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Tests Detect Alzheimer's Risks, but Should Patients Be Told?

By **GINA KOLATA**

Marjie Popkin thought she had chemo brain, that fuzzy-headed forgetful state that she figured was a result of her treatment for [ovarian cancer](#). She was not thinking clearly — having trouble with numbers, forgetting things she had just heard.

One doctor after another dismissed her complaints. Until recently, since she was, at age 62, functioning well and having no trouble taking care of herself, that might have been the end of her quest for an explanation.

Last year, though, Ms. Popkin, still troubled by what was happening to her mind, went to Dr. [Michael Rafii](#), a neurologist at the [University of California, San Diego](#), who not only gave her a thorough neurological examination but administered new tests, like an [M.R.I.](#) that assesses the volume of key brain areas and a spinal tap.

Then he told her there was something wrong. And it was not chemo brain. It most likely was [Alzheimer's disease](#). Although she seemed to be in the very early stages, all the indicators pointed in that direction.

Until recently, the image of Alzheimer's was the clearly demented person with the sometimes vacant stare, unable to follow a conversation or remember a promise to meet a friend for lunch.

Ms. Popkin is nothing like that. To a casual observer, the articulate and groomed Ms. Popkin seems perfectly fine. She is in the vanguard of a new generation of Alzheimer's patients, given a diagnosis after tests found signs of the disease years before actual [dementia](#) sets in.

But the new diagnostic tests are leading to a moral dilemma. Since there is no treatment for Alzheimer's, is it a good thing to tell people, years earlier, that they have this progressive degenerative brain disease or have a good chance of getting it?

"I am grappling with that issue," Dr. Rafii said. "I give them the diagnosis — we are getting pretty good at diagnosis now. But it's challenging because what do we do then?"

It is a quandary that is emblematic of major changes in the practice of medicine, affecting not just Alzheimer's patients. Modern medicine has produced new diagnostic tools, from scanners to genetic tests, that can find diseases or predict disease risk decades before people would notice any symptoms.

At the same time, many of those diseases have no effective treatments. Does it help to know you are likely to get a disease if there is nothing you can do?

"This is the price we pay" for the new knowledge, said Dr. [Jonathan D. Moreno](#), a professor of medical ethics and the history and sociology of science at the [University of Pennsylvania](#).

"I think we are going to go through a really tough time," he added. "We have so much information now, and we have to try to learn as a culture what information we do not want to have."

Some doctors, like Dr. [John C. Morris](#) of [Washington University](#) in St. Louis, say they will not offer the new diagnostic tests for Alzheimer's — like M.R.I.'s and spinal taps — to patients because it is not yet clear how to interpret them. He uses them in research studies but does not tell subjects the results.

"We don't know for certain what these results mean," Dr. Morris said. "If you have amyloid in your brain, we don't know for certain that you will become demented, and we don't have anything we can do about it."

But many people want to know anyway and say they can handle the uncertainty.

That issue is facing investigators in a large federal study of early signs of Alzheimer's. The researchers, who include Dr. Morris, have been testing and following hundreds of people aged 55 to 90, some with normal memories, some with [memory](#) problems and some with dementia.

So far, only investigators know the results. Now, the question is, should those who want to learn what their tests show be told?

“We are just confronting this,” said Dr. [Richard J. Hodes](#), director of the National Institute on Aging. “Bioethicists are talking with scientists and the public about what is the right thing to do.”

Risk Levels, but No Scores

Dr. Rafii learned about the new tests and how to use them because he is an investigator in that large federal study. But many who come to the memory disorders clinic at the University of California, San Diego, where Dr. Rafii works, are not part of that study, the Alzheimer's Disease Neuroimaging Initiative, and simply want to know what is wrong with their brains.

So Dr. Rafii sometimes offers the study's diagnostic tests: spinal taps and M.R.I.'s to look for shrinkage in important areas of the brain; PET scans to look for the telltale signs of Alzheimer's in the brain. He calls it “ADNI in the real world,” referring to the study's acronym. Others, too, offer such tests, although doctors differ in how far they will go.

Dr. [Mony J. de Leon](#) of [New York University](#), for example, takes a middle ground. He is studying people at increased risk for Alzheimer's or other dementias, especially those whose mothers had Alzheimer's. That sort of family history, he has found, makes the disease more likely.

Many who come to his clinic have no memory problems, but are worried. So Dr. de Leon enrolls them in a study and regularly subjects them to an array of tests — ones that probe their memory, and ones like spinal taps and brain scans that look for signs of Alzheimer's. But he only provides people with a sort of general assessment, telling them they are at increased risk, decreased risk or somewhere in the middle.

“We do not reveal their scores,” Dr. de Leon said.

Some are satisfied with that.

Enzo Simone, for example, learned that, at age 43, his tests results do not indicate an increased risk. He was glad to know, but is not convinced he has escaped what he sees as a family fate. His

mother, grandmother and great-grandmother had Alzheimer's. They got the disease in their 60s. Mr. Simone, who lives in Amawalk, N.Y., reasoned that he had 20 years before it was likely to strike. And he intends to continue being tested as part of Dr. de Leon's study.

And for those who demand more details than just a "yes," "no" or "maybe," Dr. de Leon refuses.

"We say, 'It is a statistical exercise, it is a proof of concept, it is a baby test,' " Dr. de Leon said. "Some say: 'That's not good enough. I come back to you every year, and if you want me to continue I need more than that.' "

But Dr. de Leon said he was constrained by his hospital's ethics board, which has to approve his studies. It is extremely difficult, he says, to convince the board that giving out uncertain information about risk can help people, given that there is no effective treatment. And so, he says, he tells patients, "You are here to do an experiment."

Others, like Dr. [Lawrence Honig](#) of [Columbia University](#), say they sometimes see patients with no symptoms of [memory loss](#) who are nonetheless worried about their risk. Some of them have already gotten one of the early diagnostic tests, like a spinal tap or brain scan, from a neurologist in private practice, and have been told they were on their way to developing Alzheimer's. They come to Dr. Honig, hoping he will say it is not true.

That situation, Dr. Honig says, "has become more and more common over the last few years." He says that when test results are consistent with Alzheimer's, he is honest about it, telling patients that the results are "suggestive of Alzheimer's" but adding that all he can say for sure is "at some point in the future, you might be faced with that condition."

He agonizes, though, over telling people news like that.

"I think it's pretty terrible," Dr. Honig said. "It is psychologically invasive."

But for neurologists like Dr. de Leon, the future is fast approaching, as patients increasingly demand to know.

"The floodgate is about to open," Dr. de Leon said.

Information's Burden

At **Boston University**, Dr. **Robert Green** faced an ethical dilemma. He wanted to test people for a gene, APOE, that has three variants. People with two copies of one of the variants, APO e4, have a 12- to 15-fold increased risk of Alzheimer's disease. People with even one copy of the gene variant have about a threefold increased risk.

Five different published consensus statements by ethicists and neurologists had considered the question of whether people should be told the results of APOE tests. And every one of those committee said the answer is no, do not tell.

Dr. Green wondered if that answer was right.

"It seemed rather strange to be in a position where family members are coming to you and saying, 'I really understand APOE genotyping and the idea of a risk gene, and I want to know my genotype,' and then to say to them, 'I could tell you that, but I'm not going to.'" After all, he said, "Part of what we do in medicine is to inform."

He knew what it meant to tell people they were at high risk.

"Alzheimer's is a fearsome disease," he said. "You can't get much more fearsome than Alzheimer's." And yet, he said, "People still wanted to know."

He decided to do a study to see what would happen if he told.

The first surprise was how many people wanted to know. To be in the study, a person had to have a first-degree relative who had had Alzheimer's, making it more likely that they would have an APO e4 variant. Dr. Green thought maybe a small percentage of the people he approached would want to have the genetic test. Instead, nearly a quarter did.

"Frankly, we were terrified in early days of this study," Dr. Green said. "We did not want to harm anyone. We were very, very thoughtful and intense. We sat with people beforehand and asked if they were really sure they wanted to do this."

But his subjects were fine with the testing. After they gave the subjects their test results, researchers looked for psychological effects, observing participants in conversations and administering standardized questions designed to detect anxiety or **depression** or suicidal thoughts. They found nothing.

The main difference between those who found out they had APO e4 and those who found out they did not have that gene variant is that the APO e4 subjects were more likely to buy long term care insurance, were more likely to start exercising and were more likely to start taking [vitamins](#) and nutritional supplements, even though these practices and products have never been shown to protect against Alzheimer's.

For many, though, the news was good — they did not have APO e4.

That is what happened with Alan Whitney, a 66-year-old radio astronomer at the [Massachusetts Institute of Technology](#), whose mother and mother's father both had Alzheimer's. He wanted the test, he said, knowing what it meant to have APO e4.

"That was a gamble I took," he said.

And he was lucky. If he had had an APO e4 gene, he said, he might have taken early retirement and traveled.

"Now I feel I have some time." Dr. Whitney said.

Robert Stuart-Vail, an 83-year-old retired columnist for his local newspaper in Lincoln, Mass., was not so lucky. He found out he has one copy of the APO e4 gene. His father had Alzheimer's and so did his wife, who died from it, so he knows full well what the disease entails

"I wanted to know," Mr. Stuart-Vail said. "I wanted to be able to tell my children."

When he told them, though, they did not say much, Mr. Stuart-Vail said.

"I don't think it meant that much to them. Alzheimer's — that's something that happens to old people." Mr. Stuart-Vail's children are middle-aged.

As for Mr. Stuart-Vail, he believes staying active will help stave off the disease if it is in his future. And he has come to terms with his [genetics](#).

"You play the cards you are dealt," he said.

The Days Get Harder

In San Diego, Marjie Popkin said her memory problems had gotten steadily worse in the year since she first saw Dr. Rafii.

For example, she says, she has two cats. "I have to remember when I walk out that door that they can't come with me."

She used to read "all the time." Now, she says, reading is difficult. She depends on a friend, Taffy Jones, who took her to her appointment with Dr. Rafii, and who visits often and calls her every day.

But that is hard for Ms. Jones.

In many respects, Ms. Jones said, Ms. Popkin is perfectly normal. She remembers to feed her cats, she changes their litter box every day, she showers.

"Other things she is not able to deal with at all," Ms. Jones said. Getting dressed has become a problem, and Ms. Jones has to call Ms. Popkin every morning and every night to remind her to take her pills. Ms. Popkin can no longer drive and relies on Ms. Jones to help with routine things, like getting groceries. Helping Ms. Popkin has become a time-consuming chore.

Ms. Popkin is all too aware of the situation she is in, dependent on the kindness of neighbors and Ms. Jones.

"I am trying to adjust, but it's not easy," Ms. Popkin said in a telephone conversation. "I am pretty pragmatic. I know what the score is."

Sometimes she sits in her apartment and just cries and cries. She has no family, and Ms. Jones is her only remaining friend; the others have drifted away.

The diagnosis of early-stage Alzheimer's disease was a shock, Ms. Popkin said, like "a punch in the stomach."

"This brain's been with me since I was born — how can it change like that? Sometimes I have to think, 'Is this really happening to me?'"

Her only consolation, she says, is that her father, her last remaining family member other than a cousin in North Carolina, died a few years ago, before she got the diagnosis. "He would have

been devastated.”

And Ms. Popkin — is she glad now that she found out what is wrong?

“I wish I didn't know,” she said.