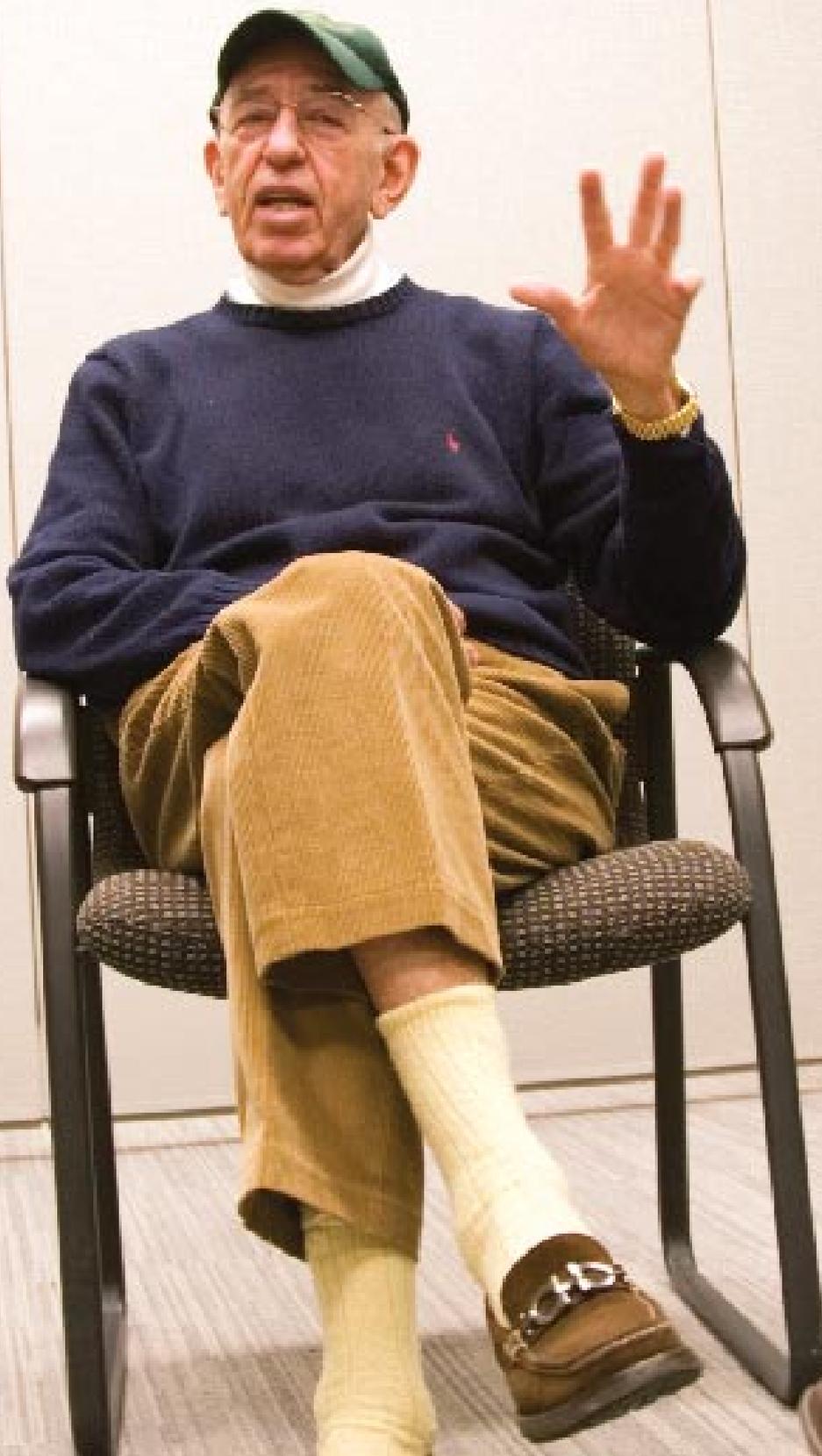


# *“Hey, I Got Dementia—and I’m Still Here!”*



# Diagnosing and Treating Early-Stage Alzheimer's

BY GINA SHAW

**G**eorge Rapoport didn't think he had Alzheimer's disease. In his mid-60s, recently retired from a lifetime in retail, he ran four miles every morning around the reservoir in Central Park near his Manhattan home, and then headed to his gym for another workout. "I had two kids, two grandchildren, and a very nice life," he says, sitting in a discussion group at the offices of the Alzheimer's Association of New York City. "Then, whoosh, I was here."

It was a little more complicated than "whoosh," of course. Diagnosed with early-stage Alzheimer's disease less than a year ago, Rapoport becomes vague when asked what the first signs of his dementia had been. But his wife, Evelyn, had noticed his increasing memory lapses and occasional, uncharacteristic bursts of anger—so she brought him to a forum at the Alzheimer's Association that included people with early-stage disease talking about their condition.

"I was amazed that they were up there, actually talking about having dementia," he says. "Initially when I started coming here, I was uncomfortable. But I'm mature enough to say, I've got a problem. And I'm not embarrassed that I have Alzheimer's disease. I'm almost, like, proud. Hey, I got dementia—and I'm still here!"

Rapoport is one of the more than 4.5 million Americans living with Alzheimer's disease today—a number that's expected to jump to 16 million by the year 2050. Many of these people, like Rapoport, are in the early stages of the disease.

Not long ago, early-stage Alzheimer's disease support groups, like the one Rapoport attends at the Alzheimer's Association's New York office, were few and far between. That's because, up until about 15 years ago, it was virtually impossible to reliably detect Alzheimer's disease in its early stages. The diagnosis of Alzheimer's could only be made when the disease was so advanced that the affected person had lost much of his cognitive abilities. Today, a battery of cognitive, neurological, and imaging tests makes it possible to detect Alzheimer's disease earlier than ever, and more advanced diagnostic tools are on the horizon.

## Detecting the Seeds of Alzheimer's

Everyone jokes about "senior moments"—those occasional memory lapses when you forget where you put the car keys, or can't recall the name of a business colleague. But sometimes those "slips of the brain" that become more common as we age—even in people without dementia—start to look like something more insidious.

Instead of forgetting what you went to the kitchen for or what you were going to say next, you might find yourself having difficulty performing very familiar tasks, like using the phone or making dinner. Instead of just dropping her keys on a shelf and forgetting where she left them, your mother or your wife might be putting them in a strange place like the freezer.

Symptoms like these bring approximately 500 people each year to the Gertrude Sergievsky Center of Columbia University Medical Center in northern Manhattan, where an interdisciplinary team of some of the nation's top Alzheimer's disease experts provides the latest diagnostic and treatment options for people with Alzheimer's disease (as well as other dementias and brain disorders).

Even at centers like these, however, the best diagnosis experts can offer is "probable" Alzheimer's disease. Currently there are no available tests for a living person that can show the accumulation of the characteristic "plaques" of Alzheimer's disease, the sticky buildup that forms when a protein called amyloid divides improperly and creates a toxic form called beta-amyloid. That can only be seen after death in pathology slides of the brain at autopsy.

But the array of neurological, neuropsychiatric, and imaging tests offered at these specialized centers—a process that can take much of a day, or even multiple days—is accurate about 90 percent of the time when it labels someone's condition "probable Alzheimer's."

A new patient at the Sergievsky Center will start by meeting with a neurologist, who takes a clinical examination—assessing things like reflexes, coordination, and muscle tone and balance—and an extensive family history. That conversation

More than  
**4.5 MILLION**  
Americans  
are living  
with  
Alzheimer's  
disease  
today—  
a number  
that's  
expected to  
jump to  
**16 MILLION**  
by the year  
2050.



## George Rapoport

It seemed like nothing at the time, eight or nine years ago. George Rapoport, then in his late 50s and still running a successful men's clothing and sporting goods store, was having dinner with a longtime friend. "Something's wrong with your speech," the man said. "You don't seem to be the way you used to be."

Offended, Rapoport dismissed his friend's comment and thought little more of it—until recently, when it came back to him as he discussed his Alzheimer's diagnosis with members of his support group at the Alzheimer's Association of New York. "Maybe that was a very, very early sign that something was wrong," he muses now.

Rapoport can still recall in great detail the time, many decades ago, when a young John F. Kennedy visited the Manhattan clothing store he and his mother then ran, and tried to make a purchase with traveler's checks only to have Rapoport's mother not recognize him. But he can't say exactly what pushed his wife Evelyn to make the call to the Alzheimer's Association. Anger, maybe? "Occasionally," he admits. "Sometimes it gets a little loud. Evelyn doesn't get aggressive."

He still drives to a country home upstate, after taking a long and thorough test at an agency in New Jersey. "Evelyn didn't want me to drive and I wanted to continue, so I took this test and we drove and drove for two hours. Eventually the instructor said, 'You can drive.'"

But despite his morning runs in Central Park, workouts at the gym, and weekly lunches with his daughter, Rapoport says his biggest problem is isolation. "I need something to do. I can't behave in a store, working for somebody else after having my own business all my life," he says. "If I could have something to do, to give back to somebody, that'd be perfection."



**“Initially when I started coming here, I was uncomfortable. But I’m *mature enough* to say, I’ve got a problem.”** —GEORGE RAPOPORT

alone can often take over an hour.

“We try to determine when the problems began,” says Karen Marder, M.D., a professor of neurology in the Sergievsky Center and chief of the division of aging and dementia in Columbia’s department of neurology. “When was the last time the person was completely fine? Often people can pinpoint problems by referring back to holidays and other occasions. We’ll ask whether they can learn something new, and if they have problems with tasks they’ve done for a long time.”

Careful questioning will often reveal that family members have taken over tasks that the person with Alzheimer’s used to do: “Oh, it was just faster, so I pay Mom’s bills for her now.”

## Words and Pictures

This history is complemented by a comprehensive neuropsychiatric exam, a process that can take four hours or more. “This is a series of tests measuring different cognitive domains,” explains Yaakov Stern, Ph.D., professor of clinical neuropsychology in the Sergievsky Center. “They assess memory for paragraphs, words and pictures, language, spatial ability, and abstract reasoning.”

One abstract reasoning question might ask the person how an orange and a banana are alike, with the expected answer being that they are both fruits. A question about memory for words and language might be: “Name as many items of clothing as you can in one minute.” Spatial testing asks the patient to put puzzles together or copy a drawing. These tests are usually “weighted” to take into account a person’s educational level and age—for example, a 70-year-old who only completed the 8th grade wouldn’t be expected to score as high as a 40-year-old with a college education.

While neurologists and neuropsychiatrists are studying the patient’s behavior and history, a comprehensive set of tests is being run on the patient’s blood and urine. You can’t diagnose Alzheimer’s disease with a blood test, but sometimes you can rule it out. For example, an underactive thyroid and vitamin deficiencies—particularly a lack of the B vitamins—can cause symptoms that mimic Alzheimer’s disease and other dementias.

## Visualizing Alzheimer’s

Several kinds of brain scans are used in diagnosing early Alzheimer’s disease, including magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET).

“MRI shows us the structure of the brain,” explains Law-

## EARLY DETECTION: TESTS ON THE HORIZON

### → Biomarker “signatures” found in cerebrospinal fluid.

One test, now under investigation, is a “bar code” panel of 23 proteins developed by researchers at Cornell University and Weill Medical College. It was recently found to be accurate between about 80 percent to 90 percent of the time in differentiating people with Alzheimer’s from normal subjects.

### → Imaging of areas of the brain where Alzheimer’s disease may begin.

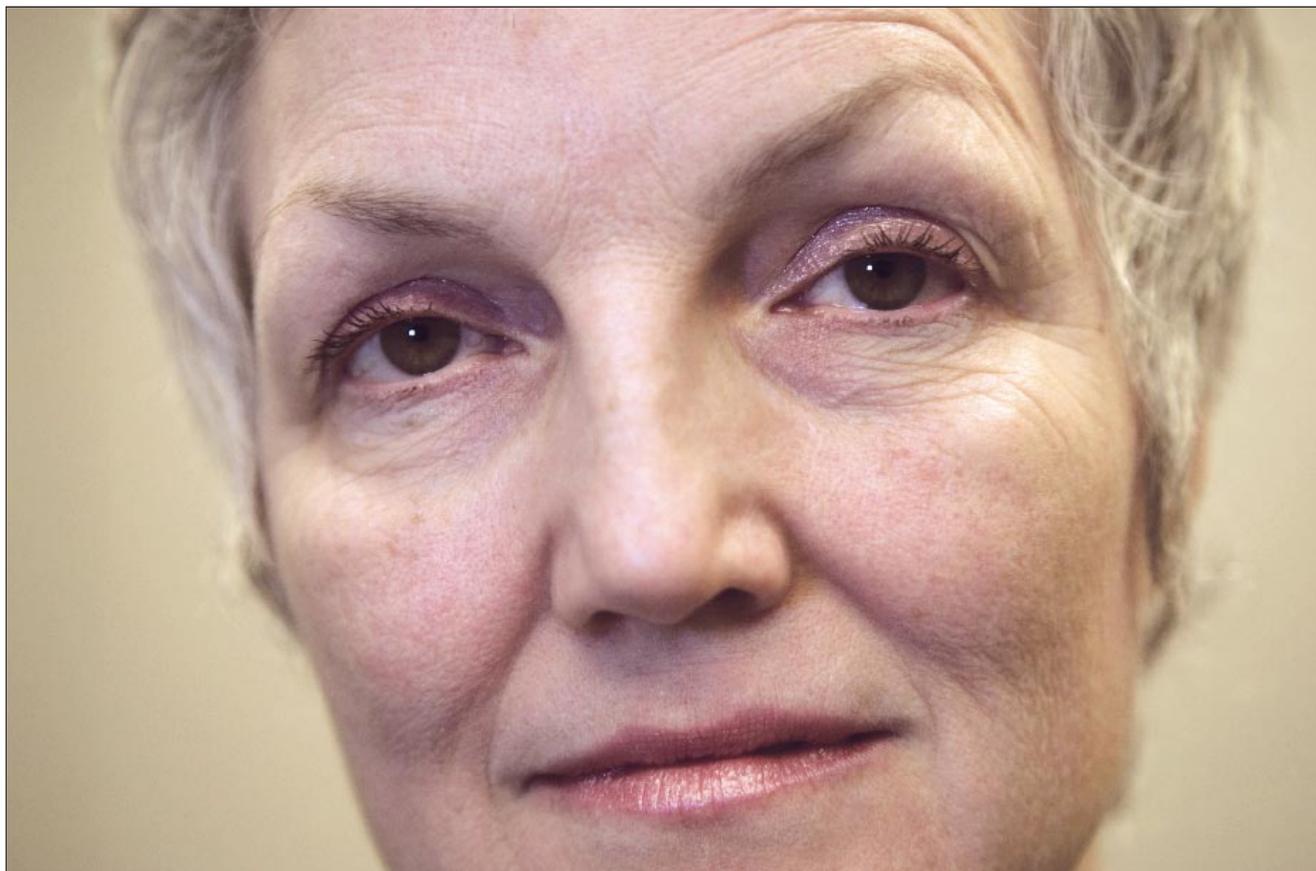
The Sergievsky Center’s Scott Small, M.D., has used high-resolution spatial imaging in mice to show that a molecule called VPS35 is involved with the development of Alzheimer’s disease. He calls VPS35 the “smoking gun” because it regulates the levels of beta-amyloid in the brain, and suggests that it could both point to a new test for Alzheimer’s disease and potential treatments.

### → New PET imaging compounds.

Areas of the brain affected by Alzheimer’s disease metabolize sugar more slowly than normal, something that can be seen on the PET scan. But a new contrast agent, called Pittsburgh Compound-B (PIB), is designed specifically to seek out the abnormal amyloid plaque in the brain that is characteristic of Alzheimer’s. Using PIB, doctors may someday be able to follow the progression of the disease and identify people who are at increased risk for Alzheimer’s disease long before any symptoms occur.

rence Honig, M.D., Ph.D., an associate professor of clinical neurology in the Sergievsky Center. “With Alzheimer’s disease, typically you will see shrinkage of the brain in areas related to cognitive function, such as the medial temporal lobes and particularly within the hippocampus, which are important to the formation of memory, and the parietal lobes, which are associated with the analytic process and complicated thoughts. There can also be global shrinkage in other areas of the brain.”

Although researchers have made headlines in recent years with the use of PET scanning, which can show biologic changes in the brains of people with Alzheimer’s even



## Mary Carver

"Growing up, I was always ditzzy," says Mary Carver, 55. "That's what I thought this was at first—just an extension of the way I've always been. Or maybe I had an instinct that it was something I didn't want to know, so I wasn't asking."

But Carver's husband Steve, an electrician for big Broadway theater productions, noticed her increasing memory lapses, started doing research, and persuaded Mary to go to a meeting at the Alzheimer's Association.

"I was angry at first," Carver says. But in time, she came to realize that she shared a lot in common with the people in the support group.

"I'd completely segregated myself from everybody," she says. Husband Steve's theater career keeps him away from their Manhattan apartment a lot, and with her 20-year-old son having moved out and 17-year-old daughter's typical teen rebellion exacerbated by her anger at her mother's condition, Carver spends most of her days either watching TV or walking her spaniel mix in a tight five-block radius around their building.

The weekly support group and "Memory Works classes" bring Mary out, but Paulette Michaud and staff at the Alzheimer's Association are trying to find more ways to break her isolation. "I still stay in my small space," she says. "I used to love going to the Natural History Museum—I'm fascinated with dinosaurs. And every day I say I'm going to go. We don't live that far from there. But somehow I always find a reason not to go."

The hardest part of having Alzheimer's disease, Carver says, is the uncertainty. "It's not knowing what to expect—any time, in a few days or in a few years. Maybe by then there will be better medications. But even as scary as it is, the best thing is to find out. Once you know that you have the disease, then you can get help."



**“Maybe I had an instinct that it was something I *didn’t* want to know, so I wasn’t asking.”** —MARY CARVER

before the onset of symptoms, the scientists at the Sergievsky Center often do not need PET to make their diagnosis. “We use it most often in trying to determine whether a patient has Alzheimer’s disease or another form of dementia,” Dr. Marder explains.

Ultimately, she says, “There’s no one test we hang our hat on.” That’s because every single test available—even pathologic tests of the brain at autopsy—has been known to be wrong.

“It’s important to distinguish between a risk profile and the disease,” says Dr. Honig. “Alzheimer’s disease isn’t like a broken foot, where you didn’t have it five minutes ago and now you do. The biochemical and molecular changes involved in Alzheimer’s occur over many years, and with better imaging techniques, it’s possible to see the early molecular signature of the disease. But someone with those molecular signs might live to 80 or 90 without ever having functional Alzheimer’s disease.”

“Even when we study someone at autopsy, and there are clear, significant Alzheimer’s changes in the brain, the pathologist will ask, ‘Was this person demented?’ That’s because there have been people whose brains have looked like they had Alzheimer’s disease, but they showed no sign of it while they were alive,” says Dr. Stern.

That’s why the team at the Sergievsky Center holds a multidisciplinary case conference on every patient before making a diagnosis of Alzheimer’s disease.

## Envisioning the Future

Once someone has been diagnosed with early Alzheimer’s disease, what does the future hold? That’s hard to know, says Nikolaos Scarmeas, M.D., an assistant professor of neurology at the Sergievsky Center. “We can’t predict for individual patients what will happen. We can offer a rough estimate, but every person follows their own trajectory of decline.”

That decline can’t be slowed or stopped—but the symptoms of the disease can be treated. By combining medications and other therapies, many people with Alzheimer’s and their families have found that they are able to improve the quality of their lives, delay the need for a nursing home, and steal precious time together back from this insidious disease.

## Keeping an Active Brain

If you ask George Rapoport, though, he’ll probably tell you that the most important part of his treatment for Alzheimer’s disease are the afternoons he spends at the offices of the Alzheimer’s Association of New York. Every Friday, he treks to the Association’s building on Lexington Avenue, where he spends an hour or so talking, laughing, and sometimes crying with the members of the Association’s support group for people in the early stages of the disease. There, he’s become friends with people he might never have met otherwise, like Mary Carver, a 55-year-old mother of two who recently lost her job as a massage therapist in part because of her increasing dementia symptoms, and Lee Robins, a 78-year-old retired litigator.

“I’ve gained a great deal from this... class,” says Robins, struggling for a moment to think of the word “group,” and then settling on another. “Someone else will talk about a problem they’re having, and I’ll look back and say, ‘That’s me!’”

“It gives me a sense of normalcy,” says Carver. “I’m not alone. There are other people in the same situation, fighting the same problems.”

Carver and Rapoport also attend weekly meetings of a group called Memory Works, where they do puzzles and brain exercises

aimed at keeping their minds sharp and active. “It’s the highlight of my week!” Carver says. “Something wonderful happens in that room. We laugh and we learn.”

At the Alzheimer’s Association, education and training coordinator Paulette Michaud, who runs the early-stage disease support group and the Memory Works program, is constantly trying to develop new ways to engage people with early-stage Alzheimer’s.

“A common symptom of early Alzheimer’s disease is loss of initiative,” she says, pointing to Robins’ tendency to sleep until two or three in the afternoon and Carver’s isolation in a five-block area around her apartment. “One of the biggest challenges is what to do with your time and your days, when you don’t need someone to do it for you yet, but you do need a companion with you. We’re trying to work with people to expand their world.”

Still in the planning stages is a “volunteer buddy” program. “People often call us wanting to contribute by working directly

**THE COMPLETE WORK-UP**

- comprehensive medical and clinical history
- basic medical screenings, like blood work and urine tests
- neuropsychiatric testing
- brain imaging

## Lee Robins

Born in the Bronx, Lee Robins retired from his law firm at 65 but kept on in private practice until well into his 70s, and only at 78 did he finally write to the New York state bar to withdraw his membership.

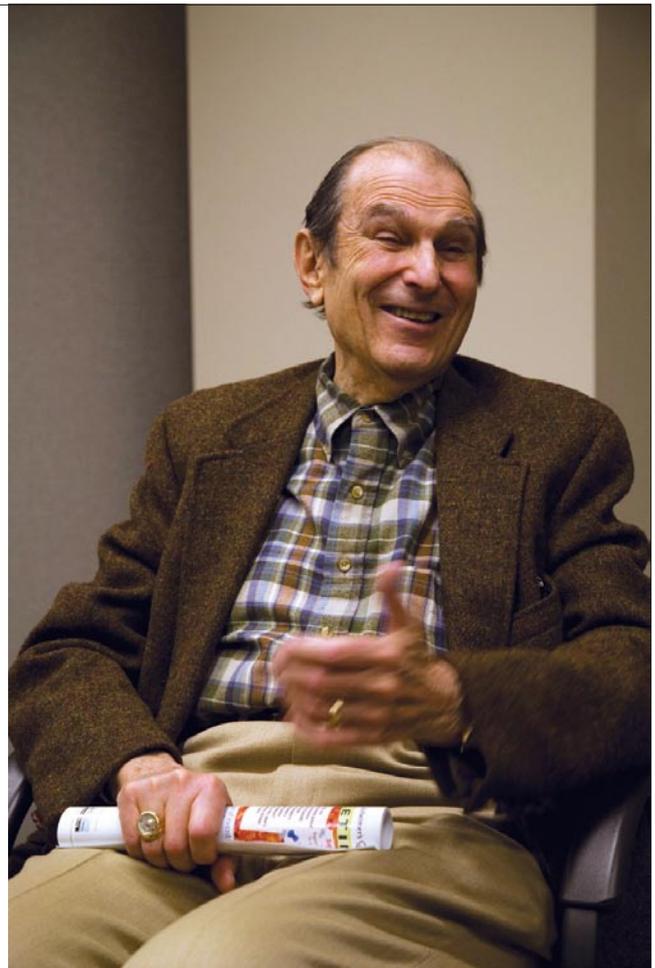
Robins didn't think there was anything unusual about what was happening with him at first. "My wife Natalie was the first to pick it up. She has a doctorate in education from Columbia, and she was wise enough to notice it," he says. "But now I'm learning that I have it, and am questioning certain of my acts."

What acts? He finds it hard to be specific. But before he stopped driving—after two accidents in a three-month span—Robins found himself getting lost on his way to his new apartment in Guttenberg, N.J.

He's finding that these small memory gaps are sometimes growing wider. To attend the support group at the Alzheimer's Association, he takes a bus from New Jersey, changes to the subway and takes it cross-town, and then looks for Grand Central Station to orient himself. "It's a very specific routine. But just today, I found that I didn't know where the 7th Avenue subway line was," he says. "So I asked a police officer, and she showed me where it was."

"My father was a loner, and slept most of the day," he says. "I must admit I'm beginning to emulate him—sometimes I sleep until 2 or 3 in the afternoon. Our days really are quite stagnant."

Is he depressed? "What's depression? Am I withdrawn? Well, yes, I certainly am, but that's nothing new. I do look forward to coming here, though," he says. "I had never really heard much about Alzheimer's disease before being diagnosed with it. Now, I think the world needs to know more about this disease. I'd be the first one to buy a license plate frame that said 'Alzheimer's: Get Checked!'"



**“I’d be the first one to buy a license plate frame that said ‘Alzheimer’s: Get Checked!’”** —LEE ROBINS

with patients who have Alzheimer’s disease as volunteers, and we don’t really have anything like that right now,” Michaud says. “What we’d like to do is match people with Alzheimer’s disease with a trained buddy, and help them find worthwhile projects to do together.” For example, Rapoport envisions using his years of experience in retail to talk to teenagers in inner-city schools about career opportunities.

Do support groups, activities, and “brain exercises” actually combat the symptoms of Alzheimer’s disease? It’s not clear, but “there are hints that it may be helpful,” says Dr. Scarmeas. Recently, the results of a large five-year study called ACTIVE, reported in the *Journal of the American Medical Association*, showed for the first time that a program of intensive “brain calisthenics” can help seniors maintain better mental acuity and function better in their daily lives.

A smaller study published by researchers from the University of California in 2006 indicated that mental exercise may help people who are already showing signs of cognitive decline. People with mild cognitive impairment (often a precursor to Alzheimer’s disease) participated in the “Brain Fitness Program” for about an hour and a half each weekday for about six weeks. After completing the program, they showed gains in memory on standard cognitive tests. (The program can be purchased online at [positscience.com](http://positscience.com).)

And while support groups may not actually slow the rate of mental decline, says Dr. Marder, “It’s good to be stimulated and socially interactive. Mood plays a big role in Alzheimer’s symptoms, and if you can stay engaged, that’s important.” Research has also found that support groups for people who care for loved ones with early Alzheimer’s disease can stave off the need for a nursing home. A recent study from New York University School of Medicine, published in the journal *Neurology*, found that a psychosocial support program delays the time when someone with dementia is put into a nursing home by an average of a year and a half.

## Treatments on the Horizon

But the ultimate goal of Alzheimer’s treatment is to slow or even stop the disease’s relentless assault on the mind.

Scientists soon expect the results of the first large-scale randomized clinical trials of “anti-amyloid” drugs—designed to either decrease the production of the harmful beta-amyloid, or improve the rate at which it’s cleared from the brain. “If this can be done successfully, it could decrease the rate of decline and keep brain cells alive,” says Dr. Honig. “Before, we were learning a lot about Alzheimer’s disease but didn’t necessarily

## IN THE MEDICINE CHEST: THE CHOICES

There are now five medications on the market that specifically treat Alzheimer’s symptoms. Four of them—donepezil (Aricept), rivastigmine (Exelon), galantamine (Reminyl), and tacrine (Cognex)—act in a similar way. They’re designed to slow the breakdown of a substance in the brain called acetylcholine, a chemical messenger important in memory and thinking. (Cognex is rarely prescribed today, because of side effects.)

The other drug, memantine (Namenda) regulates the activity of glutamate, a specialized messenger chemical that’s involved in information processing and is essential to learning and memory.

have very much to offer patients yet. We’re hopeful that that may change soon.”

George Rapoport is participating in a clinical trial of intravenous immune globulin (IVIg) as a possible treatment for Alzheimer’s disease. An antibody product derived from human plasma, IVIg contains antibodies that latch onto beta-amyloid proteins in the blood, and may be able to draw the beta-amyloid out of the nervous system and reduce the buildup of amyloid in the brain. Because it’s been used for other purposes, doctors already know a great deal about IVIg’s safety record.

“At my last appointment, my doctor [Weill Cornell Medical College’s Norman Relkin] told my wife that the plaque in my brain seemed to be lessening,” says Rapoport. “That sounded good! Now, he’s doubling the dosage. Even if it doesn’t benefit me, maybe it will be good for someone else in a few years.”

A few years can make a huge difference for people with early Alzheimer’s disease, says Dr. Scarmeas. “Our rate of knowledge is increasing exponentially. If we can genuinely delay the disease long enough, that would be almost like curing it.”

In the meantime, says Rapoport, “There is so much out there for people like us. We’re here, we’re functioning well, chatting and laughing. There is life beyond the diagnosis.” **NN**

*Gina Shaw is a health and science writer whose articles have appeared in Redbook, Glamour, and WebMD.*



For more information on the programs featured here, see **RESOURCE CENTRAL** on page 46.