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Use of Micronutrient Supplement for Preventing Advanced Age-Related Macular Degeneration in Japan

In accordance with the results of the Age-Related Eye Disease Study (AREDS),¹ a randomized controlled trial performed in the United States, patients with age-related macular degeneration (AMD) in the United States have been instructed to take micronutrient supplements when their lesion fits the inclusion criteria.² We conducted a survey about the patients' supplement use and the ophthalmologists' attitudes toward supplements in Japan, where the use is not based on ophthalmologists' prescription.

Methods. The questionnaire was given to patients diagnosed as having AMD at the Medical Retina Division, Department of Ophthalmology, Keio University Hospital, Tokyo, Japan, between January 8, 2010, and June 25, 2010. Another questionnaire was given to the ophthalmologists in our department. Supplements containing more than 50% of the AREDS-recommended levels of vitamin C, vi-

tamin E, and zinc were designated AREDS-like supplements, and those that contained reduced amounts of beta carotene and included lutein were designated AREDS plus lutein supplements. This study was approved by the ethics committee of the Keio University School of Medicine.

Results. Patient Survey. Of the 163 patients with AMD who completed our questionnaire, 159 gave valid answers (119 male, 40 female; all ethnic Japanese; age range, 50-95 years; mean age, 73.9 years). Oral supplements of any type were used by 90 participants (56.6%); 23 used an AREDS-like supplement and 35 used an AREDS plus lutein supplement. Among the 139 candidates eligible for an AREDS supplement judged by the modified AREDS classification system based on fundus findings² (Table), 48 (34.5%) used an AREDS-related supplement under their ophthalmologists' instruction; 17 used an AREDS-like supplement and 31 used an AREDS plus lutein supplement. Ninety-one participants (65.5%) had not used a supplement (Table), of whom 61 (43.9%) had not been given any instruction.

Doctor Survey. All of the 6 retinal specialists and 11 of the 12 non-retinal-specialized ophthalmologists considered AREDS-like supplements effective. All of the retinal specialists and 10 non-retinal-specialized ophthalmologists instructed their patients based on AREDS. However, 5 retinal specialists and 3 of the others included some additional information.

Comment. Overall, 56.6% of the participants in this study were taking supplements, which is lower than the proportion reported in the United States (93%).²

Surprisingly, all of the candidates who used the supplements were instructed to do so by ophthalmologists, suggesting that the patients' main source of information about supplements was their ophthalmologists.

Table. Age-Related Eye Disease Study-Related Supplement Use by 159 Participants According to Age-Related Macular Degeneration Category^a

AMD Category	Total, No.	No Evidence to Support AREDS Supplement Use, No. (%) (n = 20)		Candidate for AREDS Supplement Use, No. (%) (n = 139)	
		Using	Not Using	Using	Not Using
Group 1, no AMD	0	0	0	NA	NA
Group 2, early AMD	13	4 (30.8)	9 (69.2)	NA	NA
Group 3, intermediate AMD	14	NA	NA	3 (21.4)	11 (78.6)
Group 4, unilateral AMD					
Unilateral CNV	101	NA	NA	36 (35.6)	65 (64.4)
Unilateral central GA	1	NA	NA	1 (100.0)	0
Group 5, bilateral AMD					
Bilateral CNV					
VA ≥20/100 in better eye	19	NA	NA	6 (31.6)	13 (68.4)
VA <20/100 in better eye	6	5 (83.3)	1 (16.7)	NA	NA
Bilateral GA	1	1 (100.0)	0	NA	NA
Unilateral CNV or unilateral GA					
VA ≥20/100 in better eye	4	NA	NA	2 (50.0)	2 (50.0)
VA <20/100 in better eye	0	0	0	NA	NA
Total	159	10	10	48	91

Abbreviations: AMD, age-related macular degeneration; AREDS, Age-Related Eye Disease Study; CNV, choroidal neovascularization; GA, geographic atrophy; NA, not applicable; VA, visual acuity.

^aThe patients were categorized into 5 groups according to a modified AREDS classification system (with group 5 added) based on fundus findings. Patients classified into group 3, group 4, and a subgroup of group 5 who had visual acuity of 20/100 or better in 1 eye with neovascular AMD were candidates for an AREDS-like supplement.²

In this study, only 34.5% of the candidates used AREDS-related supplements, which is far lower than in the previous report in the United States (67%). This was in contrast to the high level of adherence among the candidates (48 of 78 participants [61.5%]; no significant difference according to age or sex). It should be noted that the instruction rate of the ophthalmologists was more critical than the adherence rate of the patients for taking supplements. Interestingly, AREDS plus lutein supplements were used more often than AREDS-like supplements in this study, in contrast to a US-based study.² A recent survey in a Japanese cohort reporting the protective association of the serum levels of carotenoids with AMD³ and studies in animal models showing the tissue-protecting effects of lutein as a blue-light filter and antioxidant^{4,5} may have promoted the use of AREDS plus lutein supplements.

The ophthalmologists did not always recommend supplements in accordance with AREDS. Some ophthalmologists were not completely confident that the AREDS results are applicable to Japanese or other Asian patients with AMD because of the differences in the clinical features of Asian and white patients with AMD.^{2,6}

The increased incidence of AMD and the resulting vision loss are now serious issues. Preventive therapy is important for both patients' personal health and their continued contributions to society. Reliable evidence based on a randomized controlled trial is still needed for ophthalmologists to appropriately instruct patients' use of supplements to prevent the progress of AMD in Japan.

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Novel Clinical Manifestation of Congenital X-Linked Retinoschisis

Traditionally, congenital X-linked retinoschisis (CXLRS) has been defined as a juvenile macular dystrophy.¹ It is characterized by foveal schisis accompanied by an abnormally reduced b-wave on electroretinography.² The gene for CXLRS, *RS1*, has been mapped to the short arm of the X chromosome and encodes for the protein retinoschisin.^{3,4} Schisis spaces, visible on optical coherence tomography (OCT), have been reported in the fovea in virtually all cases.⁵ We report a case of CXLRS followed up for 6 years with no evidence of foveal schisis on OCT and excellently maintained central vision.

Report of a Case. The patient was referred to the Associated Retinal Consultants, Royal Oak, Michigan, in 2004 at age 9 years. At this time, he had a 2-year history of recurrent vitreous hemorrhages in the left eye with a recent spontaneous vitreous hemorrhage in the right eye. His visual acuity was 20/30 OU. Dilated fundus examination revealed bilateral nasal dragging of his discs, absent foveal reflexes, and bilateral peripheral schisis cavities (**Figure 1**). A diagnosis of probable CXLRS was given, and the patient was scheduled for electroretinography as well as an examination under anesthesia with OCT. His OCT findings confirmed the presence of bilateral peripheral schisis cavities, and electroretinography showed decreased a- and b-waves. A detailed family history revealed a maternal grandfather diagnosed as having retinitis pigmentosa, which likely represents a misdiagnosed case of CXLRS. Unfortunately, it was not possible to examine the patient's grandfather to confirm or disprove this

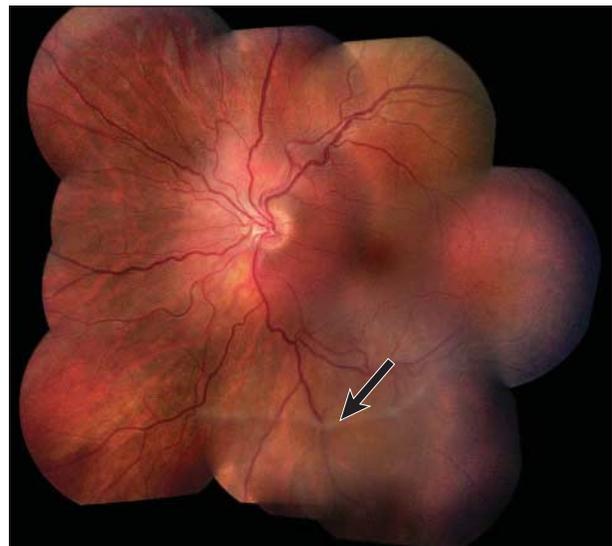


Figure 1. Montage fundus photograph of the left eye demonstrating peripheral schisis (arrow).