Diet and age-related macular degeneration: expanding our view

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In the current issue of the Journal (1), Chiu et al describe their observations of a new aspect of diet that may be related to one type and stage of age-related macular degeneration (AMD) of the eye: a diet that is high in foods with a high glycemic index. This aspect of the diet adds to the long and growing list of dietary attributes that have been related to early and later stages of AMD in different study samples over the past 15 y. Because there is no cure and limited treatments for the end-stage condition of AMD, it is the leading cause of blindness in persons older than 50 y in developed countries. Diet is potentially one of the most cost-effective strategies to prevent the development of AMD, the incidence of which is expected to increase by 50% by 2030 in the United States. The scope of dietary-related degenerative conditions such as AMD may not only increase in the near future in the United States, but may become an increasing concern in the developing world as a result of sweeping social, economic, and dietary changes that accompany the economic development of these areas (2).

The results of several previous epidemiologic studies and clinical trials suggest that diets high in antioxidant nutrients (vitamins C and E, carotenoids such as lutein and zeaxanthin, fruit and vegetables that contain these nutrients, and nonnutritive antioxidants) or zinc are associated with a decreased occurrence of early or late AMD (3). A high dietary intake of fat was associated with a higher prevalence or incidence of early or late AMD in numerous studies (4), whereas higher intakes of fish or n-3 fatty acids were associated with lower rates of AMD (4).

Because of evidence that the pathogenesis of AMD likely involves a complex interaction of cellular and vascular factors, which may be promoted by light damage, oxidative stress, and inflammation, it comes as no surprise that numerous nutrients and other dietary components may play several different roles that could be additive or complementary. A substantial body of experimental data in animals and clinical and pathologic studies in humans support the biological plausibility that the several dietary attributes discussed above may be protective. The authors of the present study cite several potential biological mechanisms by which the glycemic index might also be related to AMD. Although advanced glycation end products have been found in drusen, it is not yet known whether they are a cause or a consequence of degenerative changes. Degeneration of the retinal vasculature is a well-known complication of diabetes mellitus. Yet, the presence of diabetes has not often been related to AMD in previous epidemiologic studies. The biological plausibility that elevations in blood sugar promote AMD, particularly in the absence of diabetes, remains untested.

As is common in most of the published investigations of the relation between diet and AMD, this editorial describes the degree to which this one dimension of diet, ie, glycemic index, is related to AMD. It may be that a low glycemic index score is a marker for other combined aspects of diet that could protect against AMD. Diets with a low glycemic index often include plenty of fruit, vegetables, whole grains, legumes, and milk and few refined grains and sugars. Obviously, such diets are richer in a variety of nutritive and nonnutritive antioxidants. Diets with a high glycemic index, like high-fat diets, may be associated with higher rates of AMD because they are simply poorer in a wide variety of protective nutrients and other dietary components. Having a diet with a low glycemic index score might also be related to health-conscious fat choices that might also protect against AMD, such as low or moderate intakes of saturated and polyunsaturated fats and high intakes of fish and n-3 fats from nuts, seeds, and whole grains.

Unfortunately, we have no simple way of accounting for these multiple simultaneous aspects of diet that may be related to AMD. As did these investigators, we assume that we account for all other aspects of diet by adding the level of consumption of other dietary components to the regression model. When risk estimates do not change, we discount their influence on the observed association. Because our measures of specific diet attributes are imprecise with regard to the level and timing of diet exposure, residual confounding makes the approach of adding individual estimates of numerous other nutrients (that are often highly correlated) insufficient for completely removing this influence. Moreover, persons with low glycemic index scores may have slightly or moderately higher intakes of a broad array of micronutrients that would be harder to statistically adjust for than would be larger intakes of a few nutrients.

It may be that the glycemic index score reflects a broader diet pattern that protects against AMD. No studies of the relations of diet patterns with AMD have been published. In the past decade, increasing numbers of studies have found that overall diet patterns are related to the slower development of chronic conditions, such as hypertension and cardiovascular diseases. Because these conditions may be risk factors for AMD, patterns that slow these conditions may be risk factors for AMD, patterns that slow these
conditions may slow AMD as well. Evidence from the Dietary Approaches to Stop Hypertension (DASH) Study (5) indicates that several combined aspects of diet lower blood pressure more than does any single component alone. The adoption of the Mediterranean diet pattern in the Lyon Diet Heart Study was proven to have a stronger influence on lowering cardiac outcomes than prudent Western-type dietary approaches (6). Higher scores on the Healthy Eating Index were shown to be related to a lower prevalence of nuclear cataract (7), a risk factor for AMD in some previous studies. Research on the influence of long-term diet patterns on the development of AMD is needed.

More research on the influence of diet on the development of early stages of AMD, determined photographically as done by Chiu et al, is also needed. Early AMD is a strong predictor of developing advanced AMD (8). Therefore, slowing the development of early stages of AMD may ultimately reduce the number of persons with advanced AMD more than would slowing the progression from intermediate to late stages of AMD. Chiu et al found that the glycemic index was related to 1 of the 2 major earlier stages of AMD: the presence of pigmentary abnormalities, which is thought to signal that this single layer of retinal pigment epithelial cells that support the renewal of rods and cones is in distress. The presence of a different early stage of AMD that is characterized by large or diffuse drusen deposits, which accumulate between retinal pigment epithelial cells and the choroidal blood supply, was not related to the glycemic index score. Likewise, zinc in cross-sectional and prospective analyses in the Beaver Dam Eye Study (9) and dietary lutein and zeaxanthin in the third National Health and Nutrition Examination Survey (10) were related to the presence or incidence of retinal pigment abnormalities. The incidence of large drusen was related to the low intake of vitamin E and fruit and vegetables in The Beaver Dam Eye Study (9). Recently, in the largest prospective study of diet and AMD that photographically assessed the early stages of AMD, the incidence of AMD that was primarily composed of large or soft drusen was related to lower intakes of vitamin E, zinc, or a combination of antioxidant nutrients (3).

We currently have the tools necessary to quantify diet patterns and to evaluate their effect on AMD. Given the large number of likely dietary influences on the pathologic processes that promote AMD, the magnitude of effect of diet on AMD may be larger than early studies of single diet components suggest. Indeed, van Leeuwen et al (3) found that diets high in several antioxidant nutrients lowered the risk of AMD to a greater extent than did diets high in single antioxidant nutrients. Moreover, studies of diet patterns in relation to AMD increase the likelihood that solutions will emphasize healthy lifelong dietary practices rather than the consumption of high amounts of a narrow range of specific nutrients in supplements that are costly and potentially harmful. We are poised at the brink of expanding our view of the relations between diet and the development of AMD—an increasingly common and debilitating condition of aging.

The authors had no conflicts of interest.

REFERENCES