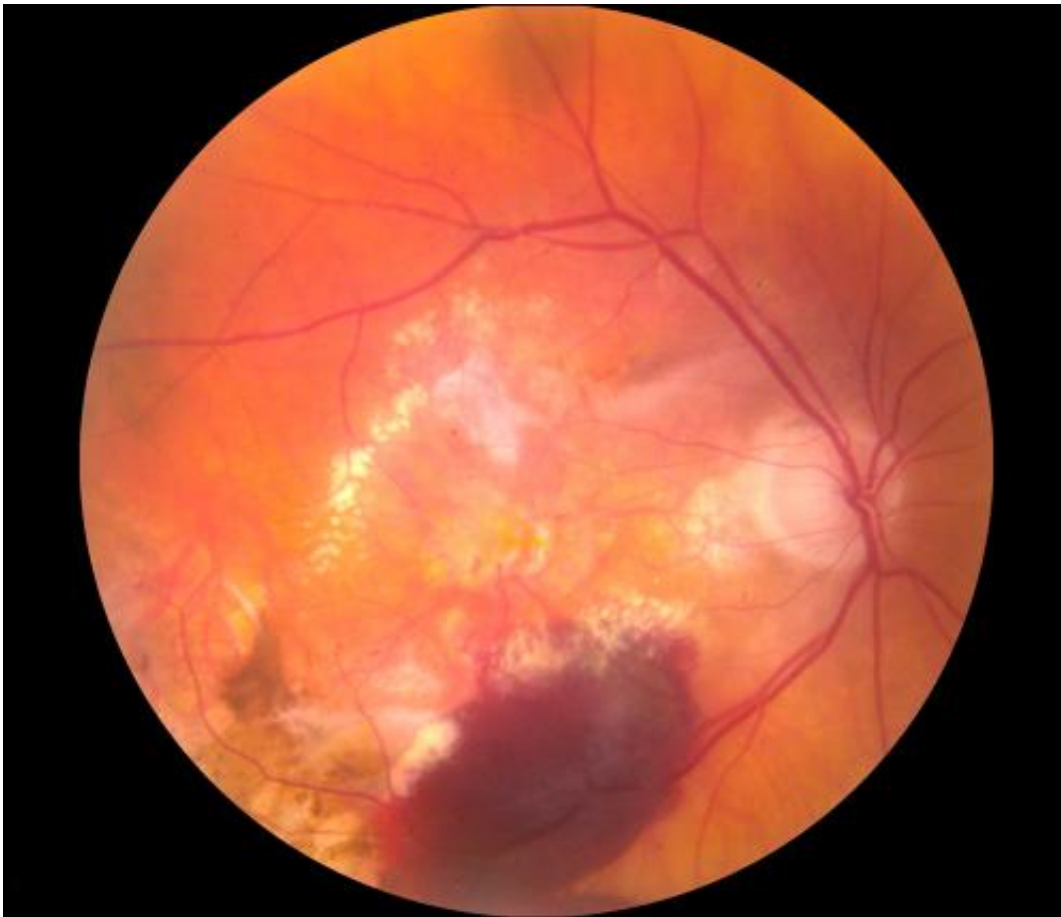


Cholesterol-lowering eye drops could treat macular degeneration

April 2 2013, by Jim Dryden



A photograph of a retina affected by advanced neovascular (wet) age-related macular degeneration (AMD) as characterized by new blood vessels with bleeding (red) and scar tissue resulting in severe vision loss. Credit: *Cell Metabolism*, Sene et al

A new study raises the intriguing possibility that drugs prescribed to lower cholesterol may be effective against macular degeneration, a blinding eye disease.

Researchers at Washington University School of Medicine in St. Louis have found that age-related macular degeneration, the leading cause of [vision loss](#) in Americans over 50, shares a common link with atherosclerosis. Both problems have the same underlying defect: the inability to remove a buildup of fat and cholesterol.

The new study is published online in the journal *Cell Metabolism*.

Working in mice and in [human cells](#), the researchers shed new light on how deposits of cholesterol contribute to macular degeneration and atherosclerosis and even blood vessel growth in some [types of cancer](#).

Patients who have atherosclerosis often are prescribed medications to [lower cholesterol](#) and keep arteries clear. This study suggests that some of those same drugs could be evaluated in patients with macular degeneration.

"Based on our findings, we need to investigate whether vision loss caused by macular degeneration could be prevented with cholesterol-lowering eye drops or other medications that might prevent the buildup of lipids beneath the retina," says senior investigator Rajendra S. Apte, MD, PhD.

The new research centers on macrophages, key [immune cells](#) that remove cholesterol and fats from tissues. In macular degeneration, the excessive buildup of cholesterol begins to occur as we age, and our macrophages begin to malfunction.

In the "dry" form of age-related macular degeneration, doctors

examining the eye can see lipid deposits beneath the retina. As those deposits become larger and more numerous, they slowly begin to destroy the central part of the eye, interfering with the vision needed to read a book or drive a car.

As aging macrophages clear fewer fat deposits beneath the retina, the [macrophage cells](#) themselves can become bloated with cholesterol, creating an [inflammatory process](#) that leads to the formation of new blood vessels that can cause further damage. Those vessels characterize the later "wet" form of the disease.

"Ultimately, that inflammation creates a toxic mix of things that leads to new [blood vessel growth](#)," Apte explains. "Most of the vision loss from 'wet' macular degeneration is the result of bleeding and scar-tissue formation related to abnormal vessel growth."

As part of their research, the scientists identified a protein that macrophages need to clear fats and cholesterol. As mice and humans age, they make less of the protein, and macrophages become less effective at engulfing and removing fat and cholesterol.

Apte, the Paul A. Cibis Distinguished Professor of Ophthalmology and Visual Sciences, and his team found that macrophages, from old mice and in patients with macular degeneration, have inadequate levels of the protein, called ABCA1, which transports cholesterol out of cells. As a result, the old macrophages accumulated high levels of cholesterol and couldn't inhibit the growth of the damaging blood vessels that characterize the "wet" form of the disorder.

But when the researchers treated the macrophages with a substance that helped restore levels of ABCA1, the cells could remove cholesterol more effectively, and the development of new blood vessels was slowed.

"We were able to deliver the drug, called an LXR agonist, in eye drops," says first author Abdoulaye Sene, PhD, a post-doctoral fellow in the Apte lab. "And we found that we could reverse the macular degeneration in the eye of an old mouse. That's exciting because if we could use eye drops to deliver drugs that fight macular degeneration, we could focus therapy only on the eyes, and we likely could limit the side effects of drugs taken orally."

Sene and Apte also say that since [macrophages](#) are important in atherosclerosis and in the formation of new blood vessels around certain types of cancerous tumors, the same pathway also might provide a target for more effective therapies for those diseases.

"We have shown that we can reverse the disease cascade in mice by improving macrophage function, either with [eye drops](#) or with systemic treatments," Apte says. "Some of the therapies already being used to treat atherosclerosis target this same pathway, so we may be able to modify drugs that already are available and use them to deliver treatment to the eye."

More information: Sene A, Khan AA, Cox D, Nakamura REI, Santeford A, Kim BM, Sidhu R, Onken MD, Harbour JW, Haqbi-Levi S, Chowers I, Edwards PA, Baldan A, Parks JS, Ory DS, Apte RS. Impaired cholesterol efflux in senescent macrophages promotes age-related macular degeneration. *Cell Metabolism*, vol. 17(4), published online April 2, 2013. [dx.doi.org/10.1016/j.cmet.2013.03.009](https://doi.org/10.1016/j.cmet.2013.03.009)

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