ALZHEIMER'S DISEASE

FOR PATIENTS AND FAMILIES

Alzheimer's disease is the most common and well-known form of degenerative **dementia**. By definition, dementia is a **syndrome**, a cluster of symptoms, of impaired memory and cognition. Dementia is a **cognitive disorder** that impairs an individual's memory and ability for reasoning, awareness, and judgment. Cognitive impairment in Alzheimer's disease may involve disturbance of language (**aphasia**), loss of ability to carry out complex motor activities (**apraxia**), and loss of ability to recognize or identify familiar people or objects (**agnosia**). Another common manifestation of Alzheimer's disease is the disturbance of **executive functioning**, which is the ability to initiate, plan, assess, and carry out complex tasks in a logical sequence of steps. The abilities to plan a shopping list, drive to the store, and shop for the items are examples of skills requiring executive functioning.

Alzheimer's disease affects approximately 2.5 million Americans and accounts for 50%–60% of all cases of dementia. It affects less than 1% of people at age 65 in the United States, but the rate doubles approximately every 5 years to 2% at age 70 and 4% at age 75, and by the age of 90 the rate is over 20%. As the segment of population older than 65 years is rapidly increasing in the United States, managing Alzheimer's disease will present a major public health challenge.

COURSE OF ILLNESS

Alzheimer's disease, like many other types of dementia, has an insidious onset. An early manifestation of the disease is memory impairment, which is often overlooked and attributed to aging. As cognitive symptoms appear, the individual may undergo dramatic lifestyle changes. A person who was once active may show loss of motivation and energy, complaining of fatigue and lassitude, which is often diagnosed as depression. Memory disturbance is usually the earliest obvious sign that something is wrong. This may be perilous for the elderly person, who may, for example, forget to turn off the stove or leave the car engine running. Usually, the diagnosis of Alzheimer's disease is not made until the individual develops behavioral symptoms and is brought to the attention of a physician. Behavioral problems may include temper outbursts, daytime wandering, poor hygiene, suspiciousness, making accusations, and physical violence.

The disease as a general rule follows a progressive course of declining cognitive function and memory loss. For some patients, and particularly for those who benefit from medications, the progressive deterioration may stabilize for several years, with a plateau in overall functional impairment, before the progression of the disease continues and cognitive functioning declines further. In the advanced stages of Alzheimer's disease, impairment may be so profound that the patient may no longer be able to recognize family members or perform the most basic tasks of self-feeding and personal hygiene. The patient may become incontinent, hostile with extreme emotional outbursts, and assaultive. Hallucinations and delusions are not uncommon in advanced stages of cognitive deterioration. The management of the patient often takes a heavy toll on the caretakers. From the time symptoms are recognized and a diagnosis is made, the degenerative course of Alzheimer's disease may continue for years until death ensues. The mean survival for patients of Alzheimer's disease is about 10 years but may range from 1 to 20 years.

CAUSE OR ETIOLOGY

The definitive diagnosis of Alzheimer's disease is made at postmortem examination of the patient's brain, from microscopic findings that are hallmarks of the disease. These findings include **neurofibrillary tangles**, which are formed when a type of protein found in neurons (brain cells) is defective. The defective protein twists in "tangles" and becomes ineffective in carrying out normal cellular functions. Ultimately, this leads to cell death and Alzheimer's disease.

Another important finding is **amyloid plaques**. Amyloid plaques are derived from the aberrant formation of a neuronal protein. The resultant abnormal protein makes up the core of amyloid plaques. How these plaques result in cellular damage and destruction is unclear. One explanation is that plaques cause cellular inflammation and damage. The abnormal deposit of amyloid plaques may be analogous to cholesterol deposits and plaque formation along arterial walls, causing arteriosclerosis and arterial damage. Ultimately, the destruction of brain cells is the final pathway leading to the cause Alzheimer's disease.

Recent advances in genetic mapping provide compelling evidence that the formation of tangles and plaques in Alzheimer's disease may be genetically linked. Alzheimer's disease may be due to mutations (i.e., random changes in the genetic material) on particular chromosomes (i.e., the DNA in our genes). One explanation is that the neurons with the abnormal gene result in the production of an altered protein that causes formation of amyloid deposits that leads to Alzheimer's disease. Another explanation is that an amyloid transport protein, which binds and transports amyloid from the brain, is abnormal and therefore ineffective in removing amyloid. The amyloid transporting protein is called **apolipoprotein E** (ApoE). Several genes that code for ApoE are associated with the risk of developing late-onset Alzheimer's disease, the most common type of Alzheimer's disease. One of the genes for ApoE is found on **chromosome 19** and is linked to late-onset Alzheimer's disease.

DIAGNOSIS

The diagnosis of Alzheimer's disease is made on the basis of exclusion of other forms of dementia. The initial workup by the physician is to establish that the dementia is not caused by another medical condition. For example, some elderly patients with depressive illness may present with **pseudodementia** with clinical features similar to dementia, including memory and cognitive impairment, but generally the symptoms of pseudodementia are not as severe as those of true dementia. The important distinction is that pseudodementia resolves when the depression is successfully treated. Another important differentiation is to exclude **delirium**, which can also cause disturbance in cognition and may be misdiagnosed as dementia. Once the diagnosis of dementia is made, clinical history, neurological and psychological testing, and laboratory tests will help the physician differentiate Alzheimer's disease from another form of dementia.

For the diagnosis of Alzheimer's disease to be made, the patient's symptoms must meet the diagnostic criteria for dementia of Alzheimer's disease. The diagnosis must include symptoms in two major areas: 1) memory impairment, showing loss of ability to learn new information or to recall previously learned information; and 2) disturbance in one or more areas of cognition, including aphasia, apraxia, agnosia, and executive functioning. The cognitive deficits also cause significant impairment in social and occupational functioning, showing a continuous decline.

Physicians commonly use the **Mini-Mental State Examination** (MMSE) to assess the patient's cognitive functioning. The initial test score is compared with routine testing to evaluate the extent of cognitive decline. It is common for patients with Alzheimer's disease to have a significantly lower score on each subsequent examination.

CLINICAL MANAGEMENT

There is no cure for Alzheimer's dementia. Treatment is aimed at palliating the symptoms of the disease. Management of the disease rests largely on supportive care for the patient, which usually involves the spouse and other family members, taking care of the patient at home until late in the course of the illness when placement in a skilled nursing facility is needed for around-the-clock care.

The treatment of Alzheimer's disease is directed primarily at preserving cognitive functions. The medications for this purpose are known as **cognitive enhancers**. These agents maintain memory and cognitive function but do not alter the course of the disease. As previously discussed, the widespread destruction of neurons is the cause of cognitive deficits in Alzheimer's disease. The neurons involved are predominantly **cholinergic neurons,** which have a role in memory and learning. Cholinergic neurons require **acetylcholine** as the neurotransmitter (i.e., the brain chemical that facilitates transmission of impulses between neurons). Destruction of cholinergic neurons in Alzheimer's disease results in a deficit of this neurotransmitter. Cognitive enhancers increase levels of acetylcholine in the brain, which help to improve memory and other cognitive functions. Patients are more likely to respond to these agents during the early stages of the disease when more cholinergic neurons are intact.

The cognitive enhancers include **tacrine** (Cognex), **donepezil** (Aricept), **rivastigmine** (Exelon), and **galantamine** (Reminyl). These agents exert their action by inhibiting **cholinesterase,** an enzyme that breaks down acetylcholine, to enhance levels of the neurotransmitter. For further discussion of these agents, refer to the handout *Information About Cognitive Enhancers for Patients and Families* (Form 3–28).

Antipsychotic medications may be needed to manage psychotic symptoms associated with late stages of Alzheimer's disease. Psychotic symptoms usually take the form of delusional thinking or nighttime hallucinations. For example, the patient may become assaultive, thinking his or her spouse is an imposter, or the patient may see and talk to imaginary visitors. A low-dose of antipsychotic medications may be prescribed to control agitation, aggression, and assaultiveness. Physicians today are shifting away from prescribing the older, first-generation antipsychotic agents, such as **haloperidol** (Haldol), **fluphenazine** (Prolixin), and **thioridazine** (Mellaril), and are prescribing the newer, second-generation antipsychotic medications, such as **aripiprazole** (Abilify), **olanzapine (**Zyprexa), **quetiapine** (Seroquel), **risperidone** (Risperdal), and **ziprasidone** (Geodon). The second-generation antipsychotics are usually well tolerated compared with the older antipsychotic medications. They are associated with significantly lower incidence of movement disorders known as **extrapyramidal side effects**, such as Parkinson-like symptoms, muscle spasms, and gait disturbance. In general, the lowest effective dose of antipsychotic medication should be used and for the shortest possible duration. Patients with dementia often do not tolerate the central nervous system (CNS) side effects of antipsychotic medications very well.

Other symptoms associated with Alzheimer's disease include depression, anxiety, and other mood disturbances. Mood stabilizers such as **divalproex** (Depakote) may be prescribed to reduce agitation and other mood symptoms. Depressive symptoms occur frequently with Alzheimer's disease. The **selective serotonin reuptake inhibitors** (SSRIs) are generally well tolerated and the preferred antidepressants for patients with dementia. Tricyclic antidepressants, such as **amitriptyline** (Elavil), should be avoided because these agents have significant sedation and anticholinergic (i.e., opposes the action of cholinergic neurons) activity and may further compromise the patient's cognitive function. Anti-anxiety medications are occasionally needed to manage anxiety. The long-acting benzodiazepines, particularly diazepam (Valium) and chlordiazepoxide (Librium), should be avoided in patients with dementia. These agents are slowly eliminated from the body, and the drug and their metabolites may accumulate and could further impair memory and cognition. Because patients with dementia are generally very sensitive to side effects of centrally active medications, psychotropic medications must be used selectively and cautiously in these patients.

If you have any questions about this handout, please consult your physician.

SUPPORT AND ADVOCACY GROUPS

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