Can You Catch Alzheimer's?

Original Content | November 02, 2009
http://www.oprah.com/health/A-Link-Between-Alzheimers-and-Cold-Sores

Photo: © 2009 Jupiterimages Corporation

It's a memory-destroying disease that has baffled scientists for decades, but one researcher has a controversial theory: that we can catch it with a kiss.

Rich P. is only in his 20s, but these days he finds himself obsessing over something most guys his age never think twice about: *Am I doomed to lose my mind?*

In some ways, Rich's anxiety is understandable. "My girlfriend is a social worker who works with the aged, specifically people with Alzheimer's," he says. "So I've seen close up what the disease does to you." Indeed, Alzheimer's disease is characterized by memory loss and confusion, and typically ends with complete disconnection from the world. People in its advanced stages can't care for themselves, recognize loved ones, or remember the lives they lived.

There's also another, even more personal connection for Rich: His girlfriend's father recently passed away from Alzheimer's. He was one of more than 70,000 Americans who die from the disease every year.

Still, what should worry Rich most isn't what he's witnessed in other people, but what he sees in the mirror. Because there, literally right under his nose, is evidence that the monster that could be responsible for Alzheimer's is already skulking about inside his body, preparing itself—at some point, decades down the road—to attack and destroy his brain.

So here's the question: Is it in you too? For years, physicians and Alzheimer's experts have said that the earliest symptoms of the disease typically don't appear until you're in your 60s, 70s, or beyond. But now there's reason to believe that the first warning signs may actually crop up much earlier than that, and in a seemingly much more benign way: as cold sores, those embarrassing blisters that can erupt on the lips of people who are sick or run-down.

The sores are triggered by the herpes virus—most often, herpes simplex virus type 1 (not to be confused with HSV-2, which predominately causes genital herpes). In

recent years, a growing body of research, much of it championed by a British scientist, has begun to suggest a startling fact: The same virus known for sabotaging people's social lives could be responsible for the majority of Alzheimer's cases.

"There's clearly a very strong connection," says the researcher, Ruth Itzhaki, Ph. D., speaking one afternoon in her office at the University of Manchester, in northwestern England. A neurobiologist, Itzhaki has spent the better part of two decades studying the link between herpes and Alzheimer's. "I estimate that about 60 percent of Alzheimer's cases could be caused by the virus."
As viruses go, herpes is a particularly devilish bugger. The ancient Greeks were among the first to record the sores it causes (the virus's name is derived from a Greek word meaning "to creep"), and today the microbe is ubiquitous. As many as 85 percent of us have been infected by it, though experts say as few as 15 percent show symptoms. Worse, once you have it, you have it forever: After the initial infection, the virus lies dormant in your peripheral nervous system, occasionally flaring up during periods of stress, illness, or fatigue. But it never completely disappears.

And it's that fact—herpes as the viral equivalent of The Thing That Wouldn't Leave—that lies at the heart of the herpes-Alzheimer's relationship. Research suggests that as we age, HSV-1 actually spreads to our brains, where in certain people, Itzhaki theorizes, it can cause the buildup of deposits—known as amyloid plaques and neurofibrillary tangles—that attack and destroy the cells responsible for memory, language, and physical functions. In short, those people develop Alzheimer's.

It's a provocative theory, one that would sound preposterous if it weren't for the steadily accumulating evidence. Last January, for instance, Itzhaki and her colleague, Matthew Wozniak, Ph. D., published a study in the *Journal of Pathology* in which they searched for the presence of the herpes virus in people's brains. They found that it resided in 90 percent of the amyloid plaques.

"The link between herpes and Alzheimer's has been there for a while, but more people are starting to pay attention," says Howard Federoff , M.D., Ph.D., an expert on neurodegenerative diseases and the executive dean of the school of medicine at Georgetown University. "It's no longer just a curiosity."

Unfortunately, while the theory may be on more researchers' radar, it's perhaps becoming a blip in the one area that matters most: the fight for funding. Sure, on the surface, the possible discovery of a cause for Alzheimer's looks like Nobel-caliber news because it suggests a way forward in treating a disease that scientists have struggled—largely unsuccessfully—to understand. What's more, if a new treatment does emerge, it could be just in the nick of time: Thanks to a combination of changing demographics and longer life spans, experts are predicting nothing less than an Alzheimer's epidemic in the decades ahead.

And yet all the promise held in the herpes connection may vanish as quickly and completely as the memories of an Alzheimer's patient. That's because despite Itzhaki's nearly 20-year struggle to get her work noticed, an entrenched Alzheimer's research establishment remains skeptical. Worse, she now finds herself on the brink of having to shut down what may be the most promising avenue of investigation in ages.

"Our remaining funds are sufficient for only several more months," she says, "so unless we obtain a donation or grant, the work will then stop completely, because nobody else in the world is directly doing such research."

For young men like Rich P., who wonders what's in store for him in the decades ahead, this would appear to be an enormous scientific misstep—particularly since Rich believes he's seen firsthand the link between herpes and Alzheimer's.

His girlfriend's father, the one who passed away from Alzheimer's? He battled cold sores all his life.

Itzhaki says there are two reasons why herpes became a Virus of Interest in the hunt for an Alzheimer's cause. First was the observation, almost three decades ago, that a rare infection called herpes encephalitis affects the same regions of the brain that Alzheimer's does. Like people with Alzheimer's, encephalitis patients can be plagued by memory problems. The other factor, she says, is the prevalence of the herpes virus itself.

"Most people get it as children," Itzhaki says. "It's in your saliva, and it can easily be passed along with a kiss from a family member." She says it's not really that puzzling that most people who carry the virus never show symptoms—as she puts it, not everyone who's infected with a microbe is necessarily affected by it. "It depends on the person harboring the virus," she says. "It's probably based on genetic factors."

How might a germ you could have contracted from, say, a grandparent potentially destroy your brain when you *become* a grandparent?

In the early 1990s, researchers, including Itzhaki, found evidence suggesting that as we age, the herpes virus begins moving from its hideout near the bottom of the skull directly into the brain (possibly because our immune systems lose some bite). Indeed, one *Journal of Pathology* study found the virus in a high proportion of postmortem brain samples taken from people who'd died in their later decades, while it was absent in those from people who'd died in youth or middle age.

What effect does the virus have when it reaches your brain? The short answer: That depends. In certain people it seems to do much less damage than in others; just as some of us never develop cold sores, some of us can have the herpes virus inside our brains without any horribly ill effects. But Itzhaki believes that in other people—specifically those who carry APOE e4, a gene form, or allele, strongly linked to Alzheimer's—the virus is not only reactivated by triggers like stress or a weakened immune system, but also actually begins to create the proteins that form the plaques and tangles presumed to be responsible for Alzheimer's.

If you're looking for evidence, Itzhaki can show you a stack of it. In two studies, for example, she and several colleagues took brain samples from 109 deceased people—61 of whom had had Alzheimer's, 48 of whom hadn't—to search for any correlation between herpes, APOE e4, and Alzheimer's.

Their results: People who had both the APOE e4 gene and the herpes virus in their brains were *15 times* more likely to have Alzheimer's than people who had neither. (The researchers also found, intriguingly, that people who suffered from recurrent cold sores were almost six times as likely to have the APOE e4 gene as those who didn't get cold sores.)
A decade later, Dr. Federoff, then working at the University of Rochester, administered the herpes virus to four different groups of mice, each of which had a different variation or absence of the APOE gene. He found that in mice with the specific APOE e4 variation, the virus was slower to become dormant than it was in mice with APOE e2, APOE e3, or no APOE gene, suggesting that the virus could be replicating faster in the e4 mice. "The results definitely suggest there's something different about having APOE e4," says Dr. Federoff.

Still other research shows the direct impact of HSV-1 itself. In 2007, a study by Itzhaki and Wozniak found that infecting lab samples of brain cells with the virus caused a buildup of the protein (beta amyloid) that's the primary component of the plaque clogging the brains of Alzheimer's patients. The same study also found a similar result in the brains of mice that had been infected with HSV-1.

Then there was January's study in the Journal of Pathology. In it, Itzhaki and Wozniak looked at brain samples from 11 deceased people; six had had Alzheimer's and five hadn't. While both groups had plaques (not surprisingly, the Alzheimer's group had far more) and evidence of the herpes virus in their brains, there was a crucial difference in the concentration of the virus: In the Alzheimer's patients, 72 percent of the virus's DNA was found in the plaques, compared with only 24 percent that was found in the plaques of the non-Alzheimer's brains. Not surprisingly, all but one of the Alzheimer's sufferers also carried the APOE e4 gene, compared with none of the samples from the non-Alzheimer's people.

Wozniak is confident that these last two studies point to the same conclusion: "The results strongly suggest that HSV-1 is a major cause of amyloid plaques—and probably of Alzheimer's disease."

For Wozniak and Itzhaki, the next step is to test whether antiviral drugs like Zovirax and Valtrex, both of which are used to shorten the duration of cold sores, might alleviate or slow the progression of Alzheimer's. The pair is seeking funding for two experiments with antiviral drugs—one testing them on mice, the other testing them on Alzheimer's patients.
"If the treatment is successful, it would stop progression of the disease, rather than just stopping the symptoms," Itzhaki says.

But that funding isn't likely to materialize if the rest of the research community continues to dismiss Itzhaki's theory—or ignore it altogether. When I e-mailed John Trojanowski, M. D., Ph. D., a respected Alzheimer's researcher at the University of Pennsylvania, to find out his take on the connection between Alzheimer's and herpes, he shot back a one-sentence reply: "Do not know of any connection."

When I pressed and asked him to take a look at two of Itzhaki's recent studies, he was equally dismissive. "This is an old story," he said, "so I do not think there is much new news here."
Even those more familiar with the research remain skeptical. "One of the things we see a lot in science is relationships—two things happening together," says Bill Thies, Ph. D., chief

medical and scientific officer at the Alzheimer's Association. "But they often turn out to be independent events, or you can't tell which thing is causing which. It could be, for example, that there's something about amyloids that attracts HSV."

Wozniak says that the study he published with Itzhaki—in which the herpes virus caused amyloid accumulation in cells and mice—refutes that criticism. He also dismisses another critique—that he and Itzhaki haven't established the mechanism by which HSV-1 brings about that accumulation. Again, he argues, this study indicates an increase in the enzymes that are responsible for forming amyloid from its precursor protein, called APP.

"Surely, the mechanism is clear: HSV-1 causes an increase in these enzymes, which in turn causes degradation of APP, leading to amyloid formation." He pauses, and then adds wryly, "It's interesting that people raise this criticism when, until our research, no other underlying causes of amyloid production linked to Alzheimer's disease were known."

Itzhaki is more sanguine about the skepticism. "We've seen this before when a virus or bacterium is suggested as the cause for a chronic illness," she says, noting the reticence people had when *H. pylori* was suggested as a cause of ulcers and when the human papilloma virus was suspected as a cause of cervical cancer. Both are now largely considered medical fact. "And the Alzheimer's establishment is very conservative."

Georgetown's Dr. Federoff agrees that in some ways the theory isn't conventional enough to be embraced by many mainstream Alzheimer's researchers. "Herpes is a common virus, but in this case we're talking about it behaving in an atypical way," he notes. That said, would he like to see further research on the connection between HSV and Alzheimer's? Absolutely.

There is one matter on which the opposing camps agree: With each passing day, the stakes for Alzheimer's research grow higher. Over the past century, the only thing that has prevented the disease from becoming even more widespread and devastating is that most people passed away from something else before they were old enough to develop it.

Drop dead of a heart attack when you're 52, and Alzheimer's is one malady you probably won't have to worry about. But the more progress we make against our most common killers—heart disease, stroke, and cancer—and the more we extend our life spans, the greater the number of Alzheimer's cases we're likely to see. Indeed, as the 33-million-plus-strong baby boom generation enters its golden years and sees its risk of Alzheimer's increase, we are potentially looking at an epidemic. By 2010, the number of cases is expected to have increased 10 percent from its 2000 total, and from there the number is projected to more than double—to more than 950,000 new cases a year—by 2050.

"Alzheimer's has always been a big problem, but it's going to be even bigger," says Thies. "And the people who are now in their 20s, 30s, and 40s are the ones it's especially going to affect."
So what do you do if you're part of that group—especially if you tend to develop cold sores? One future option could be to have yourself tested for the APOE e4 gene—though Wozniak isn't a fan of that idea. "It would just cause a lot of worry for the person involved and his or her family."

Another possibility might be to take an oral antiviral drug preventively—essentially, to attempt to keep the herpes virus in check before it can do any damage to your brain. The hitch here, however, is that no clinical trials have ever evaluated the safety of taking a daily antiviral, such as Valtrex, for longer than a year. Plus, the average physician would consider the link to Alzheimer's too tenuous to let you play guinea pig.

In the end, the best option may simply be to wait, and hope. When I ask Wozniak whether he and Itzhaki feel like they're running out of time, he says, "Of course. We are all getting older. Our parents are getting older. Soon we'll all be affected one way or another by Alzheimer's disease...if we haven't already."