You Don't Have to Go Blind from Macular Degeneration (AMD)

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I would like to preface this letter by saying that I have no financial, intellectual or emotional conflicts of interest with the science that I will be summarizing in this letter. My main motivation in writing this letter is not to sell or market vitamins, or tout my invention or even describe my own experimental work. My main motivation is to summarize the evidence that points to the importance of Meso-Zeaxanthin as the critical nutrient for the protection of the macula from the corrosive effects of age and light induced oxidation(rust) which underlies the pathophysiology of age related macular degeneration the leading cause of visual impairment in our aging population. In addition, it is my strong hopes that patients will take a pro-active interest in protecting against AMD starting with taking the one soft gel per day in the Macuhealth
Formula or like ocular supplements.

Before reading further I also need to answer the question of my background. What are my qualifications for reviewing this important scientific evidence.
My name is Michael Tolentino MD and I am retina specialist who specializes in macular degeneration
. My father Felipe Tolentino MD wrote
one of the first books on Vitreo-Retinal surgery as a faculty member at Harvard Medical School. This exposure at an early age allowed me to understand the pathophysiology of retinal disease and started me on a lifelong passion to develop treatments for blinding conditions by understanding the science and using that knowledge to develop treatments.

This exposure lead me in the early 1990's to work as a member of a team at Harvard Medical School who discovered the leading role of a molecule called VEGF and developed injection treatments that now preserve and prevent blindness for patients with wet macular degeneration and diabetic retinopathy.
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The discovery of this molecule was actually the conclusion of a 50 year search.
In the 1940's ophthalmologist realized that new blood vessels that bled in the back of the eye resulted in blindness in elderly patients. Researchers hypothesized that discovering a factor produced by the retina, induced by oxidation and hypoxia and that caused blood vessels to grow in the back of the eye, would enable development of effective treatments.

In the early 1990's advances in molecular biology allowed us not only to identify the critical factor, but also enabled us to prove that VEGF without a shadow of a doubt was that critical factor. We performed the critical experiments that demonstrated the central role of VEGF in retinal new blood vessel growth and I was fortunate to have also tested in an eye disease model for the first time a molecule currently called Avastin which is being used clinically to treat wet macular degeneration , diabetic retinopathy and retinal vein occlusions.(4, 5) While the basic science proved that VEGF was the critical factor, it took another decade for these treatments like Avastin, Lucentis and Macugen to be available to patients.

Having helped discover the critical factor that causes the development of wet macular degeneration and also having helped develop the initial drugs to treat wet macular degeneration, I sought out to discover a means of slowing down the disease using the same methodology used to discover VEGF.
Finding the critical molecule is similar to crime scene investigation. One must use clues from the crime scene to help catch the perpetrator.
In the case of macular degeneration, the crime is blindness. But how does macular degeneration cause blindness? To answer this initial question one has to understand the disease of macular degeneration
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Macular degeneration is a genetic disease that does not manifest until patients are much older. This is the source of the name age-related macular degeneration (AMD) . It manifests initially as the development of yellow deposits under the retina.
If one analyzes these deposits it consists of inflammatory byproducts and other large waste molecules. But one major commonality is that these products are oxidized. Oxidation is just

another word for rust. So simplistically the hallmark signs of macular degeneration (drusen) just represent rusting junk.
What is interesting is that rusting junk does not cause visual loss.
But the rusting junk can promote corrosion which is called geographic atrophy or it can stimulate the up regulation of the critical factor VEGF to initiate the development of wet macular degeneration
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Knowing that oxidation is the culprit gives us a target. But figuring out how to stop oxidation is not as easy. The search for the best anti-oxidant for the macula has been on going now for over 30 years. The first attempt to search for the best anti oxidant for macular degeneration started with the Age related Eye Disease Study. This study clinically tested Vitamins A, C and E along with zinc .
While the study was well executed, the anti-oxidants tested did not meet the criteria for being the
critical anti-oxidant for macular degeneration. Furthermore, the success of the study supports the hypothesis that anti-oxidation is the correct strategy to fight this devastating disease.

What are the characteristics for an optimal anti-oxidant for the macula? This critical anti-oxidant would need to be highly localized in the macula, diminish as patients age, be a potent anti-oxidant, be able to protect the macula from blue light photo oxidation and be difficult to obtain from the diet. The AREDS formulation did not meet any of these criteria. Both basic and epidemiological studies done prior to the start of the AREDS study demonstrated no beneficial effect of these nutrients. The Eye Disease Case Control Study demonstrated that increase of Vitamin A intake did not decrease the likelihood of developing macular degeneration. The study did describe a strong protective effect of the carotenoids lutein and zeaxanthin.
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These carotenoids had been only just characterized and identified in the eye which made their inclusion into a large study such as the AREDS study impossible.
While difficult to study carotenoids as a class of molecule possessed many of the criteria to be considered the critical anti-oxidants.

Carotenoids are a class of pigment(protects against light damage) that represent some of the

most potent anti-oxidants in nature. Of the 600 known carotenoids in nature which provide the color in vegetation, only 3 of these carotenoids are found in the posterior segment of the eye. These carotenoids are Lutein, Zeaxanthin and Meso-Zeaxanthin. While these molecules are actually identical in chemical structure they do represent distinct isomers.
So like triplets who may appear identical, these molecules are actually different in terms of their localization, and anti-oxidant potency.

While it is apparent that all three of these carotenoids could be considered the critical carotenoid, recent studies have shown that Meso-zeaxanthin is likely the most important of the three. The properties of Meso-Zeaxanthin that support its critical role in protecting the macula are extensive and conclusive. 1) Meso-Zeaxanthin is localized predominantly in the foveal and macular region where the signs of macular degeneration typically manifest. Lutein and Zeaxanthin are predominantly localized in the periphery. 2) Meso-Zeaxanthin is the most potent anti-oxidant of the three and when combined with lutein and zeaxanthin the anti-oxidant property of combining these carotenoids are greater than even meso-zeaxanthin alone.
3) Meso-Zeaxanthin is also not readily available in the western diet, this makes a potential for deficiency states in many patients. 4) Lastly the concentration of Meso-zeaxanthin diminishes with age.
These properties clarify the role of Meso-zeaxanthin as a critical macular protectant that needs to be replenished.

As mentioned, meso-zeaxanthin is very difficult to get in the diet so supplementation is probably the only practical means of obtaining this nutrient. The inability to get Meso-Z in the diet both provide evidence of its critical role but also prevents researchers from studying the role of Meso-Z in large epidemiological studies. Most nutritional supplementation studies are done by studying dietary questionnaires to see what nutrients patients with macular degeneration are deficient as compared to those patients who do not have macular degeneration. Because Meso-Z is not readily available in western diets it is not possible to ascertain differences in dietary consumption .

Clinical studies have been performed looking at the effects of Meso-zeaxanthin in conjunction with lutein and zeaxanthin on the pigmentary levels of the macula.

The identification of carotenoids in the macular region were first postulated from an observation . The presence of a yellowish pigmentation in the macular region which was postulated to protect the macula from the damage of blue light lead to the isolation of carotenoids as the substances that provided this yellowish pigmentation. The study of pigmentation of the macula has lead to the understanding of the critical role that pigmentation

plays in protecting the macula from macular degeneration. One can analogize the protection of the skin from sun damage by melanin. If one sees a Caucasian patient who has less melanin concentration and therefore less protection against sunlight damage one can see that sun damaged skin in the elderly is more prominent in patients who do not have protective pigmentation. It is similar in eyes with low levels of pigmentation.

Measuring the pigmentation in the macular region actually is a reasonable measure of the carotenoid content of the macula. Lower macular pigmentation is correlated with progression of macular degeneration
. While the main component of this macular pigmentation is meso-zeaxanthin taking lutein alone may increase the levels of meso-zeaxanthin in some individuals but
the conversion process of Lutein to meso-z is unknown at this time and it is clear that there are many individuals who cannot convert lutein to meso-zeaxanthin. It is for this reason that any macular nutritional supplementation requires therapeutic doses of Meso-zeaxanthin.

What This Means To You:

AMD is a lifelong disease. The rusting process starts early and only shows up later in life. As there is no cure for this disease it is important to utilize products like Macuhealth which has the correct amounts of Meso-Zeaxanthin 10 mg, Lutein 10 mg, and Zeaxanthin 2 mg to begin slowing its progression. In addition, as the goal is to "slow the AMD progression" it is critical that you are compliant taking the one soft gel each day. By taking action now for yourself and your family members you can potentially slow the rusting process that occurs with age and delay the underlying process that leads to visual loss. Protect yourself and your family by visiting www.nomoreamd.com .

In summary, the critical carotenoids are lutein, zeaxanthin and most importantly meso-zeaxanthin.

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