



“I JUST DO IT!”
Lea Thompson takes a break at her home in Studio City, CA.

Some Kind of Wonderful, Indeed

For actress **Lea Thompson**, Alzheimer’s disease advocate is the role of a lifetime.

BY SUSANNAH GORA

She’s charmed audiences with her unforgettable performances in movies like *Back to the Future* and *Some Kind of Wonderful* and on well-loved TV shows such as *Caroline in the City*. Now, after many years working as a tireless advocate for Alzheimer’s disease (AD) awareness, Thompson is the host of the American Academy of Neurology Foundation’s new educational video and guidebook, *Alzheimer’s Disease: A Guide for Patients and Families*. (To watch the video and download a copy of the guidebook, visit aan.com/patients. To order a free copy of the video and guidebook, call (800) 879-1960. Supplies are limited.)

“It’s something that doctors can give to people when they’re first diagnosed, and to their families,” Thompson explains. The video provides helpful and much-needed information to

patients who have recently learned they have AD. It answers “questions that they might have, and questions they don’t even know that they have yet,” says Thompson.

Her connection to the disease is painfully personal. Both of Thompson’s grandmothers, her stepfather, and her father-in-law all suffered from AD. “A lot of people in my life have been affected by it,” she says. Thompson’s story of losing loved ones to this debilitating neurologic disease is something that far too many of us can relate to. More than five million Americans suffer from AD.

FROM CAREGIVER TO ADVOCATE

Thompson’s journey as an AD advocate began when a colleague of hers, legendary TV director James Burrows (who had directed her in many episodes of *Caroline in the City*) asked her to sing in

Thompson **fights fiercely** in the battle to raise Alzheimer's disease awareness: "I've gone to Washington, D.C., I have talked to lobbyists, I've marched, I've spoken out."

"A Night at Sardi's." Burrows founded the yearly musical revue for the Alzheimer's Association to honor his father, Broadway director Abe Burrows, who had AD. Once Thompson got involved with the event, she says, "I realized how much AD was affecting my life." She enjoys performing in the star-studded fundraiser because "it's a way to give back."

Because of her personal experiences, Thompson—who has also been part of the Alzheimer's Association's "Champions" campaign—is particularly sensitive to how painful it can be for those watching family members struggle with the symptoms of AD.

"One of the hardest things about it is the way it can bring out different parts of someone's personality," she explains. "One of my grandmothers and my father-in-law both became angry and were very difficult to deal with. It was really trying. The other two didn't get that way—they were very loving and peaceful, which was a lot less of a challenge, emotionally."

She urges caretakers to remember that "it's not the fault of the person who's going through this, and it's certainly not your fault. And," she adds, emphatically, "it's not your fault if you have all kinds of negative feelings. Because it is a huge amount of work—both the physical work that it takes to take care of someone like that, and the emotional toll that it takes."

One of the reasons Thompson raves about the Alzheimer's Association is the support they provide for caregivers. "They have outlets and phone numbers and booklets and support groups for people who are going through this—who are watching someone they love change, sometimes drastically." Thompson advises families "to access the resources and not be ashamed. The best thing is to remind caregivers to use the resources to get help. They shouldn't feel alone or struggle silently."

Thompson also offers this stark advice to family members of people with AD: "I found it was really useful not to try to get them back" to the way they were before. "Sometimes they will remember certain things, sometimes they won't." Above all, she says, "It's important to have a sense of humor if possible, and to be really loving with them."

Thompson fights fiercely in the battle to raise awareness of AD. "I've gone to Washington, D.C., I have talked to lobbyists, I've marched, I've spoken out," she says. Plus, she adds, laughing, whenever the Alzheimer's Association calls her and asks her to do something, "I just do it!"

For Thompson, volunteering is a family affair. She has two daughters with longtime hubby, movie director Howard Deutch. Their

older daughter, Madelyn, who hopes to pursue a career as a professional singer, has sung with Thompson numerous times at AD fundraising events. Their younger daughter, Zoey (herself a budding actress who has appeared on The Disney Channel), has gotten in on the act as well. "It's really fun to be involved in something with a group of wonderful professionals all donating their time," Thompson explains, "and to set that example for your kids, that it's important to donate your time to causes. Volunteering is a great opportunity to meet new people and feel a part of something bigger than yourself." Thompson says that singing in the AD fundraisers multiple times has particularly helped her daughter Madelyn combat some of "the hopelessness that she felt watching both of her grandpas go through this. It's nice to feel like you can do something to fight back."

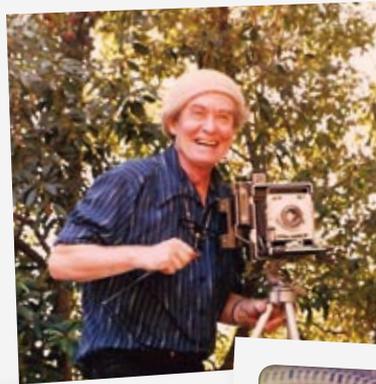
THE IMPACT OF GENES

It's important that families stick together in the fight against AD—especially since in many cases the disease can run in families.

"Three genetic mutations have been identified that cause AD in families. One-half of the children of a parent with one

ALZHEIMER'S DISEASE STRIKES MORE THAN TWICE

Lea with her maternal grandmother, Agnes Barry, in 1972 (bottom left); and with her paternal grandmother, Reva Thompson, in 1977 (bottom right). Lea's stepfather, Rob Hanson (top) probably had AD too.





STEPPING OUT

Lea with her husband, Howie Deutch, and daughters, Madelyn and Zoey.

of these mutations will, on average, inherit the mutation and develop the disease as well,” says Roger N. Rosenberg, M.D., Abe (Brunky), Morris, and William Zale Distinguished Chair in Neurology and professor of neurology and director of the Alzheimer’s Disease Center at the University of Texas Southwestern Medical Center at Dallas. “Further, a number of variations in the structure of genes have been identified in patients with AD,” says Dr. Rosenberg, who specializes in the genetic aspects of the disease.

Since Thompson has two grandparents with the disease, her risk of developing AD “is increased, compared to the general population,” Dr. Rosenberg says. But having a parent with the disease would put one at an even higher risk. “If there is one parent affected, your risk of developing AD is about three-fold compared to the general population,” says Dr. Rosenberg, “and if you have two parents affected, it’s between a seven- and ten-fold increase.”

Great strides have been made in terms of diagnosing the disease at earlier stages (although there is much debate about whether people want to be informed that they are likely to develop AD later in life—see box, “To Know or Not to Know”). Once a person has been diagnosed with AD, medications are available that “slow down the symptoms for a year or so,” says Dr. Rosenberg. The U.S. Food & Drug Administration (FDA) has approved four medications that have been shown to improve memory and slow the progression of AD: donepezil, rivastigmine, galantamine, and memantine.

“These medications allow a person to have improved memory and focus for a short period of time,” says Dr. Rosenberg. “They don’t address the underlying disease, but at the moment,

Singing in Alzheimer’s disease-fundraisers has helped Thompson’s daughter Madelyn combat “**the hopelessness** she felt watching both her grandpas go through this.”

they’re the best we have. It’s like taking aspirin if you’ve got a bad cold. It reduces your fever and decreases your headache, but it doesn’t stop the virus.”

THE IMPACT OF LIFESTYLE

There is much debate among experts concerning the impact of lifestyle on AD risk and progression. Although lifestyle changes may not prevent a person from developing AD, some experts believe that healthy choices (such as eating a so-called Mediterranean diet and being physically active) might lessen the effects of the disease.

“It’s a very important area of investigation,” says Victor Henderson, M.D., professor of health research and policy and of neurology and neurological sciences at Stanford University in Palo Alto, CA. He suggests that “the benefits of aerobic exercise and eating certain kinds of foods—such as vegetables and foods high in omega-3 fatty acids—are supported by fairly strong observational data and by evidence from laboratory

animals but haven’t been subjected to the kind of rigorous proof we like to see in humans.” (See “Proof and Consequences” at <http://bit.ly/aOY54V> for an explanation of the different kinds of evidence.)

The bottom line, says Dr. Henderson, is that “we *think* that physical exercise, perhaps mental exercise, maintaining close social ties, and the right diet make a difference, but we aren’t positive. The scientific proof behind these lifestyle interventions is largely lacking.”

Unfortunately, suggests Randall Bateman, M.D., assistant professor of neurology at Washington University in St. Louis, MO, “there is nothing one can do to guarantee that you will not get AD.” However, he does tell patients that “you want to be socially, physically, and mentally active in things you enjoy doing. My guess is that future research will show that [healthy lifestyle habits] can help lower the risk of AD by some amount, or slow the progression if you have AD. But it’s not going to be a cure-all.”

Lea Thompson’s point of view is that regardless of the current science, it seems

To Know or Not to Know: That Is the Question

Now, doctors are often able to diagnose Alzheimer’s disease (AD) at earlier stages, which raises the question: If you could find out that you are at a high risk of developing AD in the future, would you want to know, even though there’s currently no cure for the disease? This medical and ethical quandary is a hotly debated subject.

“Some people desperately want to know exactly what their risk factor is,” says Dr. Rosenberg, “particularly if they are going to be making important life decisions—starting a new business, moving to a new community, taking on additional responsibilities, and so on.” Also, he adds, “people want to know things such as when will I need additional assistance to function? What’s the genetics, based on my family history, for my children? People want to be informed, and knowledge of one’s future is important.”

like good advice to “keep yourself mentally and physically active, learn new things, and maintain a positive attitude.” If nothing else, by adopting healthier habits, says Dr. Bateman, “people actually enjoy their lives more” and add quality to their years.

RESEARCH

With treatment options limited, finding a cure for the disease is of the utmost importance. In addition to the enormous personal toll AD takes, it is also “a huge drain on the health care resources of our country as people get older,” Thompson points out.

Fortunately, says Dr. Henderson, “Alzheimer’s disease is very much on the national scientific radar—a lot of advocacy and work is going into trying to find effective treatments.” A flurry of scientific findings in recent years suggests that the eventual discovery of a cure is worth hoping for. “They have made some interesting breakthroughs,” says Thompson, “so we have our fingers crossed.”

Some of the most promising research focuses on learning more about a protein fragment called amyloid beta (A beta for short). Amyloid beta is a normal protein produced in the healthy brain. But in the brains of people with AD, it forms “toxic plaques that injure connections between nerve cells and contribute to the degenerative disease process,” Dr. Rosenberg says. A second protein, called tau, is also thought to play a role. “Alzheimer’s disease produces a progressive change in the brain resulting in nerve cell loss associated with the storage of two proteins: A beta and tau,” says Dr. Rosenberg.

“It’s thought that A beta plays a critical role in AD,” says Dr. Bateman, “but the exact mechanism of why or how it builds up in the brain in such high levels [in patients with AD] has not been well understood.”

To help understand that mechanism, Dr. Bateman conducted an important new study, which was published in the December 2010 issue of the medical journal *Science*, “trying to answer a basic question: Does the brain make too much A beta protein? Or does it clear it away too slowly once it’s made?”

Dr. Bateman and his colleagues had already learned that young healthy people “make A beta protein all the time as the result of neurons firing, but also clear it away very rapidly. Some of our first studies showed that over about a nine-hour time period, young healthy people will make and clear away half of the A beta in their central nervous system—a very rapid turnover.” Dr. Bateman’s more recent study “showed that in older people with AD, their A beta clearance rates were much slower—about 30 percent

Alzheimer’s Disease: The Basics

WHAT IS IT? Alzheimer’s disease (AD) is an “an age-related, non-reversible brain disorder that develops over a period of years,” according to the American Academy of Neurology. Alzheimer’s disease causes problems with memory, thinking, and behavior.

WHO HAS IT? Over five million Americans have AD. “The overall prevalence of AD is about 20 percent of the population over 80 years of age,” says Dr. Rosenberg, “with a reduction in percentages down to perhaps one or two percent at age 65.” A small percentage of people get AD as young as their forties and fifties (known as early-onset AD).

WHAT ARE THE SYMPTOMS? A common early symptom of AD is difficulty remembering recently learned information. After the disease has progressed, symptoms can include worsening confusion and disorientation, behavior changes, and difficulty speaking or walking.

HOW IS IT DIAGNOSED? Doctors use a variety of tools to determine if a patient has AD, including neurologic exams, mental status tests, spinal taps (low levels of amyloid beta in the cerebrospinal fluid can point to AD because this indicates that the protein is being stored in the brain itself), and positron emission tomographic (PET) brain scans.

HOW DOES ALZHEIMER’S DISEASE CAUSE DEATH? According to the Alzheimer’s Association, the disease is the sixth-leading cause of death in the United States. It can cause death in a number of ways, including, says Dr. Rosenberg, “lack of mobility, impaired clearing of secretions (such as mucous), and lack of appetite leading to poor nutrition.” Mainly though, AD puts people at a higher risk for infection, “which is the major cause of death,” he says.

WHAT ARE THE CURRENT TREATMENTS? There is currently no cure for AD, although scientists are working hard trying to discover one. In the meantime, drugs including cholinesterase inhibitors and memantine can ease cognitive symptoms for a period of time.

slower than people the same age who did not have AD.”

A drug that lowers production of A beta was recently tested. Unfortunately, it “did not benefit patients,” says Dr. Bateman. But he still believes an effective treatment will one day be found by studying A beta.

“When you look back on the work that has been done over the past 30 years in A beta, there is really a mountain of convincing evidence that all points to the same thing: A beta plays a critical role in AD,” he says. “How to develop the right drug [to target A beta]—at the right dose without significant side effects—is an important question. But in developing treatments, a cure doesn’t happen the first time out of the gate.”

Dr. Bateman points to a famous episode in medical history to support his optimism. “There are great lessons to be learned from reading the story of how penicillin was proven to work,” he says. “Things don’t always work the very first time you try them, and the details are important—how much of a dose you take and over what time period, for example. With all the evidence behind it, I’m still very enthusiastic that A beta is a great target. And there are new treatments in development that promise to be better than the first attempts.”

Others, such as Dr. Rosenberg, are doing research in the field of AD and immunotherapy. Specifically, he is working to develop

“These are exciting times. But nobody is satisfied with where we are right now. **We all need to do better.**”

—VICTOR HENDERSON, M.D.

a DNA vaccine. “When we give a DNA vaccine to mice, their immune systems make an antibody against A beta. And we have shown that making this antibody reduces the level of A beta in the brains of these mice by half,” he explains. (An antibody is a substance produced by the immune system to neutralize a foreign or dangerous substance.) “We are in the process now of trying to extend those studies to people—and working as fast as we can.”

“There are a number of different studies underway, taking various approaches. But,” Dr. Henderson cautions, “we still haven’t had the breakthrough that all of us hope for.”

Even with doctors doing everything they can to outsmart AD, it’s an uphill battle. “The disease is much more complex than any of us appreciated 10 or 15 years ago,” warns Dr. Henderson, who feels that “it is probably not a matter, for example, of simply too much A beta in the brain, which if removed would solve the problem of AD. There are a lot of other complicated, interdependent factors that need to be deciphered. Until these factors are better understood, we’re left with trying to find step-by-step approaches to delaying onset and slowing symptoms. That doesn’t mean that we won’t eventually find a cure. But a cure in the traditional sense of the word may still be a long way off.”

“Perhaps the most hopeful thing,” says Dr. Bateman, “is that there continues to be a good number of drugs that are approaching Phase 3 clinical trials.” Phase 3 trials are conducted to see if an experimental drug or treatment works better or has fewer side effects than the standard treatment for a condition. “If those drugs work, then they may have a significant impact by changing the course of the disease.”

Says Dr. Henderson, “These are exciting times. But nobody is satisfied with where we are right now. We all need to do better.”

LOOKING FORWARD, GIVING BACK

While doctors work as hard as they can for a cure, Thompson works hard to raise awareness of the disease and to help cure



SOME KIND OF CAREER

Thompson in *Back to the Future* (1985) with Crispin Glover and Michael J. Fox; with Eric Stoltz in *Some kind of Wonderful* (1987); and with the cast of *Caroline in the City* (1995-1999).

the loneliness and fear that people feel in the face of AD. When she goes to Washington, D.C., she meets many brave people living with AD. “It’s very emotional to get to talk to people and be with them,” she admits. “It’s devastating to hear them talk about it, and to see what it does to their family.”

Thompson finds time to give back despite a demanding professional schedule. She recently co-starred in the upcoming film *The Convincer* with Billy Crudup, Greg Kinnear, and Bob Balaban, which was screened at the 2011 Sundance Film Festival. “It was the first time I ever got to shoot a movie in Minnesota,” her native state. “It’s a great little indie movie,” says Thompson.

She’ll also be starring in *The Cabin*, a romantic comedy for The Hallmark Channel, and she produced and starred in the comedy film *Mayor Cupcake*. Recently she co-starred in *The Trouble with the Truth*, which she says is “kind of like *My Dinner with Andre*: two characters basically talking through most of the movie.” On top of all that, Thompson also recently starred in a pilot for ABC Family, and she has a part in the upcoming Clint East-

wood movie *J. Edgar*. “I’ve had a really good run lately,” she says, gratitude in her voice.

Even though she’s always tackling new projects, Thompson continues to be very proud of her involvement in the iconic *Back to the Future* series from decades ago. “It’s awesome that people are showing the movie to their kids and grandkids now,” she says. Thompson believes *Back to the Future* is so enduring because “it’s rare that you can have a movie that’s funny, incredibly well-crafted, and has such an interesting idea at its premise: that how you live your life can totally change the outcome. It’s life-affirming.”

Hopefully, the future will bring a cure for AD. But in the present, Thompson is doing everything she can to make the lives of patients and their families a little easier. “I do what I can do,” she says, but “there’s so much to be done.”