

## **Resolution of macular drusen following supplementation with *meso*-zeaxanthin**

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### **Introduction**

Age-related macular degeneration (AMD) is the leading cause of blind registration in people over 50 years of age in the developed world. Late AMD results in loss of central and colour vision, with consequential difficulty in performing fine-detail visual tasks such as reading, driving, and recognizing faces, therefore impacting greatly on one's independence and quality of life. It is estimated that late AMD affects more than 1.75 million individuals in the United States, and this figure is expected to rise to almost 3 million by 2020.<sup>1</sup>

Early AMD is characterized by drusen and/or retinal pigment epithelium (RPE) hyper- or hypo-pigmentation.<sup>2</sup> Drusen are whitish-yellow spots that lie external to the neurosensory retina or the RPE. Histologically, drusen are focal deposits of heterogeneous debris, situated external to the RPE basal lamina and internal to the inner collagenous layer of Bruch's membrane. Drusen have been found to contain acute-phase reactants, markers of inflammation, complement proteins, lipoproteins, and neutral lipids.<sup>3</sup> Late AMD is characterized by either geographic atrophy (any sharply delineated area of hypopigmentation, or depigmentation, or apparent absence of the RPE, in which the choroidal vasculature is more visible than in the surrounding area; the area of atrophy must be  $\geq 175\mu\text{m}$  in diameter), or choroidal neovascularization.

Macular pigment (MP) is a yellow pigment, entirely of dietary origin that accumulates at the macula, and there is a biologically plausible rationale, with growing supporting evidence, that MP protects against the development and/or progression of AMD. MP is composed of the xanthophyll carotenoids: lutein (L); zeaxanthin (Z); and *meso*-zeaxanthin (*meso*-Z). L and Z are found in a conventional western diet in the yolk of eggs, leafy green vegetables, and in yellow and orange colored fruits and vegetables. *Meso*-Z is not found in a conventional western diet, but may be found in less commonly eaten types of fish and shell-fish.<sup>4</sup> However, *meso*-Z is also formed in the retina by

isomerization of L. MP is understood to protect the macular photoreceptors by acting as a filter of actinic short-wavelength (blue) light and/or by its innate antioxidant activity. Here we present two cases, the first of whom has late AMD and the second of whom has early AMD. Both subjects received supplementation with all three macular carotenoids in the form of the commercially available product, Macushield™, with demonstrable clinical improvement.

## Report of cases

### Case 1

A 73 year old male emmetropic patient, diagnosed with neovascular AMD in April 2001 in his right eye, and macular drusen in his left eye [Figure 1]. Visual acuity (VA) at this time was 20/40 OD and 20/20 OS. He is a non-smoker with a past medical history of a myocardial infarct in 1988, following which he has been on treatment with aspirin, anti-hypertensives, and a statin. His family history of AMD consists of a sister, aged 72, who has recently been diagnosed with geographic atrophy.

VA rapidly decreased to counting fingers OD, and between 2005 and 2007 VA OS decreased from 20/20 to 20/30. He also volunteered a history consistent with an increased photostress recovery time and poor colour vision during this time period. In April 2007 he was commenced on supplemental L, Z and *meso*-Z (Macushield™) once daily. Over the succeeding months, he reported subjective improvement in vision. Examination in March 2008 revealed an improvement in VA to 20/20+4 OS and resolution of centrally located macular drusen [Figure 2]. Since commencing Macushield™ he does not report any other significant changes in his diet or lifestyle.

### Case 2

A 63 year old female emmetropic patient, diagnosed with bilateral early AMD in 2004. She smokes two cigarettes per day and has done so for the past 25 years. She has a past medical history of non-metastatic breast cancer, osteoporosis and hypertension, for which she is treated with aspirin and antihypertensives. She has no known family history of AMD, but reports a low intake of fruits and vegetables during her lifetime.

VA is currently 20/20 OU. Examination in March 2008 showed a MP optical density of 0.4 at 0.25° retinal eccentricity, and 0.64 at 0.5° retinal eccentricity, measured by heterochromatic flicker photometry, prior to commencement on Macushield™. Previous to this she had been taking a supplement containing L and Z only. Follow-up assessment in June 2008 revealed an increase in MP optical density at 0.25° retinal eccentricity to 0.79, and an increase at 0.5° retinal eccentricity to 0.72 [Figure 3]. Fundal appearance and VA have remained stable [Figure 4].

## Comment

The concentration of MP peaks at the foveal center and declines with increasing retinal eccentricity. Within the layer structure of the retina, MP reaches its peak concentration in the photoreceptor axon layer and the inner plexiform layer. Interestingly, *meso*-Z followed by Z are the dominant carotenoids centrally, whereas L is found in higher concentrations in the parafoveal region. Supplementation studies in humans have shown that MP levels increase following supplementation.

Spontaneous resolution of drusen has been previously documented in 16 (34%) of 47 participants in the Waterman study, after five years of follow-up.<sup>5</sup> However, spontaneous resolution of drusen is understood to be associated with atrophy of the overlying RPE and subsequent photoreceptor atrophy leading to vision loss. In Case 1, the resolution of drusen centrally was not accompanied by RPE atrophy, but rather an apparent re-establishment of normal anatomy and an improvement in vision. In Case 2, the MP optical density showed a dramatic increase centrally following supplementation with all three macular carotenoids, despite the fact that this individual had previously been supplementing with a product containing L and Z only. This suggests that *meso-Z* supplementation was required to maximize her MP levels centrally. Such a suggestion is also consistent with the central resolution of drusen seen in Case 1, perhaps resulting from the superior anti-oxidant activity of *meso-Z*, which is greater than that of either L or Z. Despite the fact that *meso-Z* can be formed by isomerization of L, certain individuals may lack the ability to effect this conversion in the retina, and may therefore benefit from direct supplementation with *meso-Z*.