Objective: To examine the age- and sex-specific prevalence of age-related maculopathy (ARM) and age-related macular degeneration (AMD) in citizens of Reykjavik, Iceland, who were 50 years and older.

Design: Random sample, cross sectional.

Materials and Methods: Response rate was 75.8%. The presence and severity of various characteristics of drusen and pigmentary changes that are typical of ARM and AMD were determined by grading stereoscopic color fundus photographs, using the international classification and grading system for ARM and AMD.

Results: We were able to evaluate 1021 right-eye and 1020 left-eye macular photographs. There was no statistically significant difference between right and left eyes. In people aged 50 to 59 years, 4.8% of participants (95% confidence interval [CI], 2.6-7.0) were found to have intermediate soft drusen measuring 63 to 125 µm in either eye; 1.2% (95% CI, 0.0-2.3) had large soft distinct drusen larger than 125 µm; and 0.6% (95% CI, 0.0-1.4) had large soft, crystalline, or semisolid drusen. The same figures for those 80 years and older were 18.2% (95% CI, 9.8-26.6), 10.9% (95% CI, 4.0-17.8), and 25.5% (95% CI, 18.4-32.6), respectively. Geographic atrophy was found in either eye in 9.2% of those participants 70 years and older (95% CI, 5.6-12.7), and exudative macular degeneration was found in 2.3% of participants 70 years and older (95% CI, 0.5-4.1).

Conclusion: Geographic atrophy was found to be more common in our study than in other population-based studies.

tion. The participants were citizens of Reykjavik 50 years and older who were randomly sampled using the national population census. The sample included 6.4% of the Reykjavik population for each year of birth and for both sexes. The examination took place in 1996. Of those 1635 randomly sampled, 1379 could be contacted and were eligible. Of these, 1045 elected to participate, 461 were men and 584 were women, at a response rate of 75.8%. All were white. They were examined at the University Eye Department in Reykjavik. All were required to answer a questionnaire regarding lifestyle, such as outdoor exposure, alcohol and smoking habits, health, disease, previous surgery, and medication, including eye medication.

EXAMINATION

All participants went through a standard examination protocol including keratoreflectometry (ARK 900; Nidek Co Ltd, Gamagori, Japan), air puff tonometry (NT 2000; Nidek Co Ltd), Scheimpflug photography of the anterior segment (EAS 1000; Nidek Co Ltd), and visual acuity measurements. The pupils were maximally dilated with tropicamide 1% and phenylephrine 10%. We then performed slitlamp biomicroscopy of the fundi using a 78-diopter lens. Two simultaneous color stereo fundus photographs (30°) were taken, with one centred on the fovea and the other on the optic disc (Figure) (3Dx/NM; Nidek Co Ltd). This was done by a single trained ophthalmic photographer. The 35-mm slide transparencies were put into a frame and analyzed using the pocket stereoscope (Cartographic Engineering Ltd, Hampshire, England). The grading of the photographs was based on the international classification system by Bird et al,3 which again, is based on the Wisconsin grading system. The grading was carried out in the Moorfields Eye Hospital Reading Centre (London, England).

Each patient’s unique identification number was displayed on the photographs. Image quality was graded from 1 to 6. A grade of “1” was awarded when the photograph was in perfect stereo with sharp focus; “2,” for good stereo and good focus; “3,” for acceptable stereo and focus; “4,” for poor stereo and focus, but with main features, such as end-stage AMD still gradable; “5,” for no stereo, thus not gradable; “6,” for good stereo and focus, but with the photograph not centered properly on the macula; and “0,” for a missing image. Grades 5, 6, and 9 were disregarded when analyzing the results of the detailed grading.

GRADING METHODS

The protocol of the International ARM Group was followed with minor modifications. We used a standard grid for ARM classification for the 30° fundus camera, with central, middle, and outer circles, the radii of which were 500 µm, 1500 µm, and 3000 µm, corresponding with zones 1, 2, and 3 in results, respectively. Spokes then split the circles into upper, lower, temporal, and nasal zones. Sets of the 3 circles and spokes were printed on clear plastic as well as 5 circles measuring 63 µm, 125 µm, 175 µm, 250 µm, and 500 µm, respectively, to estimate the size of drusen and pigmentary abnormalities. These were developed according to the published guidelines.2 To phenotype ARM and AMD precisely in this population, all abnormalities were graded in all 3 zones including drusen, pigment changes, and end-stage AMD. For the physical development of the grid, AutoCAD Software (Autodesk Inc, San Rafael, Calif) was used and the images were reproduced as 3 × 3 slides for easy use with stereo images. In estimating the lesion size or area, the grading circles were placed on one side of the slide (one member of the stereoscopic pair) and viewed through the stereo viewer, which was placed on a standard fluorescent viewing box. Intergrader reliability was assessed on a random subsample of gradeable eyes. This report includes only lesions of ARM present within the grid. The type, size, and number of drusen in each zone was established, as well as hyperpigmentation and hypopigmentation.

All images were graded by 2 trained ophthalmic graders, and 30% of the images were graded by the ophthalmologist trained in grading, without having access to previous grades, age, sex, and clinical information regarding the participants. Fourteen days later, an ophthalmologist trained in grading (T.P.) individually viewed all images and created the final grade based on the results of the previous gradings. In case of disagreement between the graders, one of the authors (A.C.B.) adjudicated the results, and his grading was taken as final. Ten percent of the photographs were randomly selected and regraded by the ophthalmologist after another 14 days, and thus, an audit final grade was created. These grades were compared with the original final gradings to check for internal consistency. If there was a difference between the original and the audit final gradings, the adjudicator’s (A.C.B.) decision was taken as the absolute final. Using Microsoft Access (Microsoft Corp, Redmond, Wash), we developed a database containing all information on grading, identity of graders, data entry persons, and date the photographs were graded. The data were checked for inconsistency at the end of the study by an independent observer who had not been involved in the original data entry process. There was a less than 0.5% error in the data entry process, whereby none of these errors would have affected the validity of the results.

We present the results separately, for hard drusen, early ARM, and AMD. The number of hard drusen smaller than 63 µm was established for each zone.

DEFINITION OF EARLY ARM

Grading of early ARM included the presence of soft, indistinct, or reticular drusen (≥63 µm) within the grid, and/or presence of retinal pigment epithelial abnormalities measuring 63 µm or greater within the grid.

DEFINITION OF AMD

The late stages of ARM were defined to include geographic atrophy and exudative macular degeneration—the lesions termed AMD by the International ARM study group. Geographic atrophy was defined as a discrete area of the retinal depigmentation characterized by the sharp border and presence of the visible choroidal vessels at least equaling the size of circle one (zone I). Exudative AMD included serous or hemorrhagic detachment of the retinal pigment epithelium or sensory retina, presence of subretinal or subpigment epithelium hemorrhage, or subretinal fibrous scar.
Table 1. Number of Randomized and Examined Persons and Eyes

<table>
<thead>
<tr>
<th>Age Group, y</th>
<th>No. of Eligible Persons</th>
<th>No. of Examined Persons</th>
<th>No. of Gradable Images</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M/F Total</td>
<td>M/F Total</td>
<td>M/F Total</td>
</tr>
<tr>
<td>50-59</td>
<td>262/265 527</td>
<td>216/224 440</td>
<td>167/195 362</td>
</tr>
<tr>
<td>60-69</td>
<td>229/283 503</td>
<td>182/259 441</td>
<td>144/219 354</td>
</tr>
<tr>
<td>70-79</td>
<td>181/206 387</td>
<td>160/186 346</td>
<td>116/135 251</td>
</tr>
<tr>
<td>≥80</td>
<td>68/150 218</td>
<td>61/91 152</td>
<td>34/44 78</td>
</tr>
<tr>
<td>Total</td>
<td>731/904 1635</td>
<td>619/760 1379</td>
<td>461/584 1045</td>
</tr>
</tbody>
</table>

Table 2. Exact Agreement and κ Statistics for All Variables Studied: Results of Master Records vs Audit Master Records

<table>
<thead>
<tr>
<th>Variable Characteristic†</th>
<th>% Agreement, R/L Median (Range)</th>
<th>κ, Value R/L Median (Range)</th>
<th>Probability &gt; Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drusen</td>
<td>83.335 (74.29-97.14)/81.245 (71.03-96.26)</td>
<td>0.674 (0.5617-0.8594)/0.6135 (0.4889-0.7215)</td>
<td>0.0000 all variables and zones</td>
</tr>
<tr>
<td>Pigmentary changes</td>
<td>97.14 (94.29-100.00)/95.33 (92.52-96.26)</td>
<td>0.7592 (0.5532-1.0000)/0.6280 (0.5535-0.7070)</td>
<td>0.0000 all variables and zones</td>
</tr>
<tr>
<td>Geographic atrophy</td>
<td>98.1 (97.14-98.10)/97.20 (96.26-97.20)</td>
<td>0.7937 (0.7172-0.7937)/0.7215 (0.7177-0.7774)</td>
<td>0.0000 all variables and zones</td>
</tr>
<tr>
<td>Neovascular AMD</td>
<td>99.05 (98.1-100.0)/96.24 (94.39-96.26)</td>
<td>0.8536 (0.7426-1.0000)/0.5885 (0.3809-0.6543)</td>
<td>0.0000 all variables and zones</td>
</tr>
</tbody>
</table>

To exclude photocoagulation scars resulting from treatment for subretinal neovascular membranes being mistaken as geographic atrophy, we examined the records of the only center performing fluorescein angiography and laser treatment in Iceland.

Exact agreement and κ values were calculated for all variables studied, and for master records vs audit master records, we used Staata statistical software. For other statistical analyses, including χ², Fisher exact test, and logistic regression analyses, we used SPSS version 10.1 (Statistical Package for the Social Sciences 10.1; SPSS Inc, Chicago, Ill). Prevalence rates were calculated in 10-year categories with 95% confidence intervals (CI). In logistic regression analyses, age was entered as a continuous variable.

We used the macular slitlamp grading (F.J.) for eyes with ungradable images only; these were, however, not included in statistical analyses.

Finally, we used a genealogical database to analyze whether those with AMD were more likely to be related than is expected from a random sample.

RESULTS

Of the 1635 persons in the random sample, 1379 were eligible. We were unable to contact 256 persons at the time since they had changed residences without yet notifying the authorities. Of the 1379 eligible, 1045 elected to participate (Table 1). All those not willing to participate agreed to answer a short questionnaire identifying the authorities. Of the 1379 eligible, 1045 elected to participate. Of the 1635 persons in the random sample, 1379 were eligible. We were unable to contact 256 persons at the time since they had changed residences without yet notifying the authorities. Of the 1379 eligible, 1045 elected to participate (Table 1). All those not willing to participate agreed to answer a short questionnaire identifying the authorities.

Table 3 presents the number of gradable photographs (grades 1-4), as well as percentages of hard drusen and early ARM by patient age and sex. There were slightly higher numbers of gradable photographs for women than for men, reflecting the higher participation rate of women. The results for both sexes are remarkably similar. In either eye, the prevalence of hard drusen smaller than 63 µm decreased from 85.3% in people 50 to 59 years old to 38.6% for those 80 years and older. Early ARM, including pigmentary abnormalities and drusen measuring 63 µm or more (excluding AMD), increased with increasing age. The prevalence in either eye increased from 8.9% (95% CI, 5.9-11.9) in people 50 to 59 years old to 37.1% (95% CI, 25.5-48.8) in those 80 years and older (Table 3).

Considering right eyes only, soft intermediate drusen measuring 63 to 125 µm occurred with similar frequency in zone I, zone II, and zone III; the same applies to large, soft distinct drusen larger than 125 µm. Large drusen would be more difficult to differentiate between type, size, and number of drusen than to diagnose pigmentary abnormalities and advanced AMD. Thus, the stereo and focus quality was sufficient in either eye to grade drusen in 1006 instances and to grade pigmentary abnormalities and AMD in 1022 instances. There was no statistically significant difference in photographic quality between right and left eyes. Table 2 presents agreement and κ statistics for variables studied, and results of the master records vs audit master records in the sample audit.

The most severe type of drusen and the most numerous drusen were both taken into account. Also, if the most severe was a large soft drusen, and if the most numerous were soft intermediate but there was a small hard drusen as well, then the number of drusen would be shown as the number of small hard drusen smaller than 63 µm. This allowed the grading system to account for the majority of the drusen on the photograph.

EARLY ARM

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indistinct drusen larger than 125 µm were, however, predominantly seen in zone II. Results for left eyes were similar. In people 50 to 59 years old, 4.8% (95% CI, 2.6-7.0) of participants were found to have intermediate soft drusen measuring 63 to 125 µm in either eye; 1.2% (95% CI, 0.0-2.3) had large soft distinct drusen larger than 125 µm; and 0.6% (95% CI, 0.0-1.4) had large soft, crystalline (calcified) or semisolid drusen larger than 125 µm. The same figures for those 80 years and older were 18.2% (95% CI, 18.4-32.6), respectively (Table 4).

When both sexes were combined, the prevalence of hypopigmentation 63 µm or larger in at least one eye was 1.2% (95% CI, 0.0-2.4) in people 50 to 59 years old, and 20.0% (95% CI, 9.1-30.9) in those 80 years and older (Table 5). The most common form of hypopigmentation was punctate (67%), followed by “linear” (24%), a term used if the pigment seemed to form a line. Hypopigmentation was not counted for each and every drusen; if, however, it was large enough to be taken into account, it was counted as punctate. Hypopigmentation was found in zone II in 74% of cases, in zone I in 34%, and in zone III in 8%. There was no statistically significant difference between the frequency of hypopigmentation and hypopigmentation between the sexes (P=.13).

**AGE-RELATED MACULAR DEGENERATION**

Exudative macular degeneration was found in 6 persons—3 women and 3 men, and in 3 right eyes and 3 left eyes. Their mean age was 84 years (range, 77-88 years). One of these, an 86-year-old woman, had exudative macu-
lar degeneration in the right eye and geographic atrophy in the left eye, and an 84-year-old woman and an 88-year-old man had geographic atrophy in the right eye and exudative macular degeneration in the left eye. Thus, half of those with exudative macular degeneration in one eye had geographic atrophy in the other eye. No one had definite exudative macular degeneration in both eyes, though 1 of the 3 had a questionable membrane in the second eye. Further, 3 eyes had questionable neovascular AMD, 2 of them with definite geographic atrophy in the same eye. The prevalence for those 70 years and older was 2.3% (95% CI, 0.5-4.1), and 9.8% for those 80 years and older (Table 6). The exudative lesions were generally large, including all zones (I-III) in 4 instances, and zones I and II, and zone II only in the fifth and sixth person, respectively.

**GEOGRAPHIC ATROPHY**

Twenty-nine persons had definite geographic atrophy in either eye (18 women and 11 men). The age range for geographic atrophy was 52 to 87 years (mean, 77 years). Only 1 person younger than 60 years was found to have geographic atrophy. Sixteen persons had geographic atrophy in the right eye, and 23 were affected in the left eye. In the right eye, zone I was affected in 14 instances (87.5%), and zone II was affected 12 instances (75.0%); whereas zone III was affected in 6 instances and was always affected in conjunction with zones I and II. The results in the left eyes were similar. The prevalence for geographic atrophy in both sexes combined was 0.3% for 50- to 59-year-old patients, 1.2% for 60- to 69-year-old patients, 5.3% for those 70 to 79 years old, and 25.0% for those 80 years and older. It therefore seems that geographic atrophy starts at an earlier age than exudative macular degeneration, and both increase rapidly after age 80 years (Table 6). Geographic atrophy was found in either eye of 9.2% of those 70 years and older (95% CI, 5.6-12.7).

Considering the advanced (AMD) types together, the prevalence increases from 5.8% in patients in their 70s, to 30.8% in those 80 years and older.

Thirty-nine right eyes were without gradable photographs — 4, 6, 18, and 11 in persons 50 to 59 years old, 60 to 69 years old, 70 to 79 years old, and 80 years and older, respectively. The most common cause for ungradable photographs was poor focus or stereo in 74.4%.

The results of the slitlamp grading of these 39 eyes were similar to the results of the graded images, considering the same age groups. Advanced AMD, namely geographic atrophy, was only found in one right eye (that of a 92-year-old woman) among the 39 slitlamp-graded eyes. The results for the left eyes were similar.

We did a genealogical analysis using the deCODE genetics genealogical database. All those with geographic atrophy were found to have a common ancestor 6 generations back, whereas more than 10 generations were required for those with exudative disease, with the last being similar to a random sample of the Icelandic population.

**COMMENT**

For the random sample, we use the national population census, a 9-month-old update. This results in some “dropout” due to death and change of residence during the period. The dropouts are, however, evenly distributed regarding age and sex and should not influence the results adversely. Like in other studies using uniform standardized advanced techniques of examination, there is, however, some additional drop in participation after age 80 years owing to decreased mobility. The study does seem fairly representative of the population, and this is also supported by comparing our results with the results of a previous study from Iceland using less advanced techniques and in which all those 80 years and older were examined.1

In this article, we follow the guidelines of the International ARM Epidemiological Study Group² and the Wisconsin Group.³

The results for eyes with gradable photographs are similar to those with ungradable photographs, in which slitlamp grading was used. We did, however, only use graded images for statistical analysis since the 2 methods are not strictly comparable.

There is a good agreement of the results of master records vs audit master records. We found a significantly increased prevalence of early ARM with increasing age (OR/years = 1.08; 95% CI, 1.06-1.10; P < .001). Klein et al¹² found the frequency of drusen to decrease with increasing age, and Laatikainen and Hirvelä¹³ found early age-related changes to increase until the age of 85 years. Bressler et al¹⁴ and Pauleikhoff et al¹⁵ found an age-related increase for drusen and pigmentary abnormalities.

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**Table 6. Age- and Sex-Specific Percent Prevalence of AMD in Either Eye**

| Age Group, y | Combined† Men, No. (%) | Combined† Women, No. (%) | Combined† Combined† Combined† Combined† Combined† Combined† |
|--------------|-------------------------|--------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
|              |                         |                          |                         |                         |                         |                         |
| 50-59        | 11 (2.7)                | 18 (3.5)                 | 29 (3.2)                | 0 (0.0)                 | 0 (0.0)                 | 0 (0.0)                 |
| 50-69        | 2 (1.5)                 | 2 (1.5)                  | 4 (1.2)                 | 0 (0.0)                 | 0 (0.0)                 | 0 (0.0)                 |
| 70-79        | 4 (4.0)                 | 7 (6.5)                  | 11 (5.3)                | 1 (1.0)                 | 0 (0.0)                 | 1 (0.5)                 |
| >80          | 5 (21.7)                | 8 (27.6)                 | 13 (25.0)               | 2 (8.7)                 | 3 (10.7)                | 5 (9.8)                 |
| Total        | 11 (2.7)                | 18 (3.5)                 | 29 (3.2)                | 3 (0.7)                 | 3 (0.7)                 | 6 (0.7)                 |

*Abbreviation: AMD, age-related macular degeneration.

*N = 1022.*
ties. In the present study, we found an age-related increase per year from 50 years of age for intermediate soft drusen measuring 63 to 125 µm (OR = 1.08; 95% CI, 1.04-1.11; P < .001), soft distinct drusen larger than 125 µm (OR = 1.08; 95% CI, 1.04-1.13; P < .001), and soft indistinct drusen larger than 125 µm (OR = 1.13; 95% CI, 1.08-1.19; P < .001), with the biggest rise with increasing age for the last abnormality mentioned. Conversely, we found a decrease in the prevalence of small drusen measuring less than 63 µm with increasing age, which was also observed in the Beaver Dam Eye Study. These drusen are not necessarily expected to contribute to the development of AMD, though they may in some instances break down, to later cluster, and eventually form larger more confluent drusen.

Intermediate soft drusen 63 to 125 µm in size, and large distinct drusen larger than 125 µm affect zone I and zone II with similar frequency, whereas zone II is most frequently affected (60%) by large indistinct drusen larger than 125 µm. These large indistinct drusen seem to spare fixation to some extent until late stages. Vinding found rising frequency of pigmentary changes with increasing age in Denmark, which is also in agreement with our findings. Like our group, this Danish study found geographic atrophy to be more common than the exudative type; however, they did not use exactly the same criteria as we did. Both hypopigmentation (83%) and hyperpigmentation (74%) are most commonly found in zone II, followed by zone I.

Since zone I has the highest concentration of macular pigment, it may be relatively resistant to early retinal pigmentary abnormalities. In the more advanced form (namely, geographic atrophy), this relative resistance appears to collapse since in geographic atrophy, zone I alone or with zone II are affected in more than 80% of instances. In the Beaver Dam Eye Study, for those 75 years and older, the prevalence of geographic atrophy was 3.5%, and 6.7% for exudative macular degeneration. The same age in Denmark, which is also in agreement with our findings Food and Agriculture Organization, no European nation eats more fish per capita than Icelanders,26 while their consumption of green vegetables and fruits is relatively well nourished. According to the United Nations Food and Agriculture Organization, no European nation eats more fish per capita than Icelanders, while their consumption of green vegetables and fruits is relatively low by European standards, which possibly results in relatively low levels of vitamin A. Daily intake of multivitamins and cod liver oil is, however, known to be very common among elderly Icelanders.28 Intake of zinc is similar to other Northern European populations.27 Smoking, which has been implicated as a risk factor for AMD, was relatively uncommon among those 70 years and older in our study, and fish was usually consumed several times a week.28

The main conclusion of this study is that the phenotype of ARM and AMD is different in different communities, or at least Iceland is different than most other Northern European communities. This difference is expressed by the higher prevalence of geographic atrophy in Iceland than it is in similar populations. Our genealogical analysis suggests that those affected are more related than would be expected from a random sample from this population.
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We are indebted to the Reykjavik Eye Study Group for their contribution; to Mr M. Noda (Nidek Co Ltd, Gama-gori, Japan) for fundus photography; and to K. P. Magnusson, PhD (deCODE Genetics, Reykjavik, Iceland) for help with genealogical analysis.

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REFERENCES