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THE AUTHORS REPLY: A cardinal rule of the delineation of a hereditary cancer syndrome is a comprehensive family history of cancer that includes cancers at all anatomical sites. Clinical examples such as the hereditary breast-ovarian cancer syndrome and the Lynch syndrome are legion, and the list goes on.¹ Albright et al.² quantified a statistical association in a population-based study of multiple myeloma, prostate cancer, and malignant melanoma involving all types of relatives ($P=0.027$ to $P=8.3\times 10^{-9}$). They identified 72 pedigrees with a significant excess of both multiple myeloma and prostate cancer. Our studies of familial multiple myeloma³ as well as others from the

literature⁴ that attempt to define a genetic association between multiple myeloma and prostate cancer underscore the power of tumor aggregation, yet a common molecular genetic pathway explaining this putative association with hereditary cancer remains elusive.

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Age-Related Macular Degeneration

TO THE EDITOR: The review of age-related macular degeneration by Jager et al. (June 12 issue)¹ does not refer to an editorial accompanying the report of the Age-Related Eye Disease Study (AREDS) in the *Archives of Ophthalmology* in 2001 and two subsequent letters,²⁻⁴ all of which criticized the study analysis for setting aside a negative result in which dietary supplementation with high doses of vitamins and minerals was ineffective and instead reporting on a subgroup in which the result was positive. The investigators argued that the excluded patients had too few end points to be eligible for treatment. However, the group of patients who received the supplement had greater disease progression and provided valuable data regarding early intervention.

Discarding prespecified negative analyses and reporting on positive subgroup analyses has been repeatedly discouraged.⁵ The omission of the above information perpetuates the myth that the supplement used in the AREDS was effective, at the price of a treatment that has no benefit and carries undetermined risks.

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TO THE EDITOR: The review of age-related macular degeneration contains one problem: the inaccurate use of the term “legal blindness.” The authors imply that decreased vision in one eye may make that eye legally blind. This is incorrect: one eye cannot be legally blind, but a person may be legally blind. In the United States, “Statutory blindness is defined in the law as central visual acuity of 20/200 or less in the better eye with the use of [a] correcting lens.”¹ Additional qualifications apply in the case of restricted visual fields.^{1,2} The proper definition is of financial and sociological importance to patients.

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1. Social Security Administration, 20 C.F.R. § 404.1581 (1983).
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nal Revenue Service, 2008:31. (Accessed September 26, 2008, at <http://www.irs.gov/pub/irs-pdf/i1040gi.pdf>.)

THE AUTHORS REPLY: With regard to Seigel's comments, we believe that the authors of the report of the AREDS¹ responded adequately to any concerns raised in correspondence after publication of their article. The authors of that report recognized the potential perils of subgroup analyses of nonprespecified groups and were not issuing a blanket recommendation for megadose supplements.^{2,3} Our review also acknowledges that the supplementation used in the AREDS may not be appropriate for all patients. Instead, we believe that the decision to initiate this supplementation should be based on a coordinated effort among the vitreoretinal specialist, the primary care physician, and the patient.

We disagree with the assertion that this supplementation has no benefit. In our opinion, it has clearly been shown to decrease the rate of visual loss in selected patients with age-related macular degeneration. Recommendations from the report of the AREDS are part of the evidence-based preferred practice patterns of the American Academy of Ophthalmology for the management of age-related macular degeneration, and they were rated as having the highest strength of evidence (based on study design) as well as being most important for the care process.⁴

Herm raises an important point. Indeed, one can easily infer from the article that an eye can

become legally blind: "Although neovascular age-related macular degeneration represents only 10 to 15% of the overall prevalence of age-related macular degeneration, it is responsible for more than 80% of cases of severe visual loss or legal blindness (i.e., visual acuity of 20/200 or worse) resulting from age-related macular degeneration." The words "or legal blindness" should have been omitted from the article. Herm is correct, and his point is well taken.

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Long-Term Results of Rabbit Antithymocyte Globulin and Basiliximab Induction

TO THE EDITOR: In our recently reported prospective, randomized, international clinical trial comparing rabbit antithymocyte globulin and basiliximab in renal transplantation (ClinicalTrials.gov number, NCT00235300),¹ we observed that induction treatment with rabbit antithymocyte globulin was as safe as and more effective than basiliximab at 1 year in preventing acute rejection in patients who had received kidney transplants from deceased donors and who were at increased risk for acute rejection or delayed graft function. Whether the apparent benefits of rabbit antithymocyte globulin over basiliximab persist is unknown.

The duration of follow-up in a clinical study

is limited by whether patients are willing to participate for an extended period and whether investigators can commit the additional time. Additional limitations include the need for additional informed consent and the added costs of further study. Consequently, long-term safety and efficacy data are lacking for many drugs in multiple therapeutic areas.² Postmarketing surveillance after drug approval is mandated by the Food and Drug Administration to monitor safety but depends on spontaneous reporting by health care professionals. Unfortunately, causality often cannot be ascertained from such reports. Registries of patients, sponsored by the government or