Study of aging macular degeneration in China. *Jpn J Ophthalmol.* 1987;31:349-367.
9. Jain IS. Senile macular degeneration in Northern India. *Indian J Ophthalmol.* 1984;32:343-346.
10. Hakkinen I. Vision in the elderly and its use in the social environment. *Scand J Soc Med.* 1984;35(suppl):5-60.
11. Sperduto RD, Seigel D. Senile lens and senile macular changes in a population-based sample. *Am J Ophthalmol.* 1980;90:86-91.
12. Bressler NM, Bressler SB, West SK, et al. The grading and prevalence of macular degeneration in Chesapeake Bay watermen. *Arch Ophthalmol.* 1989;107:847-852.