EYES RIGHT

How to protect your vision

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THE MACULA AT RISK

Q: *What is age-related macular degeneration, or AMD?*

A: The macula is the centre of your retina. It's where your finest vision comes from. And that area is where this degenerative process occurs.

There are two different types of AMD. One is called neovascular, or the so-called wet type. Neovascular means you have abnormal new blood vessels that may lead to bleeding and a very acute loss of vision. [See "Macular Degeneration," p. 4.]

Atrophic, or dry, macular degeneration is a slow withering away of the normal seeing cells and the underlying structures. So you have blind spots in the centre of your field of vision.

The wet type is less common, but it accounts for 80 per cent of people with severe vision loss.

Q: *Can AMD be treated?*

A: New treatments have dramatically helped the wet type. The treatments counteract vascular endothelial growth factor, or VEGF, which is important for growing new blood vessels. VEGF also plays a role in the spread of cancer and in other diseases.

We inject into the eye the same drugs that we use for cancer—Lucentis, for example. In most cases, vision remains stable, and in 40 per cent of patients, the treatment actually reduces vision loss, which is quite remarkable. So these drugs have really revolutionized treatment of wet AMD.

We've been testing treatments for the dry type and exciting research is ongoing, but nothing has worked out yet.

Q: *Is AMD a major public health problem?*

A: Yes. One million people in Canada have age-related macular degeneration. That number is expected to double by 2031. And many of those people are at risk for advanced macular degeneration. They have intermediate AMD, which is characterized by these yellow spots on the retina called drusen.

Q: *Does early AMD cause symptoms?*

A: In the beginning, you may have very few or no symptoms. Early AMD can only be diagnosed by an eye exam where your eyes are dilated. The ophthalmologist or eye care provider puts drops in your eyes to open up the pupil so he or she can look at the retina and other structures of the eye.

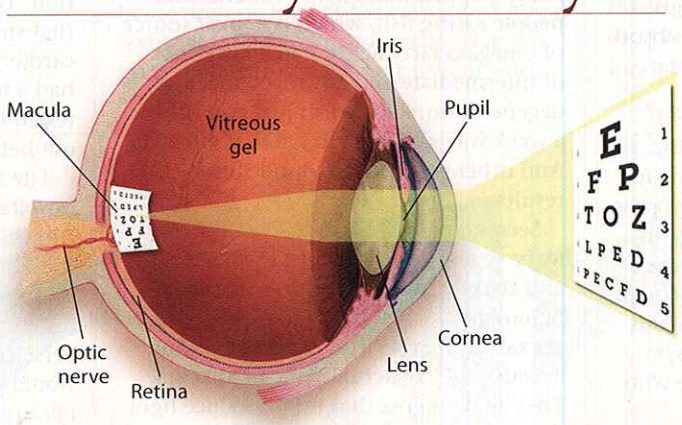
Q: *What causes AMD?*

A: The cause is unknown, but the main risk factor is age. The second most important risk factor is cigarette smoking, which can double your risk. And a number of studies have reported that people who consume more fish or green leafy vegetables have a lower risk of AMD, though that kind of study can't prove cause and effect.

Q: *The U.S. National Eye Institute recently released the results of the second Age-Related Eye Disease Study, or AREDS2. What did the first AREDS study find?*

A: The first study found that the AREDS formulation—a combination of vitamin C, vitamin E, beta-carotene, zinc, and copper—reduced the risk of progressing to advanced macular degeneration in those who had intermediate AMD. But the AREDS formulation didn't stop people with early AMD from progressing to intermediate AMD.

Anatomy of the Eye



The lens, which focuses light rays onto the retina, is supposed to be clear. Opaque areas, called cataracts, scatter light and blur vision. When the macula—the centre of the retina—degenerates, it blurs the sharp, detailed vision that you need to read, drive, sew, etc.

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Photo: © sonya etchison/fotolia.com (top). Illustration: Adapted from the U.S. National Eye Institute.

Q: *What led to the first AREDS formulation?*

A: The vitamins C and E and the beta-carotene were designed to provide anti-oxidants. And we decided to add zinc because a very small study found that it might improve vision in a very short time.

Based on that small study, zinc had taken off. It was a multi-million-dollar business. We used 80 milligrams of zinc, a dose that was considered very high by our nutritional experts. But we wanted to give the same dose that that small study gave.

five-year clinical trial ended in 2001, all the patients were told to take the AREDS formulation, so it was no longer a clinical trial. The participants were followed for five more years, through 2005.

At that point, we still saw a 27 per cent reduction in the risk of progressing to advanced disease in those who were originally assigned to take the AREDS formulation.

Q: *What led to AREDS2?*

A: When we evaluated the diets of people in the AREDS population, two nutrients

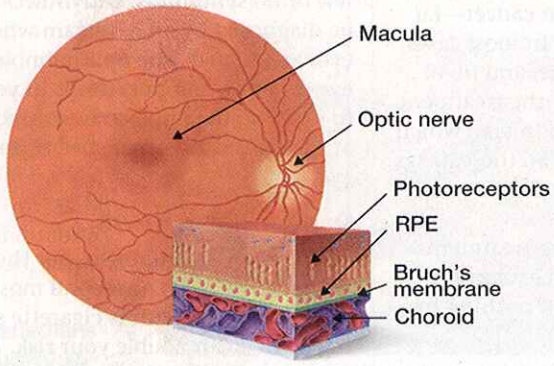
Q: *So AREDS2 tested lutein and omega-3s?*

A: Yes. We tested to see whether adding lutein and zeaxanthin and/or omega-3 fatty acids to the AREDS formulation would further reduce the risk of advanced AMD. All participants were randomly assigned to lutein and zeaxanthin, omega-3 fatty acids, the combination, or a placebo. [See "The AREDS2 Study," p. 5.]

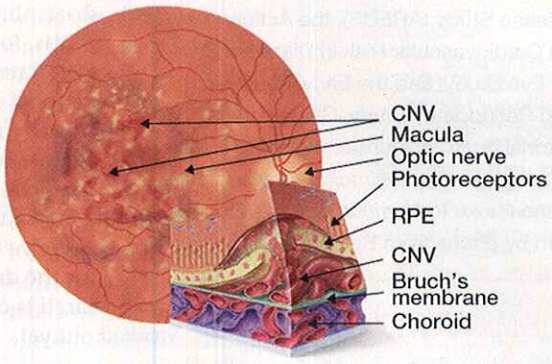
Q: *What else did AREDS2 test?*

A: We wanted to see if we could eliminate beta-carotene from the AREDS formula-

Macular Degeneration



The normal eye. Photoreceptors (rods and cones) produce waste that's removed by the retinal pigment epithelium (RPE), Bruch's membrane, and the choroid working together like a fireman's bucket brigade. Waste that doesn't get broken down collects in bundles called drusen (not shown).



The macula degenerates. If drusen build up, they can disrupt the RPE, the photoreceptors, and vision (dry macular degeneration). If abnormal blood vessels begin to grow—the process is called choroidal neovascularization, or CNV—they can bleed or leak fluid onto the retina (wet macular degeneration).

Illustrations: AMD Alliance International.

And we added copper because high doses of zinc can make it harder to absorb copper, which could result in anemia.

Q: *Did you find any adverse effects?*

A: Yes. In people who were given zinc, we found an increase in hospitalizations for urinary tract infections, an enlarged prostate in men, and stress incontinence in women. Stress incontinence is the loss of a small amount of urine when you cough, sneeze, laugh, or exercise. The problems occurred in 7.5 per cent of people who took zinc and in 5 per cent of those who did not take zinc.

Q: *Did the benefit from the AREDS1 formulation last?*

A: Yes. We recently published the results of a 10-year AREDS1 follow-up. When the

really popped out. First, we found that people eating fish, which is a great source of omega-3 fatty acids, had a lower risk of intermediate and advanced macular degeneration. Eating fish just two times a week was sufficient to see that effect. And other studies had found similar results.

Second, people who ate lots of green leafy vegetables, which are high in lutein and zeaxanthin, had a lower risk of AMD. Lutein and its virtually identical cousin, zeaxanthin, are particularly important because they're actually in the macula. They're pigments that might reduce light damage and might have anti-oxidative capacity.

We wanted to use lutein in AREDS1, but at that point, we didn't have a commercially available source.

tion. Two large trials had demonstrated that smokers given high doses of beta-carotene—33,000 to 50,000 IU a day—had a higher risk of lung cancer. So we tested the AREDS formula with or without beta-carotene.

The second issue was the increase in hospitalizations in people who got zinc in AREDS1. So in AREDS2 we tested either the original dose of 80 milligrams or a lower dose of 25 milligrams. We saw no difference in hospitalizations or other adverse effects. We can't tell if taking no zinc would have led to fewer adverse effects because everyone in AREDS2 took zinc.

Q: *Weren't the zinc takers in AREDS1 less likely to die?*

A: Yes. We found that zinc reduced the mortality rate by about 20 per cent. The

What AREDS2 Tested

AREDS2 tried to improve on the AREDS1 formula (vitamin C, vitamin E, beta-carotene, zinc, and copper).

Everyone in AREDS2 got

Vitamin C *(500 mg)*, vitamin E *(400 IU)*, and copper *(2 mg)*

In addition, people got

Either	Or
Lutein *(10 mg)* + Zeaxanthin *(2 mg)*	No Lutein + Zeaxanthin
DHA *(350 mg)* + EPA *(650 mg)*	No DHA + EPA
Beta-carotene *(25,000 IU)*	No Beta-carotene
Zinc *(80 mg)*	Zinc *(25 mg)*

Sources: *JAMA 309*: 2005, 2013 and *JAMA Ophthalmol. 131*: 843, 2013.

reduction was mostly due to fewer heart attacks and strokes. Further research is needed to follow up on those results.

Q: *So everyone in AREDS2 got a variation of the AREDS1 formula?*

A: Yes. These are people who are at high risk for advanced macular degeneration, so they all got the AREDS formulation. They all had intermediate AMD in both eyes or intermediate AMD in one eye and advanced disease in the other eye. So even the placebo group was getting the AREDS formulation.

Q: *Did the omega-3s help?*

A: They weren't beneficial or harmful for eyes. We're also looking at cardiovascular disease and cognitive function. We're still analyzing those results.

Q: *What about lutein and zeaxanthin?*

A: When the people who took lutein and zeaxanthin were compared directly to those who took beta-carotene, there was about a 20 per cent lower risk of progressing to advanced AMD in those who took lutein and zeaxanthin.

Lutein and zeaxanthin had the greatest benefit for people who were getting the least lutein and zeaxanthin from their food. Those people had a 25 per cent lower risk of progressing to advanced AMD than those who took beta-carotene.

Q: *Did beta-carotene help?*

A: The results suggested that beta-carotene probably wasn't playing much of a role. It's not in the eye, while lutein and zeaxanthin are. Beta-carotene was added because at the time we did AREDS1, it was a popular antioxidant.

Q: *Did beta-carotene cause harm?*

A: Because previous studies suggested that high doses of beta-carotene increased the risk of lung cancer in smokers, we didn't give beta-carotene to current smokers. However, in AREDS2 we found almost a two-fold increase in lung cancer in people who were given beta-carotene. The disease was diagnosed in 2 per cent of people who were given beta-carotene and in 1 per cent of those who were not. Approximately 90 per cent of these cancers occurred in former smokers.

Q: *How long ago did the former smokers stop smoking?*

A: We don't know, but it had to be at least one year before they entered the study.

Fifty per cent of the participants in our studies were former smokers. And 7 per cent of people in AREDS2 and 13 per cent in AREDS1 were current smokers. So many people with AMD have some smoking history. Beta-carotene should be eliminated from the AREDS formulation because of this adverse effect.

Q: *Didn't beta-carotene block lutein from being absorbed?*

A: Yes. Beta-carotene suppressed blood lutein levels. People who were given beta-carotene had 33 per cent lower blood levels of lutein than those who were not given beta-carotene. Beta-carotene and lutein are carried into the gut with certain proteins, and there's only so many there. If you flood the system with beta-carotene, less lutein gets in.

Q: *Are foods that are rich in beta-carotene safe?*

A: Yes. The risks associated with beta-carotene supplements haven't been found with food. People ask me, "Can I eat carrots?" Eat as much as you'd like. Eating foods rich in beta-carotene is not a problem.

Q: *Were most people in AREDS2 getting lutein in Centrum Silver?*

A: Yes. Some people in AREDS were taking multivitamins on their own before the study started. In order to make sure that they were all taking the same multivitamins, we offered all AREDS2 participants Centrum Silver, and 90 per cent accepted it.

Centrum Silver contains 250 micrograms of lutein, which was much lower than the 10 milligrams we were studying. [So is the 500 micrograms of lutein in Centrum Select 50+, the company's formula for seniors in Canada.] Ten milligrams is 10,000 micrograms. The 250 micrograms of lutein in Centrum probably didn't affect our study results. People with AMD should know that it is safe to take a multivitamin in addition to the AREDS formulation.

Q: *Can you get 10,000 micrograms of lutein a day from food?*

A: It's hard to get that much from food. People at the highest intakes get

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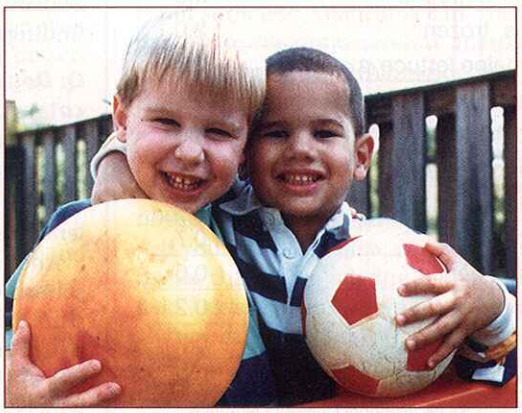
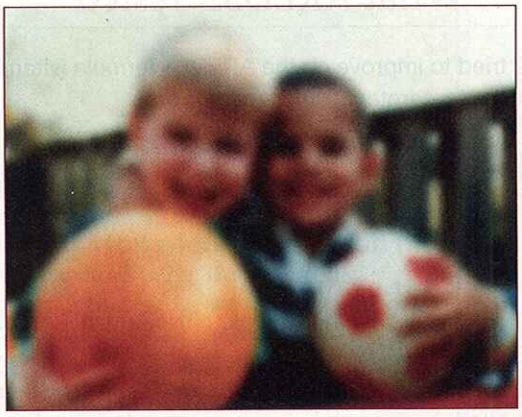


A scene as viewed by someone with a healthy retina.

A scene as viewed by someone with macular degeneration.

Photos: U.S. National Eye Institute, National Institutes of Health.



A scene as viewed by someone with a cataract.

6,000 micrograms a day, and that would be eating about a third of a cup of cooked spinach every day. That's a lot of spinach.

People with the lowest intakes eat the equivalent of maybe a third of a cup a week. And the people in AREDS consume more than the general population. They're a well-nourished, well-educated group. These are mostly people who are taking care of themselves. And the extra lutein was still helping them.

Q: *Did the AREDS2 nutrients slow both wet and dry AMD?*

A: Mostly they helped with neovascular, or wet, AMD. But the interesting thing is that most people don't just get neovascular. They get a mix. Quite often, 30 per cent of the people with dry or geographic atrophy type also develop new blood vessels within five years.

So we're really talking about everybody with macular degeneration, because you can't sort out who's going to get what. We don't have a crystal ball.

Q: *Should people who don't have AMD still take the AREDS nutrients?*

A: No. People who have a family history of AMD or who think they might be at risk should have a dilated eye exam. If they are diagnosed with intermediate AMD, then they should consider taking the AREDS formula.

On the other hand, we should all eat a diet replete with fish and green leafy vegetables, not just for the eyes but to lower the risk of cardiovascular disease, cancer, and other conditions. And even though we didn't find a benefit from omega-3 supplements, data from other studies are very compelling that we should eat fish.

Q: *Why would omega-3s help?*

A: EPA, or eicosapentaenoic acid, and especially DHA, or docosahexaenoic acid, are major building blocks of the retina. They may also play a role in reducing inflammation. We had great hopes that they would be beneficial.

Of course, the data on omega-3s and cardiovascular disease looked promising years ago, and less promising in the last five or 10 years, partly because people are receiving better care for their cholesterol and high blood pressure.

Maybe our patients were so well nourished that they didn't need extra omega-3s. Maybe just a little in the diet goes a long way.

Why didn't omega-3 fatty acids work in AREDS2? Did we use the wrong dose? Did we start too late? Is our ratio of DHA to EPA incorrect? We don't know the answers, but we're conducting further analyses.

Q: *What about B vitamins or other nutrients that AREDS didn't test?*

A: In a randomized trial of 5,442 women, the combination of vitamin B-6, vitamin B-12, and folate reduced the risk of macular degeneration. These were interesting results that are worth further investigation.

Q: *And neither vitamin C nor vitamin E helped in those women or in the men in the U.S. Physicians' Health Study?*

A: That's correct. Those vitamins slow down the progression of disease in people who already have it, but it looks like they don't prevent it.

Digging for Lutein

If you're looking for lutein-rich vegetables and fruits, here's where to start.

Vegetables & Fruits *(½ cup, vegetables cooked, unless noted)*	Lutein + Zeaxanthin *(milligrams)*
Kale	15.5
Spinach *(2 cups raw)*	10.4
Spinach	9.6
Swiss chard	9.4
Collard greens	5.3
Peas, frozen	2.0
Romaine lettuce *(2 cups raw)*	2.0
Brussels sprouts	1.1
Zucchini	1.0
Broccoli *(2 spears)*	0.9
Yellow corn	0.8
Asparagus	0.7
Green beans	0.6
Iceberg lettuce *(2 cups raw)*	0.2
Nectarine *(1)*	0.2
Orange *(1)*	0.2

Source: U.S.D.A. National Nutrient Database.

BEYOND MACULAR DEGENERATION

Q: *What are cataracts?*

A: A cataract means that the eye's lens becomes opaque. Aging is the main risk factor. One of the most common surgeries in Canada is for cataracts. If we can reduce cataracts by even 10 to 20 per cent, we'd make a remarkable dent in rates of surgery.

Diabetes is known to increase the risk of cataract. Smoking and light exposure probably increase the risk. Women tend to have a slightly higher risk than men, and people who are overweight or obese have a higher risk than those who are normal weight.

Q: *Did the AREDS nutrients prevent cataracts?*

A: The AREDS1 formula didn't have a beneficial or harmful effect on cataracts. In AREDS2, participants with the lowest intakes of lutein and zeaxanthin who were given lutein and zeaxanthin had about a 30 per cent lower risk of cataract surgery than those who got no lutein or zeaxanthin. We need to explore those findings further.

Q: *Does anything else help prevent cataracts?*

A: In AREDS1 we found that people who were taking Centrum had a lower risk of nuclear cataracts, which occur when the lens gets thicker and thicker.

And a few years later, an Italian trial sponsored by the U.S. National Eye Institute found that Centrum reduced the risk of nuclear cataracts but increased the risk of posterior subscapular cataracts, which are in the back of the visible lens. So that was a mixed message.

Photo: U.S. National Eye Institute, National Institutes of Health.

A scene as viewed by someone with diabetic retinopathy.

Q: *Which type is most common?*

A: Nuclear. But posterior subscapular cataracts cause the most vision problems earlier and most noticeably if they're right in the centre of the back of the lens. In AREDS2, 90 per cent of our patients were taking Centrum, so we don't know whether it had an effect on cataracts, but results from the Physicians' Health Study and other randomized trials should give us some idea of what's going on with that.

We didn't look at omega-3 fatty acids because there's no biological reason omega-3s would have any effect on cataracts.

Q: *How does diabetes harm eyes?*

A: Diabetes can lead to small-blood-vessel disease. And the eyes have small blood vessels. The longer you've had diabetes and the higher your blood sugar is, the more likely you are to get diabetic eye disease, or diabetic retinopathy.

The small vessels can actually close up, and the body reacts by developing abnormal new vessels, which can cause hemorrhaging and scarring. A bleed in the eye could block vision. It can actually detach the whole retina and cause blindness.

Q: *Can lower blood sugar protect against diabetic retinopathy?*

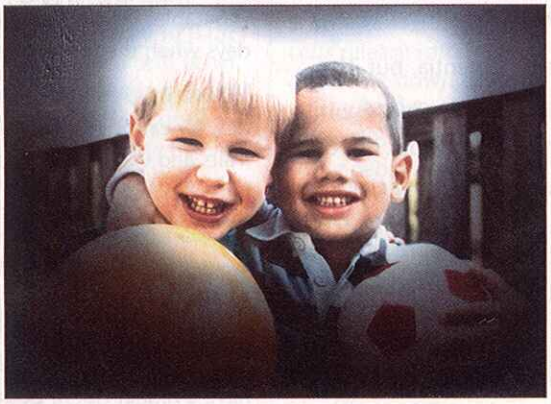
A: Yes. If you have diabetes, you're doing very well if you keep your hemoglobin A1c—that's a long-term measure of blood sugar levels—around or below 7 per cent. We've proven in studies that people with type 1 or type 2 diabetes who have tight control on their blood sugar have less progression of diabetic eye disease. It could be as much as a 70 per cent reduction.

That's tremendous. No drug can give you that. It's also crucial for people with type 1 or type 2 diabetes to manage their blood pressure and cholesterol.

Q: *Do most people get their eyes checked often enough?*

A: No. It's a problem. Everyone aged 65 or older should have an exam with their eyes dilated every one or two years. Many don't. And people with diabetes should have their eyes examined on a yearly basis.

Having an eye exam is crucial. The leading causes of blindness—macular degeneration, cataracts, and especially glaucoma—can sneak up on you without your ever knowing you have them. And if you have diabetes, your risk of eye disease and losing vision is much higher. There's so much more we can do for diabetics now.



A scene as viewed by someone with glaucoma.

Q: *That test with a puff of air isn't enough to detect glaucoma?*

A: Simply measuring the eye pressure is not sufficient. Glaucoma can cause damage to the optic nerve. A dilated eye exam allows the ophthalmologist to see if the nerve is damaged.

Testing the field of vision is also important to look for defects of glaucoma. The visual field test picks up which part of the field you're missing.

If you have glaucoma, you may not realize that you're missing the peripheral field, because if you've got two eyes, you're always scanning. But if you look straight ahead and you can't see your hands when they're held out to your sides, then it's because you don't have peripheral vision.

Q: *So you need both the visual field test and the dilated eye exam to diagnose glaucoma?*

A: Yes. And both are especially important in people who are suspected of having glaucoma or have a family history of it.

Q: *How does a dilated eye exam find macular degeneration?*

A: We look for drusen in the early stages. If you have AMD, one thing you can do to monitor yourself is to close one eye and see if you can read newsprint. Or look at straight lines on graph paper with one eye covered to see if they look crooked.

Covering one eye helps because sometimes when you have an eye disease in one eye, the other eye compensates so well that you don't notice it. People say, "I accidentally covered my eye because I was brushing my hair and I realized that I can't see out of my other eye."

Even to find cataracts, you want to have your eyes dilated. When you look into the pupil, you only see a small part of the lens. But when you dilate, you see probably 80 per cent of the lens.

Q: *What would you tell someone without AMD who wants to take the AREDS formulation?*

A: We don't have evidence that the AREDS formulation makes any difference if you don't have intermediate AMD. In AREDS1, the supplement didn't help prevent cataracts or keep the early stages of AMD from progressing. The AREDS2 supplement is for people who have intermediate disease—that is, who are at risk for advanced disease. We don't know the side effects of taking these supplements in the long term.

The Bottom Line

- To protect your eyes, eat lutein-rich foods (like green leafy vegetables) and fish.
- Get an exam with your eyes dilated every year or two.
- If you have intermediate macular degeneration, take lutein (10 mg), zeaxanthin (2 mg), zinc (25 mg), vitamin C (500 mg), and vitamin E (400 IU) every day.

Photos: U.S. National Eye Institute, National Institutes of Health.