

DEMENTIA: NEW THEORIES, NEW TREATMENTS

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INTRODUCTION

Approximately 4 million people in the United States suffer from Alzheimer's disease—an irreversible, progressive, neurodegenerative disorder. Ten percent of people over age 65 and half of people over age 85 are affected by the disease. The estimated annual cost of caring for a patient with advanced Alzheimer's disease is more than \$50,000.

Given that Alzheimer's is expected to become a much more prominent problem over the next 20 years, the Memory Assessment Clinic at Grady Memorial Hospital in Atlanta represents a cooperative effort to find answers to this puzzling disease. Morehouse School of Medicine, Emory University School of Medicine, and Grady Health Systems are partners in the clinic.

"Alzheimer's disease is diagnosed as 'irreversible' among the types of dementia," said Dr. LaRoy Penix. Other diseases that are considered "irreversible" are Pick's Disease, Huntington's Chorea, Parkinson's Disease, Diffuse Lewy-body Dementia, Multiple Sclerosis, and Creutzfeldt-Jakob Disease. Other types of dementia are diagnosed as "treatable—potentially reversible" and "treatable—not reversible."

"Alzheimer's starts with short-term memory loss of about 2 to 3 points per year on the MMSE—the Mini-Mental State Examination—and eventually affects executive functions, visual spatial orientation and language," Dr. Penix said. "Patients may survive 8 to 10 years after diagnosis or 20 years after onset."

The pathological features of Alzheimer's disease are: neurofibrillary tangles—twisted nerve cell fibers; senile (neuritic) plaques—protein deposits or clumps; congophilic amyloid angiopathy; loss of cholinergic neurons in the nucleus basalis of Meynert; and de-afferentation of the hippocampus.

Identifying risk factors is important in dealing with Al-

zheimer's. "One possible risk factor is the presence of too much amyloid precursor protein," Dr. Penix said.

The A-beta protein cascade theory of Alzheimer's disease (Mattson, 1999) is the leading theory of what causes Alzheimer's, Dr. Penix said. It includes a sequence of conditions in the brain that results in dementia.

MANAGING DEMENTIA

Dr. Penix offered the ABC's of managing dementia: Activities of daily living, Behavior, and Cognition.

Activities of Daily Living

These include the ability to use the telephone, perform household tasks, use household appliances, manage money, shop, prepare food, get around inside and outside the home, participate in hobbies and leisure activities, handle personal mail, and grasp situations or explanations. Basic activities include toileting, feeding, dressing, personal hygiene and grooming, ambulation, and bathing.

Behavior

Behavioral problems include depression, agitation and belligerence, reversal of the sleep-wake cycle, visual hallucinations and loss of inhibitions. Treatments include Haloperidol (Haldol), Risperidone (Risperdal), Olanzapine (Zyprexa), Quetiapine (Seroquel), and Benzodiazepines. "Haldol has become known as Vitamin H," Dr. Penix said. "Benzodiazepines are the drugs of last resort."

Cognition

Pharmacotherapy with cholinesterase inhibitors focuses on this area of management. They include Tacrine (Cognex)—QID (four times daily), high side-effect profile; Donepezil (Aricept)—QID, titrated dose, well tolerated; Rivastigmine (Exelon)—BID (twice daily), titrated dose, nausea and vomiting; and Calantamine (Reminyl)—BID (twice daily), titrated dose.

"Social support is important in helping the Alzheimer's patient and his or her family," Dr. Penix said. This includes providing memory aids, such as notepads and reminders posted in specific locations. The patient's home should be evaluated for safety—especially the kitchen, bathroom, and bedroom. Social

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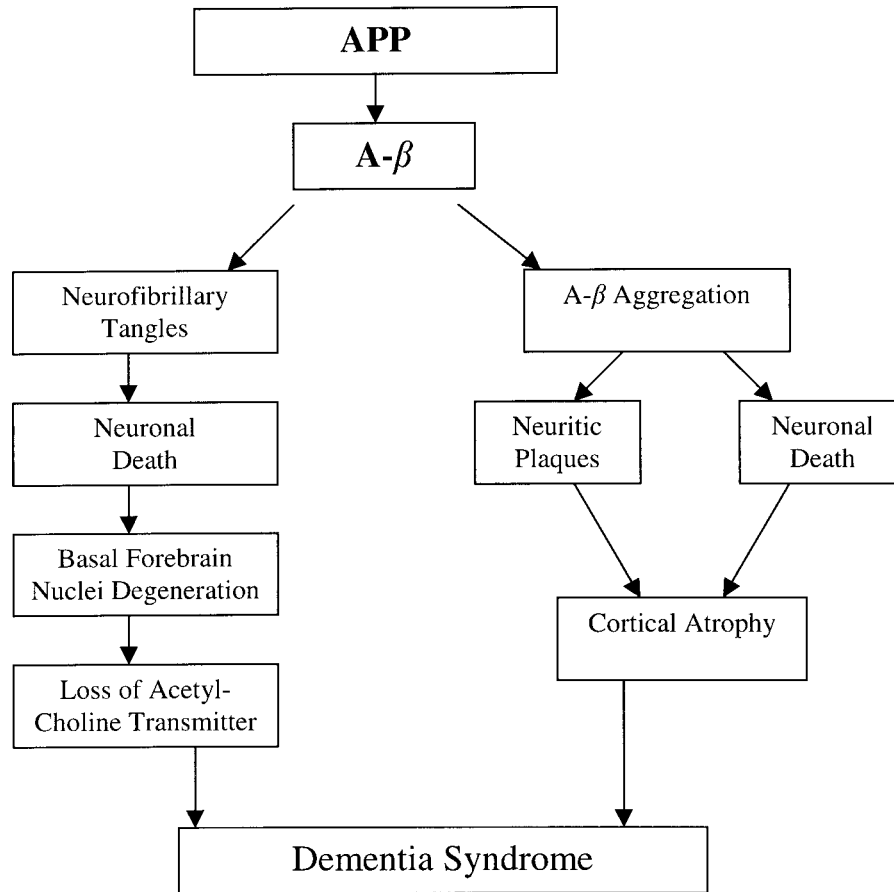


Fig 1. A- β protein cascade theory of Alzheimer's Disease

support also includes driving the patient to appointments, helping him or her pay bills, and preventing the patient from "wandering."

The following putative treatments are available but unproven, Dr. Penix said. They include administering an A-beta peptide vaccine; lowering levels of the amino acid homocysteine; and implanting a shunt to drain protein-filled cerebrospinal fluid (CSF) from the head to the stomach at a regulated rate. Patients may try eating fish or seafood at least once a week, taking ginkgo biloba, or receiving memory training. "There is also a 'cocktail' treatment consisting of several drugs," Dr. Penick said.

The list of putative neuroprotective agents includes estrogen replacement; nonsteroidal anti-inflammatory drugs (NSAIDs) and COX-2 inhibitors; Vitamin E; Vitamin C; and B vitamins, such as folate, B12 and B6.

"Recent studies have found a linear correlation between dementia and hypertension," Dr. Penix said. "In the memory clinic at Grady, we have found that 85% of our patients have high blood pressure. Fifty-nine percent of them are being treated for hypertension, with 40% controlled and 62% uncontrolled."

Alzheimer's is a "devastating disease," Dr. Penix concluded. "There are things we can do, but it will take a joint effort."