

ALZHEIMER'S DISEASE

Mary-Letitia Timiras M.D.

Overlook Hospital

Summit, New Jersey

Topics Covered

- Demography
- Clinical manifestations
- Pathophysiology
- Diagnosis
- Treatment
- Future trends

Prevalence and Impact of AD

- AD is the most common cause of dementia in people 65 years and older
- Affects 10% of people over the age of 65 and 50% of people over the age of 85
- Approximately 4 million AD patients in the United States
- Annual treatment costs = \$100 billion
- AD is the fourth leading cause of death in the United States
- The overwhelming majority of patients live at home and are cared for by family and friends

DIFFERENTIAL DIAGNOSIS

- **Alzheimer's disease**
- **Vascular (multi-infarct) dementia**
- **Dementia associated with Lewy bodies**
- **Delirium**
- **Depression**
- **Other (alcohol, Parkinson's disease [PD], Pick's disease, frontal lobe dementia, neurosyphilis)**

DELIRIUM vs DEMENTIA

- **Delirium and dementia often occur together in older hospitalized patients; the distinguishing signs of delirium are:**
 - **Acute onset**
 - **Cognitive fluctuations over hours or days**
 - **Impaired consciousness and attention**
 - **Altered sleep cycles**

VASCULAR DEMENTIA

- **Development of cognitive deficits manifested by both**
 - impaired memory
 - aphasia, apraxia, agnosia, disturbed executive function
- **Significantly impaired social, occupational function**
- **Focal neurologic symptoms & signs or evidence of cerebrovascular disease**
- **Deficits occur in absence of delirium**

DEPRESSION vs DEMENTIA

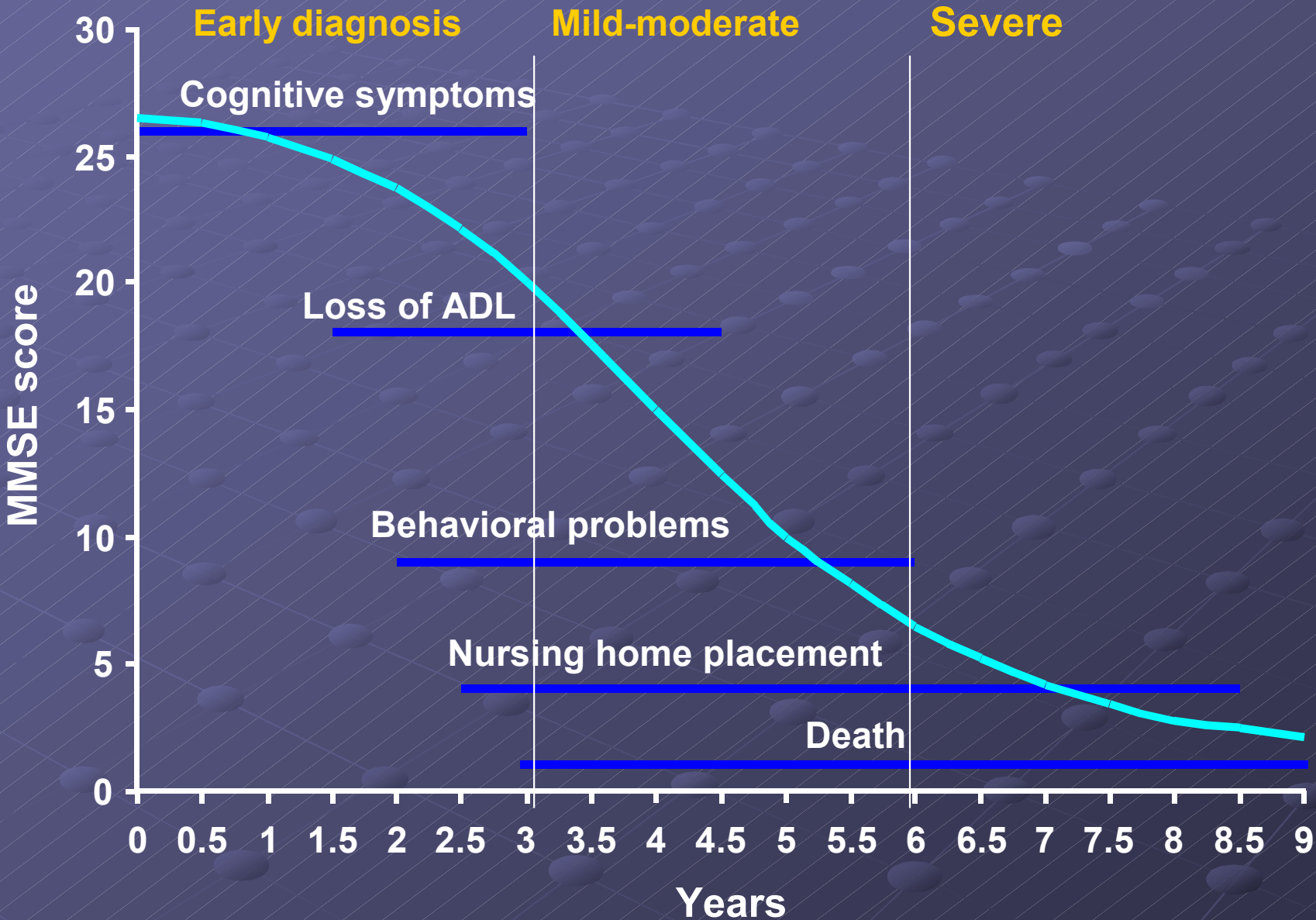
- **The symptoms of depression and dementia often overlap; patients with primary depression:**
- **Demonstrate ↓ motivation during cognitive testing**
- **Express cognitive complaints that exceed measured deficits**
- **Maintain language and motor skills**

Projected Prevalence of AD

4 Million AD Cases Today—
Over 14 Million Projected Within a Generation



The Progress of Alzheimer's Disease



Alzheimer's Disease Progresses Through Distinct Stages

Dementia/Alzheimer's

Stage	Mild	Moderate	Severe
Symptoms	Memory loss Language problems Mood swings Personality changes Diminished judgment	Behavioral, personality changes Unable to learn/recall new info Long-term memory affected Wandering, agitation, aggression, confusion Require assistance w/ADL	Gait, incontinence, motor disturbances Bedridden Unable to perform ADL Placement in long-term care needed

WHAT IS DEMENTIA?

- **An acquired syndrome of decline in memory and other cognitive functions sufficient to affect daily life in an alert patient**
- **Progressive and disabling**
- **NOT an inherent aspect of aging**
- **Different from normal cognitive lapses**

Normal Lapses

- **Forgetting a name**
- **Leaving kettle on**
- **Finding right word**
- **Forgetting date or day**

Dementia

- **Not recognizing family member**
- **Forgetting to serve meal just prepared**
- **Substituting inappropriate words**
- **Getting lost in own neighborhood**

Normal Lapses

- **Trouble balancing checkbook**
- **Losing keys, glasses**
- **Getting blues in sad situations**
- **Gradual changes with aging**

Dementia

- **Not recognizing numbers**
- **Putting iron in freezer**
- **Rapid mood swings for no reason**
- **Sudden, dramatic personality change**

RISK FACTORS FOR DEMENTIA

- **Age**
- **Family history**
- **Head injury**
- **Fewer years of education**

THE GENETICS OF DEMENTIA

- **Mutations of chromosomes 1, 14, 21**
- **Rare early-onset (before age 60) familial forms of dementia**
- **Down syndrome**

- **Apolipoprotein E4 on chromosome 19**
- **Late-onset AD**
- **APOE*4 allele ↑ risk & ↓ onset age in dose-related fashion**
- **APOE*2 allele may have protective effect**

PROTECTIVE FACTORS UNDER STUDY

- **Estrogen replacement therapy after menopause**
- **NSAIDs**
- **Antioxidants**

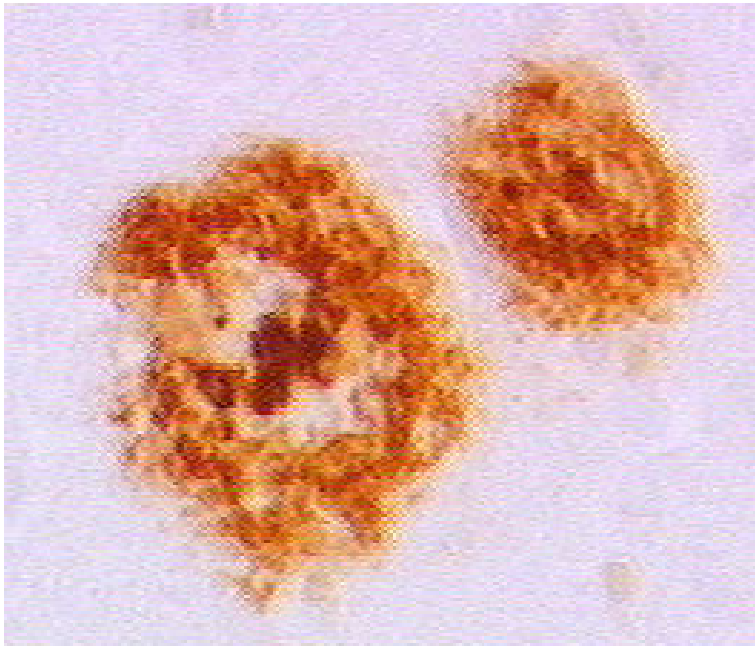
LEWY BODY DEMENTIA

- **Dementia**
- **Visual hallucinations**
- **Parkinsonian signs**
- **Alterations of alertness or attention**

Pathology of AD

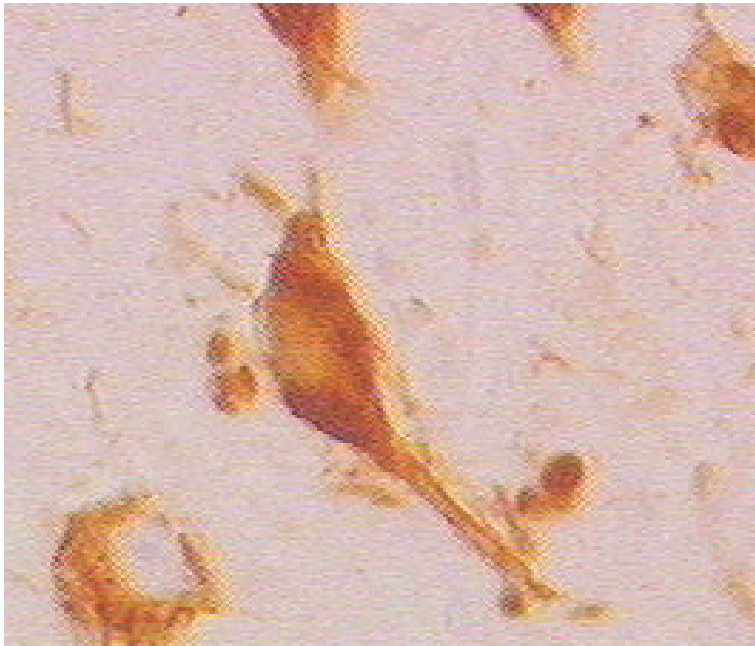
- There are 3 consistent neuropathological hallmarks:
 - Amyloid-rich senile plaques
 - Neurofibrillary tangles
 - Neuronal degeneration
- These changes eventually lead to clinical symptoms, but they begin years before the onset of symptoms

β -amyloid Plaques



Immunocytochemical staining of senile plaques in the isocortex of a brain of a human with AD (anti-amyloid antibody)

Neurofibrillary Tangles



Immunocytochemical staining of neurofibrillary tangles in the isocortex of the brain of a human with AD (anti-tau antibody)

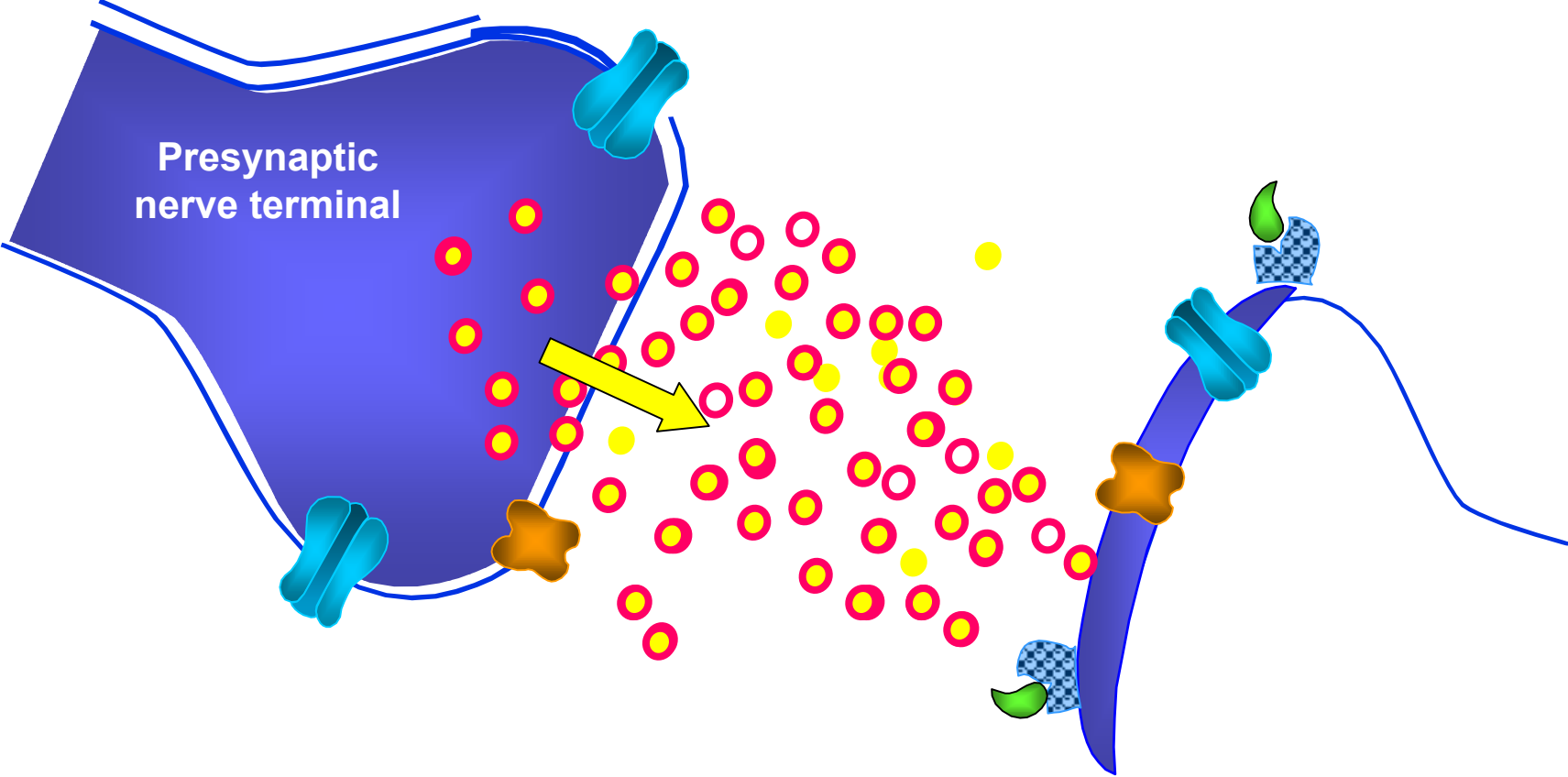
Cholinergic Hypothesis

- Acetylcholine (ACh) is an important neurotransmitter in areas of the brain involved in memory formation
- Loss of ACh activity correlates with the severity of AD

Acetylcholinesterase Inhibitors

- Drugs used to treat Alzheimer's disease act by inhibiting acetylcholinesterase activity
- These drugs block the esterase-mediated metabolism of acetylcholine to choline and acetate. This results in:
 - Increased acetylcholine in the synaptic cleft
 - Increased availability of acetylcholine for postsynaptic and presynaptic nicotinic (and muscarinic) acetylcholine receptors

Acetylcholinesterase Inhibition



ASSESSMENT: HISTORY

(1 of 4)

- **Ask both the patient & a reliable informant**
- **about the patient's:**
 - **Current condition**
 - **Medical history**
 - **Current medications & medication history**
 - **Patterns of alcohol use or abuse**
 - **Living arrangements**

ASSESSMENT: PHYSICAL

(2 of 4)

- **Examine:**
 - **Neurologic status**
 - **Mental status**
 - **Functional status**
- **Include:**
 - **Quantified screens for cognition**
 - e.g., Folstein's MMSE, Mini-Cog
 - **Neuropsychologic testing**

ASSESSMENT:

LABORATORY (3 of 4)

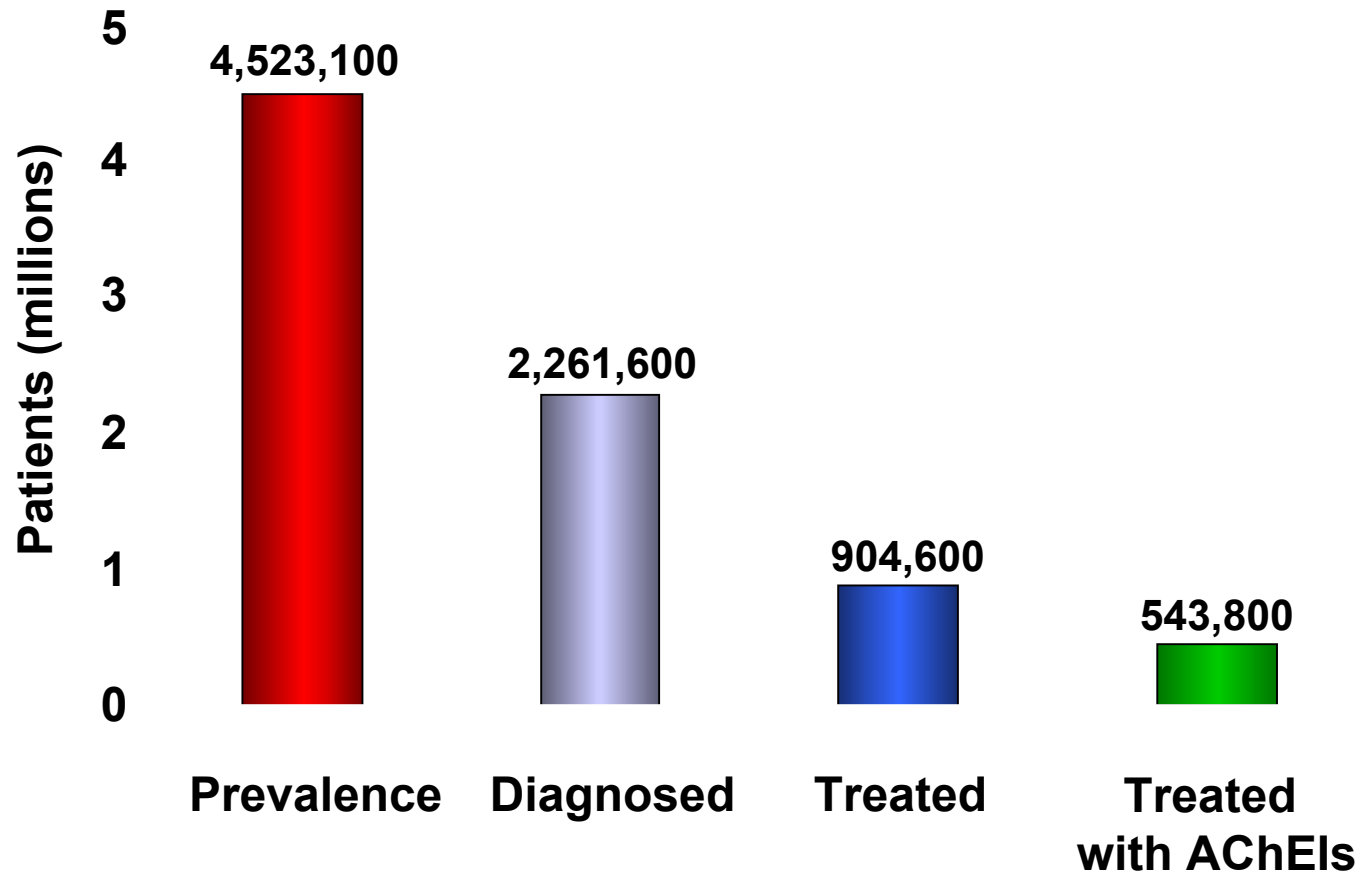
- **Laboratory tests should include:**
- **Complete blood cell count**
- **Blood chemistries**
- **Liver function tests**
- **Serologic tests for:**
 - Syphilis, TSH, Vitamin B₁₂ level

ASSESSMENT: BRAIN

IMAGING (4 of 4)

- **Use imaging when:**
 - **Onset occurs at age < 65 years**
 - **Symptoms have occurred for < 2 years**
 - **Neurologic signs are asymmetric**
 - **Clinical picture suggests normal-pressure hydrocephalus**
- **Consider:**
 - **Noncontrast computed topography head scan**
 - **Magnetic resonance imaging**
 - **Positron emission tomography**

Treatment of Alzheimer's Disease



Any drug treatment, not limited to acetylcholinesterase inhibitors.

TREATMENT & MANAGEMENT

- **Primary goals: to enhance quality of life & maximize functional performance by improving cognition, mood, and behavior**
 - **Nonpharmacologic**
 - **Pharmacologic**
 - **Specific symptom management**
 - **Resources**

NONPHARMACOLOGIC

- **Cognitive enhancement**
- **Individual and group therapy**
- **Regular appointments**
- **Communication with family,
caregivers**
- **Environmental modification**
- **Attention to safety**

PHARMACOLOGIC

- **Cholinesterase inhibitors: donepezil, rivastigmine, galantamine**
- **Other cognitive enhancers: estrogen, NSAIDs, ginkgo biloba, vitamin E**
- **Antidepressants**
- **Antipsychotics**

SYMPTOM MANAGEMENT

- **Sundowning**
- **Psychoses (delusions, hallucinations)**
- **Sleep disturbances**
- **Aggression, agitation**
- **Hypersexuality**

RESOURCES FOR MANAGING DEMENTIA

- **Attorney for will, conservatorship, estate planning**
- **Community: neighbors & friends, aging & mental health networks, adult day care, respite care, home-health agency**
- **Organizations: Alzheimer's Association, Area Agencies on Aging, Councils on Aging**
- **Services: Meals-on-Wheels, senior citizen centers**

SUMMARY (1 of 2)

- **Dementia is common in older adults but is NOT an inherent part of aging**
- **AD is the most common type of dementia, followed by vascular dementia and dementia with Lewy bodies**
- **Evaluation includes history with informant, physical & functional assessment, focused labs, & possibly brain imaging**

SUMMARY (2 of 2)

- **Primary treatment goals: enhance quality of life, maximize function by improving cognition, mood, behavior**
- **Treatment may use both medications and nonpharmacologic interventions**
- **Community resources should be used to support patient, family, caregivers**

Future Trends

- Alzheimer's as a multifactorial syndrome
- Pendulum of history
- Vaccine
- Genetic therapy