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Ophthalmologists May Detect More Alzheimer's

Ocular signs may be some of the first clues available to detect the impending onset of this devastating disease.

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The odds are that ophthalmologists, who routinely take care of elderly patients, may be the first to see a patient with undiagnosed Alzheimer's disease. The ability to recognize the earliest signs of the disease and refer a patient for prompt evaluation and treatment is becoming increasingly important as newer interventions are being developed. Alzheimer's affects more than 4.5 million Americans, mostly past the sixth decade of life. The risk of developing the disease doubles every five years. As families witness the mental deterioration of a loved one, they can't help but ask questions, and worry about the answers. Will the disease affect vision? Can an Alzheimer's patient safely undergo cataract surgery? Could the disease have been diagnosed sooner? What preventive treatments can slow progression of the disease? Am I at risk? Be-lieve it or not, the ans-wers to these quest-ions and more may soon come from their ophthalmologist.

Sixty percent of Americans over the age of 60—and 70 percent of those over the age of 75—have cataracts. Oph-thalmologists in this country will perform more than 2.9 million cat-aract procedures this year. As an ophthalmologist who regularly sees elderly patients for cataract surgery, I have some special insight into looking for patients with the characteristic symptoms of Alzheimer's. Do other ophthalmologists know that the eye examination they perform for cataract may detect the earliest signs of Alz-heimer's?

Background

In 1906, the German physician, Alois Alzheimer, first described the

characteristic pathological changes in the brain of a woman with an unusual mind-altering disease. One-hundred years later, Alzheimer's is seen with increasing frequency in our affluent society. Few of us are untouched by a patient, a friend or a loved one who has developed the disease. The effect this debilitating disease has on pa-tients, families and the health-care community can be overwhelming.

In Alzheimer's, memory loss can be severe enough to interfere with daily functioning. The disease can be cruel both to the patient, who often is un-aware of the extent of the loss of mental function, and for the spouses and family who must provide around-the-clock nursing care. Watching the downward spiral of a loved one who can no longer recognize members of her own family or perform the simplest of tasks can take a terrible toll.

There is no simple test for the disease. We still do not know the cause of Alzheimer's, but over the past 10 years, medical science has advanced our understanding of the disease process. Some believe the disease to be genetic, yet the only known risk factor is a gene that makes apolipoprotein E (ApoE) and only 15 percent of those with the gene go on to develop Alzheimer's. The vast majority of individuals develop the sporadic age-related form.

Early diagnosis is critical to prepare the patient and the family for the cascade of symptoms that will ultimately appear. More importantly, it can be critical to the success of many new drugs that could delay the onset or slow the progression of the disease. Confirming the diagnosis relies upon the findings of neurofibrillar tangles and plaques in the brains of individuals with AD, but sadly, only after an autopsy. The plaques are formed by an excess accumulation of amyloid beta protein (Aß). The pathway of this protein's biosynthesis is the basis of many of the new approaches to drug development.

There are several treatments available for Alzheimer's. The newest drugs in-clude Tacrine (Cognex), Donepezil (Aricept), Rivastigmine (Exelon), and Galantamine (Razadyne, previously known as Reminyl). These pharmaceuticals may lessen Alzheimer's symptoms for a limited time, but are only effective if started before the

development of the more ad-vanced signs. The earlier the diagnosis is made, the more effective the treatments are in slowing progression of the disease. Once the disease is established however, present day treatments become less effective. The drug memantine (Namenda) is approved to treat moderate to severe forms of Alzheimer's, but its effect is limited.

We are still far from a cure. I am confident, though, that the combined efforts of the pharmaceutical and biotechnology industry will result in newer treatments for Alzheimer's. Someday soon we may see the disease prevented altogether.

Your Role

Where do ophthalmologists fit in with the diagnosis and treatment of Alzheimer's? Over the past several years, researchers have uncovered an amazing way to discover the disease outside of the brain. Ophthalmologists have long known that amyloid appears within the eye. Pseudoexfoliation syndrome, for example, has been shown to be associated with an amyloid of a serum protein. Lee Goldstein, MD, PhD, the lead author of a paper published in The Lancet and a member of the MGH Ge-netics and Aging Research Unit at Har-vard Medical School, along with re-searchers at Beth Israel and Brigham and Women's Hospital in Boston, have discovered that Aß can be detected in lens samples from elderly individuals with and without the disorder. "The formation of Aß plaques in the brain and the de-velopment of cataracts in the lens are both examples of accumulated protein associated with age-related degenerative damage," he said, "In addition, people with Down syndrome, who develop Alzheimer's at an early age, are also prone to early onset cataracts. But as far as we know, no one had investigated whether there might be any association between the pathology of Alzheimer's disease and age-related changes in the lens."

What the researchers found was a distinctive pattern of Aß deposits that ap-pear only in the outer, peripheral portion of lenses removed at autopsy from Alzheimer's patients. This finding became the basis for

developing an ophthalmic detection system for Aß. Paul Hartung and colleagues at Neuroptix Corp. (Acton, Mass.) are developing proprietary technology that uses complementary optical techniques to detect the level of protein in the supranuclear lens.

Here is how it works. Using a modified ophthalmoscope to which is attached a low power infrared laser, the developers were able to use quasi-elastic light scattering to accurately measure the amount and size of aggregated proteins in a particular sampled region of a patient's lens. A fluorescent ligand scanner confirms that the scattering detected is caused by A-Beta proteins. In this manner, A-Beta can be detected in the lens, long before signs of the disease are present in the patient. This unique technology, which allows imaging of the same place in the lens over time, could potentially allow physicians to monitor the effectiveness of therapy by monitoring the accumulation or reduction of abnormal protein. The technology is in its early testing stages but clinical trials are underway. This area of research shows much promise for the millions affected by Alzheimer's, their families, and the physicians who care for them.

Could ophthalmologists actually be-come the sentinels who could detect this devastating mind wasting disease before anyone else? The implications are intriguing. If the early diagnosis of Alzheimer's disease becomes a reality, the elderly may someday soon see an ophthalmologist not just to improve their quality of life through cataract surgery, but by having their cataract analyzed for a degenerative brain disease.

Dr. Kershner is an ophthalmic surgeon, consultant and president of Eye Laser Consulting in Boston. He has no financial or proprietary interest in any of the technologies described in this article.

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