**ALZHEIMER'S DISEASE.**

**By**
**William Reville, University College, Cork.**

Alzheimer's disease is a very distressing condition, both for the sufferer and for all those who care about the victim. Incidence of the disease is sharply increasing and there is no cure. However, great progress is being made in understanding the basic biochemistry of the condition. Much of this work was carried out at the National Institute on Ageing in America under the direction of Zaven Khachaturian. It is hoped that effective treatments will be available soon, followed closely by a cure.

At least 16 million people worldwide suffer from Alzheimer's disease (AD). Ireland has 33,000 cases of AD. Most cases develop after the age of 65 in people with no family history of the disease, although genetic factors predispose people to the disorder. AD is the leading form of dementia in the elderly, responsible for about half of all cases. A small number of cases of AD (2% to 7%) are an early-onset variety and can afflict people as young as 30. Early-onset AD is an inherited condition distinct from late-onset AD.

AD destroys the brain silently. Usually the first symptom to appear is forgetfulness. This is followed by severe loss of memory, confusion, uncoordinated movement, garbled speech, personality changes, hallucinations and mood swings. As the brain deteriorates, the rest of the body gradually closes down until, invariably, the victims are left incapable of caring for themselves. Death ensues somewhere between 2 and 20 years after the appearance of the first symptoms.

AD has existed since ancient times and writers have often described the typical symptoms. Shakespeare's King Lear, losing his memory and growing disoriented, is a well-known example. AD was defined as a distinct disease in 1906 by a German physician Alois Alzheimer. He described a patient who presented with volatile behaviour, memory loss, disorientation, hallucinations, and paranoia. After the death of the patient, Alzheimer examined her brain and described the odd growths, called tangles and plaques, that are now considered the unambiguous fingerprint of AD. A protein called beta-amyloid protein forms sticky clumps at the core of the plaques in AD brain.

The sector of the population at greatest risk of AD are people aged 85 and over. This is the fastest growing population sector in developed countries. People are now also, on average, physically healthier at all ages than in the past. Therefore, not only are absolute numbers of AD victims on the increase, but the average duration of the disease is also increasing. Health care is very expensive and unless effective treatment or cure for AD is forthcoming soon society faces an enormous financial burden.

The brain is a very complex arrangement of interconnected nerve cells - the neurons. In the absence of brain disease the organ will continue to function well into the tenth decade of life. In AD, neurons gradually lose the ability to extract energy from glucose (the principal food for the brain), to carry out essential repairs, and eventually to connect to other neurons. Neurons often die. It is not known what causes the brain systems to deteriorate in AD.

Acetylcholine is a chemical that is necessary in the transmission of electrical signals from one neuron to another and research has shown that acetylcholine-containing neurons play an

important role in memory. The first breakthrough in understanding the biochemistry of AD was made in 1976 when it was shown that an enzyme necessary to make acetylcholine was deficient in AD brains.

Later work in the 1980s and 1990s identified genes responsible for the early-onset form of AD and genes that predispose people to develop the much commoner late-onset-AD. The identification of genes opens the possibility of genetic testing. However, a positive test for the late-onset-predisposing gene does not necessarily mean a person will get AD. One could also question, on ethical grounds, the value of a genetic test in a situation where there is no cure for the disease.

AD is a complex disorder and it is likely that genetic and environmental factors interact to initiate the process. Some years ago there was a widespread feeling that ingestion of aluminium played a significant role in AD. This hypothesis no longer finds favour with the majority of researchers in the field. The 3 systems of neuronal intercommunication, energy metabolism of glucose and neuronal repair work together to keep the brain healthy. It is probable that a disruption of any of these systems, whether caused by imbalanced nutrition, toxins, trauma or infection could start off degenerative changes culminating in AD.

To my knowledge only 2 drugs are on the market to treat AD. Both slow down the breakdown of acetylcholine in the brain and thereby help communication between damaged neurons. The drugs slow the rate of deterioration in some patients but cannot prevent the final victory of AD. Recent research findings on the protein that accumulates to form the characteristic plaques and tangles in the AD brain holds the promise of the development of a more effective drug to treat AD.

If you are in your sixties and have noticed that your memory is not what it used to be, should you worry that AD may be developing? No. Memory performance in everybody slowly declines from the age of 20. The decline becomes more noticeable beyond the age of 60 but there is a considerable range of normal variation. With any luck at all your mind will remain clear for the entire duration of your earthly journey.

*(This article first appeared in The Irish Times, June 15, 1998.)*