Breakthroughs in Alzheimer's Research: News You Can Use
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Testimony

Honorable Senators and other attendees. In my testimony I will address the availability and adequacy of current treatments for Alzheimer disease, the potential for preventing Alzheimer disease and the importance of continued support for research and care into this devastating, common illness.

Descriptions of Alzheimer disease are contained in the earliest medical writings that are 3,000 years old. However, the brain changes characteristic of Alzheimer disease were described only 100 years ago and it has only been in the past 35 years that clinicians, scientists and the public have appreciated the fact that what used to be called "senility" is a group of diseases referred to medically as dementias. Today we recognize that two-thirds of all cases of late life dementing is caused by Alzheimer disease.

Currently Available Treatments

The recognition that "senility" is most commonly caused by Alzheimer disease led to the discovery in the mid-1970s by researchers in Europe and the United States that a chemical called acetylcholine is deficient in the brains of individuals dying from the illness. Three of the treatments that are available today, donepezil (Aricept), galantamine (Reminyl) and rivastigmine (Excelon) work by increasing the amount of this chemical in the brain. These medications are all modestly effective in treating patients with Alzheimer disease; this benefit translates into improved function, behavior and cognition (thinking). On average, these drugs bring about a 6-9 month improvement in the disease. However, they do not modify the underlying biology; the death of brain cells due to the disorder continues in spite of treatment. It is important to emphasize that the modest benefit provided by these medications translates into meaningful improvement and, equally importantly, demonstrates that the symptoms of the disease are amenable to biological therapies.

A second class of medications builds upon the discovery made at Washington University, St. Louis and Johns Hopkins that the brain responds to loss of acetylcholine by stimulating or "exciting" the remaining cells with the neurotransmitter glutamate. Unfortunately, this results in "excito-toxicity" due to overstimulation of these remaining cells. The first example of this class of medications, memantine, (Namenda) was developed in Germany and recently approved by the FDA for the treatment of individuals

with moderate-severe Alzheimer. It is hoped that disease progression might be slowed by blocking glutamate but this has not yet been proven.

Potential Treatments

Tremendous strides have been made in the past 25 years in understanding the basic biology of memory and other thinking processes. Drugs are under development that seek to enhance these processes. In addition, an extensive body of research has focused on the function and metabolism of the proteins thought to be involved in the genesis of Alzheimer disease. Studies funded by the NIA, NINDS and NIMH suggest that the deposition of abnormal proteins may be the initiating and/or perpetuating cause of Alzheimer disease. Many pharmaceutical companies, biotech companies and publicly funded researchers are studying compounds that potentially interfere with the formation or deposition of these abnormal proteins, or might increase their removal from the brain. Studies of the effectiveness of these therapies has begun only recently, but the quality of research being performed now is quite extraordinary and many scientists believe that therapies that target the biology of the disease and slow its development, stop its development or reverse the abnormalities are a possibility. NIH-sponsored research has played a major role in the development of many of these approaches.

Treatment

Extensive non-drug research demonstrates the benefit of interventions that provide information and emotional support to caregivers. Intriguingly, these interventions have been shown to have 3 benefits, improving the psychological well-being of the caregiver, diminishing the prevalence of behavioral and psychiatric symptoms in the patient and delaying placement in a long term care facility, a goal of many family members and patients. Much of this research has been supported by the NIH.

Prevention

At present, the best supported preventive strategy for Alzheimer disease is treating the risk factors for brain vascular disease – controlling high blood pressure, elevated cholesterol, elevated low density level lipoprotein (LDL) levels, diabetes and obesity. The contribution of these to the development of Alzheimer disease may be modest but they could have a meaningful impact because so many people are affected.

A second potential prevention strategy is the use of non-steroidal anti-inflammatory drugs (NSAIDS) such as ibuprofen (Motrin, Advil and generic). At present, the studies supporting the preventive actions of the drugs in this class are all retrospective. That is, they depend on data collected from individuals who do have Alzheimer disease and do not have Alzheimer disease. A prospective trial (funded by the NIA) called ADAPT should tell us in several years whether drugs in this class can delay the onset or prevent Alzheimer disease. It now appears that women who take hormone replacement therapy after age 64 are at increased risk of developing Alzheimer disease. However, some research suggests that estrogen taken at the time of menopause may be preventive. More research is needed on this topic.

A third area of research that has potential for prevention is the study of genetic risk factors. This may reveal targets for medication that can prevent or delay the onset of disease.

A fourth area of intense interest and scrutiny is whether mental and/or physical activity lowers the risk of developing Alzheimer disease. To date, studies supporting this are all retrospective and thus can only suggest the possibility of such a benefit. Some research also suggests that more years of education offers some protection and some individuals raise the possibility that this may work by increasing connections among brain cells.

Future Prospects

In my opinion we are at a crucial point in the development of therapies aimed at altering the biology of Alzheimer disease. Whether such a treatment will be available in 5 years or 50 years cannot be foreseen, but the pace of research and the advances already made increase the likelihood that a disease-altering or preventing therapy will be identified. In my opinion, the need for continued research in this area should remain a high priority, given the devastation wrought by this illness on individual Americans and their family members as well as the economic costs of the disease. In many states, Medicaid nursing home benefits are one of the largest individual budget items and Alzheimer disease is the single greatest contributor to nursing home placement in the U.S..
Research should also continue to look for better strategies to diminish the emotional, financial and behavioral burdens wrought by the dementias until cures and preventions are available. This important work complements research into the basic biology of the disease and the development of more biological effects therapies.

As a clinician and clinical researcher for 30 years, I have watched Alzheimer disease change from a condition known to a handful of experts to a disorder that is feared universally. Only through continued research can these fears and burdens be relieved. The need for such research is shown in a study that I have just completed which demonstrates that fewer than 1/3 of people with Alzheimer disease who live at home are recognized by their doctor as having dementia (See Figure).