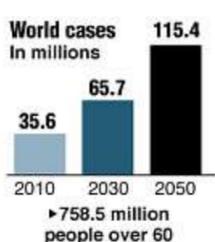


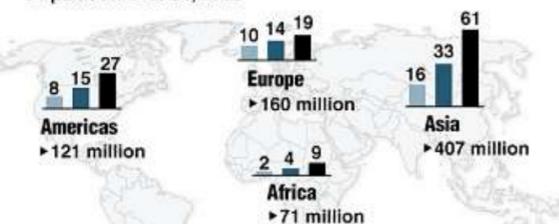
Rising cases

Dementia cases worldwide will triple in 40 years as life expectancy and medical care improve in poorer countries. Currently more than 35 million people live with dementia.



Number of people with dementia in millions

► Population over 60, 2010



Source: Alzheimer's Disease International Graphic: Melina Yingling © 2012 MCT

Alzheimer's: Patients in clinical trials are 'heroes'

Continued from 1A

that scientists know these misfolded proteins spend part of their time outside of cells — traveling from one cell to another — new drugs can target them there. This could help prevent or at least block the progression of these diseases.

"Aggregated protein causes the normal protein to misfold and spread from cell to cell," Carlson said.

Research breakthroughs on any of these diseases could offer the missing puzzle piece to Alzheimer's, or at least lead scientists toward a treatment that could delay the onset of Alzheimer's.

Delaying Alzheimer's

While scientists and doctors ultimately want to find a cure for this disease that affects 5.4 million people in the United States, delaying the onset of Alzheimer's would be a huge step in the right direction.

Delaying the onset of this disease, which is the sixth-

leading cause of death in the United States, could drop the numbers of those ever affected as many people may reach the end of their lives before symptoms emerge.

Nearly half — 43 percent — of Americans older than age 85 suffer from

Alzheimer's, which is the most common form of dementia.

Delaying the disease also could greatly reduce health care costs.

"The research that leads to a treatment that would delay Alzheimer's by five years would cut government spending for Alzheimer's disease by 45 percent by 2050," said Suzanne Belser, executive officer of Alzheimer's Association Montana.

"The costs of caring for AD patients is immense — currently \$200 billion in 2012, and projected to increase to \$1.1 trillion by 2050 if no therapy is found, putting a tremendous strain on health care providers and insurers — including Medicare," Carlson added.

Looking at the growing number of dementia patients in Montana's nursing homes and assisted-living facilities is worrisome, Dietrich said. Few people are wealthy and able to pay privately, some are poor and their care is paid through Medicare and Medicaid programs, while others pay with long-term care insurance.

"You'll spend \$60,000 to \$80,000 a year (for a care facility). There are very few people who can afford it," he said.

And with fewer people paying into those programs as the large numbers of baby boomers hit retirement age, "something has to give," he said.

Funding needed

A lack of funding is slowing research.

Belser said the United States spends far less on

Alzheimer's research than other diseases.

About \$6 billion was spent on cancer research, \$4 billion on heart disease research and \$3 billion on AIDS research in 2011, Belser said. Approximately \$480 million was spent on Alzheimer's research.

Change may be coming, however.

The Alzheimer's Association, which is the leading global voluntary health organization in Alzheimer's care and support, and the largest private, nonprofit funder of Alzheimer's research, spearheaded a national push that is leading to more funding.

The Obama administration recently released a draft national plan to address Alzheimer's disease, which included \$130 million in new funding for Alzheimer's research over the next two years.

Belser will go to Washington, D.C., this week to lobby for several U.S. House and Senate bills aimed at increasing the commitment to and funding for Alzheimer's research, and expanding diagnosis of the disease.

Currently, the diagnosis of Alzheimer's relies largely on recognizing memory loss. Typically, a loved one notices the patient has been making out-of-the-ordinary decisions. By the time the patient sees a doctor and is diagnosed,

there already has been significant brain damage.

"If we have a treatment to slow down the disease, when would you want to start it?" Dietrich asked. "Before the signs are obvious."

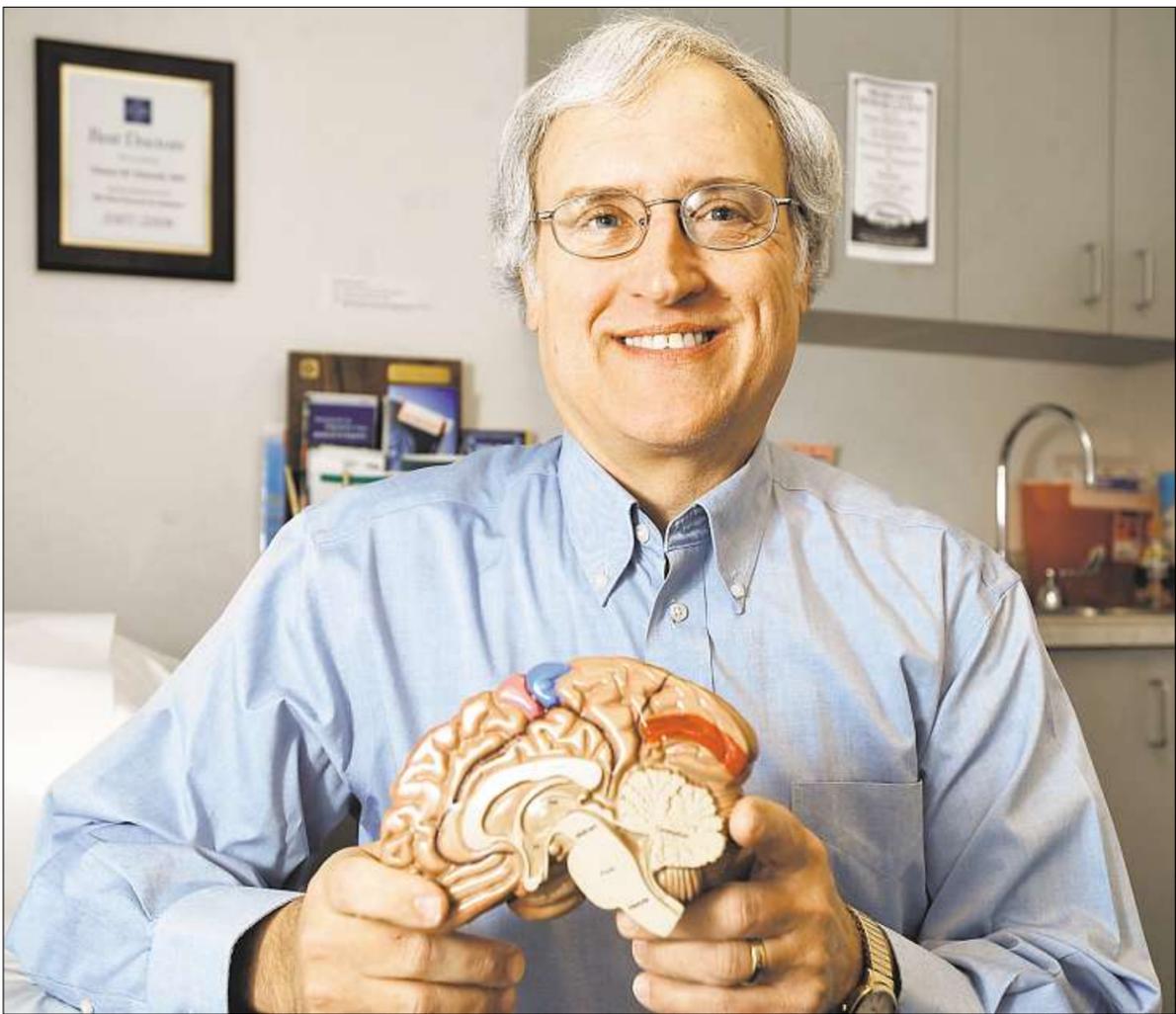
Researchers hope a biomarker can be found that would serve as an early indicator of the disease, much like high cholesterol can indicate increased risk for coronary heart disease. They are working to "validate" a biomarker, which means it needs to be confirmed by multiple studies in large groups of people.

Current research is working toward identifying biomarkers using several tools, including brain imaging, levels of proteins in cerebrospinal fluid, levels of proteins in blood and genetic risk profiling.

There isn't a treatment available to slow or stop the deterioration of brain cells in Alzheimer's disease, but the U.S. Food and Drug Administration has approved five drugs that lessen symptoms and improve daily functioning for six to 12 months, but do not prevent the disease progression.

There also are about 100 experimental therapies in clinical testing in human volunteers across the world, according to the Alzheimer's Association.

Carlson said once family members complain about dementia in their loved ones, it is less likely that newly developed therapies will be successful. Brain changes in those with Alzheimer's are thought to begin 10 years or more before the appearance of



Great Falls neurologist Dennis Dietrich is the only doctor in the state currently enrolling patients in Alzheimer's clinical trials.

TRIBUNE PHOTO/ RION SANDERS

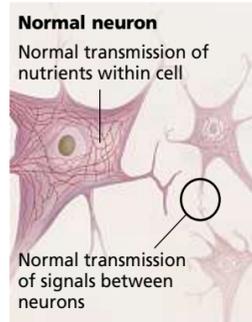
DEGENERATIVE BRAIN DISEASE

Proteins that exist in normal amounts in healthy brains build to abnormally high levels in patients with Alzheimer's disease, resulting in the death of neurons, the brain's nerve cells.

INSIDE THE BRAIN TISSUE

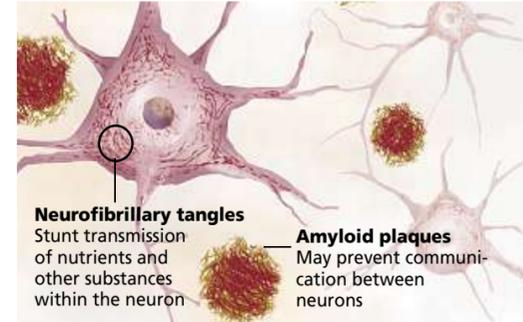
Healthy brain

The body can dissolve protein fragments called amyloids that develop between neurons



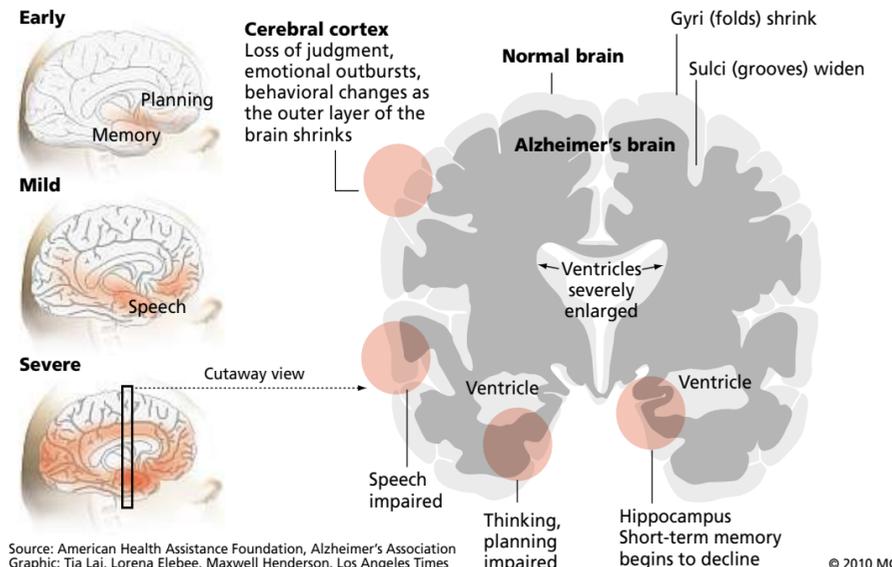
Brain with Alzheimer's disease

Amyloids build and form hard, insoluble plaques between neurons; a protein called tau within the neurons becomes abnormal, creating twisted fibers called tangles



DISEASE PROGRESSION AND FINAL STAGES

The spread of tangles and plaques through the Alzheimer's brain advances in a predictable pattern (below left); as the disease progresses and kills more brain nerves, shrinkage of the brain is obvious; neurological functions affected by areas of brain loss:



symptoms such as memory loss, according to the Alzheimer's Association.

Other obstacles

Another research obstacle is a lack of trial participants.

"It's easy to get approval for Alzheimer's patients, but it's too late," Carlson said.

However, people who have a family history of three rare familial forms of Alzheimer's have helped researchers.

In these trials, the drugs can be given to patients who know they carry the tainted gene but haven't yet displayed symptoms.

A Colombian family of more than 5,000 people is among those involved in research.

The hope is that researchers will find a drug that will work on familial forms of the disease and it also will work on the sporadic, more common form of the disease, Carlson added.

He said the McLaughlin Research Institute made its first mouse model to research Alzheimer's in 1988. These transgenic mice express a faulty human gene, called APP, which is a cause of familial early onset Alzheimer's. There are several mouse models in labs across the world, all mimicking Alzheimer's, but the disease behaves differently in mice and humans, Carlson said.

Human brains with Alzheimer's first develop beta-amyloid plaques, followed by tangles that lead to the death of brain cells. The APP mice don't develop tangles.

"These Alzheimer's mice only have plaques," Carlson said. "We'd really like to reproduce the whole (spectrum of) Alzheimer's disease."

Scientists used to think tangles came before the beta-amyloid plaques, but it has been discovered that the plaques occur first. Mice expressing a different mutant gene have been developed that accurately model the tangles seen in Alzheimer's disease and frontotemporal dementia.

This is important to researchers working on a biomarker, with advances being made in the ability to detect the accumulation of beta-amyloid plaques and neurofibrillary tangles in the brain.

"What we think is that the mice with plaques are models for pre-clinical Alzheimer's, while the mice with tangles are more relevant to later-stage disease," Carlson said.

Great Falls trials

Dietrich has administered clinical trials on promising Alzheimer's drugs for 20 years. The drug he currently has in clinical trials, Bapineuzumab, is being tested by Janssen Pharmaceuticals and

Pfizer, Inc.

The school of thought is to passively vaccinate against beta-amyloid plaques in the brain.

"If you develop an antibody, then you can attack the target with it," Dietrich said. "Bapineuzumab attaches to beta-amyloid and helps remove it from the brain."

The drug, which is administered through an IV, already has been shown to reduce the plaques in the brain, Dietrich said.

Scans have shown the drug's success in reducing beta-amyloid plaques in the brain, but researchers still are unclear as to whether it slows the progression of the disease.

"We hope to have some results from our first study by the end of this year," he said.

Dietrich is enrolling patients in a second trial for Bapineuzumab, this one through Pfizer. The trial is scheduled for completion in 2014.

To be eligible for the trial, patients need to be experiencing only mild to moderate symptoms of Alzheimer's, and be between the ages of 50 and 88, with no other major health issues, he said. Great Falls is one of 292 trial sites.

"I'm not seeing hundreds

CAN ALZHEIMER'S BE PREVENTED?

This is a question that continues to intrigue researchers and fuel new investigations. There are no clear cut answers yet — partially due to the need for more large-scale studies — but promising research is under way.

The Alzheimer's Association continues to fund studies exploring the influence of mental fitness, physical fitness, diet and environment. As the number of people affected by Alzheimer's rises, the effort to find prevention strategies continues to gain momentum, according to researchers.

NEED HELP?

- » **Alzheimer's Association 24/7 Help Line:** 1-800-272-3900
- » **Website:** Alz.org has the most comprehensive information on Alzheimer's.
- » **Medicaid Waiver Program:** In Great Falls and the Golden Triangle area, contact Benefis Spectrum at 455-2660.
- » **Clinical trials:** Call Dr. Dennis Dietrich's office at 727-3720 for more information.
- » **McLaughlin Research Institute:** For more information on the institute or to contribute to its research, go online to <http://mri.montana.edu>, or call 452-6208.

of people in this trial. It's a very small trial," Dietrich said.

To measure whether the drug works, patients will undergo extensive cognitive testing and need to sit still through a 45-minute MRI.

"If the brain shrinks, it may indicate that you've lost brain cells," Dietrich said.

The ratio of phosphorylated tau and the decreased alpha-beta in spinal fluid also is measured as a means of determining if the drug is working.

Though these trials look promising, Dietrich stops short of saying researchers are near a cure.

"I think it's incredibly complicated," he said. "We need a breakthrough, and we don't know where it's coming."

Dietrich said that one thing's for sure, however: People who enter clinical trials are heroes.

When a patient of his even considers participating in a clinical trial, he tells that person, "Without people like you, we wouldn't have any new treatments."

Amie Thompson is the specialty publications editor at the Great Falls Tribune. Reach her at 1-800-438-1431 or 791-6531 or email her at athompson@greatfallstribune.com.