ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #331

1. Title: Prevalence of Age-Related Maculopathy and Associated Risk Factors

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3. Timeline:

Analyses will begin with a set of available data of all participants with retinal photographs for which data are available. Final writing of manuscripts will begin in November l995 and be completed by March 1996.

4. Rationale:

Age-related malacular degeneratlon is the most common cause of legal blindness in Americans 65 years of age or older. Photocoagulation treatment prevents severe loss of vision in only a small percentage of eyes with this condition. Thus, there is a need to develop a public health approach to prevent this condition.

The anatomical changes associated with age-related maculopathy consisting of drusen, atrophy of the retinal pigment epithelium and/or exudative changes have been well characterized. However, the pathogenesis of this condition remains poorly understood. To date, there are no data published from population-based studies which have examined the natural history of this condition. There are few cross-sectional population based studies which have examined racial differences. Data from such studies suggest that the prevalence of early lesions associated with age-related maculopathy is similar in blacks and whites, however, late signs of age-ralated maculopathy are more frequent in whites compared to blacks.

Entironmental factors (e.g., light exposure) systemic disease (e.g., hypertension), ocular factors (e.g., iris pigmentation), and family history of the disease have been suggested as increasing the risk of age-related maculopathy and dietary factors (e.g., antioxidants such as Vitamin E and beta carotene and minerals such as zinc) as possibly decreasing it. However, with the exception of family history, the relationships are weak and/or inconsistent from study to study.

Increased blood pressure and cardiovascular disease, by their effects on the choroidal circulation, have been hypothesized as possible pathogenetic factors for the development of macular degeneration. Hypertension was found to be related to macular degeneration in a large case-control study by Hyman et al. and in two large population-based studies, the HANES and the Framingham Eye Study. However, in the large Eye Disease Case Control Study, hypertension was not significantly associated with the presence of exudative macular degeneration and in the population-based Beaver Dam Eye Study neither hypertension nor blood pressure was associated with early or late age-related maculopathy.

Similarly, data on the relationships of age-related maculopathy with cardiovascular disease are not consistent. In the large case-control study of Hyman et al. patients with exudative macular degeneration had a higher risk of stroke and cardiovascular disease than patients without macular degeneration. However, in the Eye Disease Case Control Study, the Framingham Eye Study, and the Beaver Dam Eye Study no significant relationships were found between a history of cardiovascular disease and age-related maculopathy.

Recently, Vingerling et al. reported in persons who were younger than 85 years of age who were participating

in the Rotterdam Study of the Elderly that plaques in the carotid bifurcation were associated with 4.7 times increase risk of late age-related maculopathy (95% C.I., 1.8-12.0). After controlling for other risk factors, those with plaques in the common carotid artery showed a relative risk of late age-related maculopathy of 2.7 (95% C.I., 1.5-4.8) compared to those without plaques in the common carotid artery. They concluded that "these findings suggest that atherosclerosis may be involved in the etiology of age-related maculopathy."

Lipids by their deposition in Bruch's membrane of the retina have been hypothesized as another possible pathogenetic factor for the development of age-related macular degeneration. It has been suggested that such deposition may decrease hydaulic conductivity resulting in the development of detachments of the retinal pigment epithelium. In the case-control study of Hyman et al., a strong positive relationship was found between serum cholesterol and exudative macular degeneration. Similarly, in the Eye Disease Case Control Study, higher levels of total cholesterol, but not triglycerides, were significantly associated with exudative macular degeneration. In Beaver Dam, the total serum cholesterol level was inversely related and the serum HDL cholesterol was directly related to early age-related maculopathy. This was also found in the Rotterdam Study of the Elderly (data unpublished). In the HANES there appeared to be a macular degeneration, although the relationship was not significant. No relationship of lipids and age-related maculopathy was found in the Framingham Eye Study.

Use of fundus photography and grading of the photographs to detect age-related maculopathy in the ARIC will permit examination of the relationships of blood pressure, measures of atherosclerotic disease (ankle to amr blood pressure, duplex ultrasonography of the carotid arteries (average wall IMT thickness, discrete maximal IMT wall thickness, plaques), history of heart attack and stroke), and measures of dyslipidemias (e.g., fasting serum total cholesterol, high-density lipoprotein, triglycerides, LDL-cholesterol) and other atherosclerotic disease risk factors (fasting insulin levels, plasma fibrinogen, etc) to the prevalence of early age-related maculopathy in whites and blacks.

5. Main Hypothesis:

(1) Whites will have more signs of early and late ARM than blacks after controlling for age and sex; (2) Atherosclerosis (e.g., changes in average wall thicknees of carotid artery, ankle to arm blood pressure measures, etc) and retinal arteriolar changes will be related to signs of early and late ARM; and (3) cigarette smoking and beer drinking will be positively related (adverse effect) to signs of ARM.

6. Data:

Data on signs of early age-related maculopathy (soft drusen status, increased retinal pigment, and retinal pigment epithelial degeneration) and late ARM (geographic atrophy or exudative macular degeneration), arteriolar narrowing, A-V/ratio, A-V nicking, race, aex, age, field center, visits 1-3 sitting and supine blood pressures, antihypertensive medications, diabetes status, medical history, body weight, height, body mass index, smoking status, past and current alcohol consumption by type, carotid intimal-medial wall thickness (visits 1-3 ), cerebral MRI (visits 1-3), family history of cardiovascular disease; and prevalent coronary heart disease; serum lipid profiles (total cholesterol, LDL, HDL, triglycerides), HDL subfractions, Lp(a), and Apo A1 and B (Visits 1-3).