

BY JUDITH WALL
OU Public Affairs

No Quick Fix For Alzheimer's Disease

**Is there hope for
finding a cause
or a cure?
Yes, says Roger
Brumback.
Soon?
Probably not.**



■ Alzheimer's destroys the brain in stages as indicated by the arrows from right to left. First the memory is lost; then victims cannot process information, care for themselves or communicate. Finally, with the loss of judgment and reason residing in the frontal lobe, most patients no longer can be managed at home.

Illustrations by GEORGE DOTSON
Photos by TERRI JENNINGS

The good news is Americans are living longer.

The bad news is that half of us who reach age 85 will have Alzheimer's disease and be unable to recall what happened the day before, much less have any memory of those 85 years of living.

The fourth leading cause of death for adults, Alzheimer's has become the disease most dreaded for many aging Americans. A retired Oklahoma schoolteacher said that, with the loss of dignity brought by the disease and the financial and emotional burden it brings to the families of victims, she considers Alzheimer's "a fate worse than death."

But what about all that research progress in the news? Surely in the next few years, there will be a way to treat or prevent the disease.

OU pathology professor and Alzheimer's expert Roger Brumback

agrees that scientists are continuously learning more about the disease—but, as with most new knowledge, the secrets of Alzheimer's are being revealed in small increments. All too often, he contends, the significance of a medical research finding is overstated in the media.

"So many times something has been presented as the cause or cure for a disease, and it doesn't turn out to be true," says Brumback, who is David Ross Boyd Professor and interim chair of the Department of Pathology at the OU Health Sciences Center and actively involved in Alzheimer's research.

In fact, the OU pathologist finds the practice of hyperbole in the reporting of medical news harmful. With so much hype going on, how can John Q. Public tell the difference in real science and pseudo science?

"Answers are going to come from understanding both the basic science of Alzheimer's and the risk factors for the disease," points out Brumback, who investigates the structural changes in the memory and emotion regions of the brain and how these changes relate to the progression of the disease.

"It took the Framingham Heart Study 30 years to determine that cholesterol was a major risk factor for cardiovascular disease," Brumback says. Longitudinal studies for Alzheimer's did not start until the late 1980s and early 1990s, he explains, adding that his parents are participating in one such study in Pittsburgh. "It may be another 20 years before we completely understand the risk factors for the disease."

On the basic science front, the key to developing a cure for this devastating disease seems to lie with

understanding what causes the death of brain cells—or neurons—which do not replace themselves like other cells in the body. Promising research from the lab of OU pathologist Paula Grammas indicates that microvessels in the Alzheimer's brain secrete factors that can cause neuron death.

Jordan Tang, a researcher at the

ported that its researchers had developed a vaccine that prevented the plaques from forming in the brains of genetically engineered mice, ABC News asked their panel of experts if this was the long-awaited major breakthrough. Brumback was asked to provide the skeptic's view in a *Nightline* interview with Ted Koppel.



■ Pathologists Dr. Anna Pereira, left, Dr. Roger Brumback and Dr. Paula Grammas demonstrate the differences between a normal brain and one from an Alzheimer's victim in the Neuropathology Laboratory of the Diagnostic Center for Alzheimer's Disease. Approximately 150 pro bono autopsies a year are performed at the center on the brains of any Oklahoma resident suspected of dying from Alzheimer's Disease. Diagnosis and genetic implication consultations then are available to the victims' families. The center also serves as a "brain bank" by providing tissue to researchers at OUHSC and other academic centers.

Oklahoma Medical Research Foundation, has designed an inhibitor for an enzyme that contributes to the formation of seemingly harmful "plaques and tangles" found in the brains of Alzheimer's patients. Many researchers across the country are striving to understand the significance of these plaques, which can cover the outside of neurons and become so dense they trigger an inflammatory reaction that leads to cell death.

When Elan Pharmaceutical re-

The OU pathologist explained to *Nightline* viewers that, while the vaccine might eventually prove to be an important step forward, the significance of plaques in human brains is not fully understood. And even if the vaccine did prevent plaques in mice, science is a long way from knowing if it would protect human beings from Alzheimer's.

Brumback believes that everyone should assume the role of skeptic in evaluating medical news—and infor-



■ The treatment component of the OU Health Sciences Center's Alzheimer's efforts received a big boost with the recent opening of the Center for Memory Loss and Dementia, which provides diagnosis, treatment and outpatient care and support for caregivers. From left in the new center's conference room are occupational therapist Carrie Davis; center director Dr. Elliott Ross; OU pathology department interim chair Dr. Roger Brumback; nurse manager Connie Brown; caregiver services director Marilee Monnot; and clinical services director Dr. Anton Coleman. Ross also is director and Brumback the neuropathologist at the Center for Alzheimer's and Neurodegenerative Disorders at the Veterans Affairs Medical Center.

mation gleaned from well meaning friends and the Internet.

Long active in educating people about Alzheimer's disease, Brumback is past president and a frequent spokesperson for the Oklahoma Alzheimer's Association. And as medical director of the Diagnostic Center for Alzheimer's Disease, he often meets with family members after performing an autopsy on the brain of a loved one to explain his findings and their implication.

He offers the following crash course on Alzheimer's for *Sooner Magazine* readers:

■ While memory loss and dementia are symptoms of Alzheimer's, not every person with memory loss or dementia has the disease.

Half of all the people with dementia have a treatable condition, Brumback emphasizes. The cause of the dementia often can be a patient's own medication. Other causes include endocrine disturbances, depression and cancer.

"It's critically important that patients be properly evaluated," he says.

"The diagnosis of Alzheimer's should not be made haphazardly."

After the extensive testing needed to rule out other conditions and diseases, what is left is a diagnosis of "dementia of unknown cause," which most likely means a degenerative disease of the brain. The majority of people suffering from a degenerative brain disease do have Alzheimer's. While a definitive diagnosis only can be made after death through an autopsy of the brain, the variety of degenerative brain diseases do have different characteristics, and qualified physicians usually can make an accurate diagnosis. Brumback says that on autopsy, about 10 percent of Alzheimer's diagnoses are shown to be incorrect.

■ Some people are born with a greater propensity for developing Alzheimer's.

Five genes on different chromosomes have been linked to Alzheimer's, and there are probably more. Some forms of these genes make it more likely that a person will develop the disease; others make it less likely.

Being born with a bad form of one or more gene linked to Alzheimer's does not necessarily mean a person will get the disease. Something has to trigger the process, Brumback explains, but at this point, researchers can only guess at what the trigger might be. A definitive answer will come with longitudinal studies.

■ Gene replacement probably will not be the answer for Alzheimer's.

"Some diseases, such as cystic fibrosis, are caused by a single gene," Brumback points out. "If we could replace that gene, we could cure those people. Alzheimer's and all the degenerative diseases of the central nervous system are going to be more complicated."

When risk factors are better understood, those who carry genes for Alzheimer's will be able to adjust their lifestyles to compensate.

■ People die of Alzheimer's because the disease destroys the body's control center.

Alzheimer's patients can survive as long as nursing care keeps them from dying, Brumback says.

For example, every few minutes, healthy people automatically swallow their saliva. People with Alzheimer's lose that ability. Saliva pools in the lungs, and patients repeatedly develop pneumonia, which has to be treated with increasing powerful doses of antibiotics.

Another example: Healthy people completely empty their bladders, which serves to wash out bacteria. People with dementia usually are incontinent, with the bladder never being completely emptied. As a result, they develop bladder infections, which can travel to the kidneys and be fatal. With a course of antibiotics, they do not die.

"Alzheimer's is the underlying cause of death, but the day a person

suffering from the disease actually dies is determined by some type of infection," Brumback says.

"I had one patient who, with tremendous nursing care, was kept alive in a vegetative state for nearly 25 years," he recalls.

■ **A victim of Alzheimer's will have had the disease for many years before symptoms appear.**

"The death of a brain cell is something that occurs slowly," Brumback says. "It suffers a lingering illness over many years. If we could do things to help it stay alive, we would slow the progression of the disease."

For example, some researchers believe that antioxidants found in fruits and vegetables may help keep sick brain cells alive a few years longer. Longitudinal studies will prove or disprove that theory.

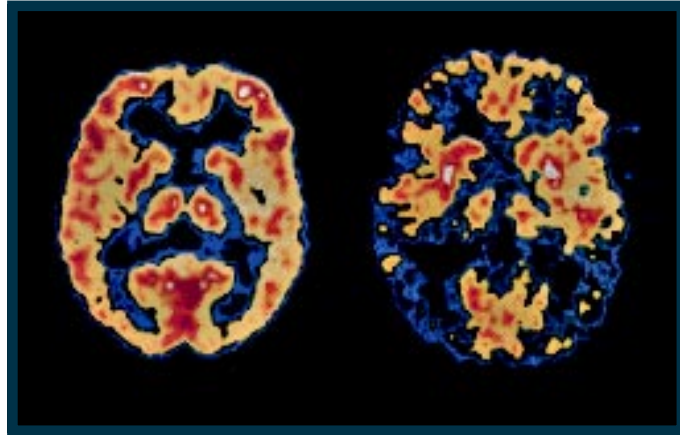
OU pathologist Ann Pereira is looking for a way to prevent the body's natural inflammatory response, which normally disposes of sick and dying cells, from killing off sick-but-still-functioning neurons in the brain of those with Alzheimer's. OU neurologist Anton Coleman is trying to determine if estrogen and other hormones offer protection from the disease.

■ **Alzheimer's begins in the hippocampus—the tiny area deep in the center of the brain responsible for memory—and spreads outward. The last part to be affected is the frontal lobe, where judgment and reason reside.**

As memory fades, people are able to compensate because they still have a frontal lobe. When they cannot remember where their car keys are, they ask their spouse to find them.

After memory is destroyed, other functions are taken in turn. People lose the ability to process information, care for themselves and communicate. But until the frontal lobe is destroyed, family members usually can manage the care of an Alzheimer's victim. A wife can even take her

husband with Alzheimer's to a restaurant for a family celebration. He will not know how to order or how to eat, but she can order for him and place the fork in his hand. When the frontal lobe is destroyed, however, she can no longer take her husband out to dinner,



■ The blue and black areas show the differences in brain activity between a normal brain (left) and a brain affected by Alzheimer's disease (right).

■ **“People with a lifelong tendency to actively use their minds still may get the disease, but not as early.”**

since he will behave inappropriately.

"When the frontal lobe goes, most people end up in a nursing home," Brumback says, adding that OU neurologist Elliot Ross is trying to better understand and manage the behavior problems that lead to nursing home confinement.

An estimated half of all nursing home residents suffer from Alzheimer's. From onset to death, the average cost of maintaining a person with the disease is more than \$175,000.

Brumback notes that with Pick's disease, another degenerative disease of the brain, the destructive wave begins in the frontal lobe. The first symptom of Pick's often is bizarre behavior, with memory remaining intact until the end.

■ **Is there really nothing people can do to protect themselves from Alzheimer's?**

When all the data from longitudinal studies has been examined, Brumback suspects that lifelong intellectual activity will be shown to offer some degree of protection against the disease. Already there are indications that people who are intellectually active tend to get Alzheimer's later in life than other people.

"People with a lifelong tendency to actively use their minds still may get the disease, but not as early," he says.

He refers to a Chinese study that suggested educated people had a later onset of Alzheimer's than illiterate people did. Delay is an important goal, he explains. "If we can delay the disease, we might outlive our chances

of getting it."

Brumback believes the intriguing research of OU neuropsychologist William Beatty will help shed light on the role of intellectual activity. Beatty studies Alzheimer's patients who have maintained their ability to play a musical instrument or play chess when they are no longer able to feed or care for themselves in any way. He hopes to learn what is preventing that particular skill from deteriorating.

■ **Eventually Alzheimer's will be conquered, Brumback says with conviction.**

In the meantime, he suggests practicing all the things now known to contribute to good health. Stop smoking. Maintain an appropriate weight. Exercise daily. Consume a diet low in fat that is composed primarily of fruits, vegetables and whole grains. Control stress. Limit consumption of alcoholic beverages. It probably would not hurt to take some sort of anti-inflammatory agent, such as ibuprofen, on a daily basis.

And after realistically evaluating your level of ongoing intellectual activity, you might want to enroll in a class at OU or work on your chess game. 🍷