Overview of Alzheimer’s and Other Dementias

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Overview

- Defining dementia
- Effects of dementia on the brain
- Stages and symptoms of Alzheimer’s disease
- Treatment options and medications
- Current research
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Dementia is defined as the loss of cognitive function that interferes with a person’s day-to-day activities.

- Thinking
- Remembering
- Reasoning
- Personality
- Behavior
How Is Dementia Different from Normal Aging?

- Normal changes in memory with aging:
  - Forgetting names or appointments
  - Having trouble sorting out complex problems
  - Having difficulty learning new things (computers, etc.)

These changes do not affect a person’s ability to manage day-to-day activities.
What Other Conditions Can Be Confused with Dementia?

- Medication side effects
- Alcohol effects
- Hormone or vitamin imbalances
- Depression
Depression

- Can lead to problems with attention and memory
- Can be confused with lack of initiation, a common early sign of dementia
- May be seen together with or precede dementia
Feeling sad, hopeless, or guilty most of the time
Feeling tired or having low energy
Crying a lot
Having thoughts of suicide or death
Sleep problems (too much or too little)
Changes in appetite or weight (up or down)
Loss of interest and pleasure in activities
Geriatric Suicide

- Studies estimate only 10-40% of elderly get care
- Overall US suicide rate 12/100,000
- White males peak from 20-40 and again over 65
- Rate in 85 and up at 50/100,000
- Est. 75% of elderly who suicide saw MD within month prior
- 20% of older pts. who suicide saw MD that day
- 25% of all completed suicides in patients over the age of 65
Dementia Terminology

New

- Dementia due to
  - Alzheimer’s disease
  - Lewy Body disease
  - Vascular disease
  - Pick’s disease
  - HIV
  - Parkinson’s disease

Older

- Chronic Brain Syndrome
- Organic Brain Syndrome
- Senility
- Acute Confusional State
- Hardening of the Arteries
Dementia can be caused by various disorders including:

- Alzheimer’s disease
- Lewy Body disease
- Vascular dementia
- Fronto-temporal dementia
- Parkinson’s disease
What Is Dementia?

- Dementia can be caused by various disorders including:
  - Alzheimer’s disease
  - Lewy Body disease
  - Vascular dementia
  - Fronto-temporal dementia
  - Parkinson’s disease
Causes of Dementia

- Alzheimer's disease
- Lewy Body
- Vascular/Multi-Infarct
- Combination
- Brain Tumors
- Parkinson's disease
- Psychiatric Conditions
- Unknown
Alzheimer’s Disease

- The most common form of dementia (up to 80% of all dementia cases)
- Prevalence increases with aging
- 2 main forms:
  - Early onset (accounts for <10% of cases)
    - Symptoms develop before age 60
    - Highly linked to 3 genes on chromosomes 1, 14, 21
  - Late onset (>90% of cases)
    - Symptoms usually develop after age 70
    - Linked to genetic risk factor apolipoprotein E4
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Alzheimer’s Disease Prevalence: Changes with Aging

Evans et al., JAMA 1989
Alzheimer’s Disease Prevalence in the United States

Hebert et al., Arch Neurol 2003
- Age
- Family history of AD
- Apolipoprotein E4 (APOE4) – genetic risk
- Low sex steroids/high gonadotropins
- Low education level
- Head trauma with loss of consciousness
- Down syndrome

Risk Factors for AD
AD Risk Factors:
APOE 4

APOE allele frequencies in general population

- APOE 3: 78%
- APOE 2: 8%
- APOE 4: 14%

AD Risk Factors: APOE 4

APOE allele frequencies in persons with dementia

Vascular risk factors associated with AD:
- High cholesterol
- High blood pressure
- Obesity
- Diabetes
- Low activity levels
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Effects of Alzheimer’s on the Brain

A. The brain of a normal elderly person

B. The brain of a person with Alzheimer's disease

C. The brain of a person with alcoholism
Effects of Alzheimer’s on the Brain
Effects of Alzheimer’s on the Brain

Normal

Alzheimer’s

Neurofibrillary tangles

Amyloid plaques
AMYLOID PLAQUES
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Stages of Alzheimer’s Disease
Stages of Alzheimer’s Disease

Cognition

Normal

“Pre-Alzheimer’s Disease”

Mild

Moderate

Severe

AD
Stages of Alzheimer’s Disease

- Normal
- Mild Cognitive Impairment (MCI)
- Mild
- Moderate
- Severe
- AD (Alzheimer’s Disease)
Mild Cognitive Impairment (MCI)

- Characterized by:
  - Memory complaint, preferably corroborated by an informant
  - Impaired memory function for age and education
  - Preserved general cognitive function
  - Intact social/occupational function
  - Not demented on testing
Mild AD characterized by:
- Short-term memory loss
- Difficulty performing familiar tasks
- Altered judgment
- Language changes
- Changes in mood, behavior, personality
- Disorientation to time and place
- Problems with abstract thinking
Moderate AD characterized by:
- Worsening memory loss
- Difficulty performing familiar tasks
- Poor judgment
- Language changes
- Changes in mood, behavior, personality
- Disorientation to time and place
- Problems with abstract thinking
- Changes in sensory perception
- Physical changes
Severe AD characterized by:
- Little or no short-term memory
- Inability to perform tasks
- Lack of judgment
- Unable to communicate
- Physical decline
What Are Some Behavioral Changes Seen with Dementia?

- Delusions
- Suspiciousness
- Hostility
- Hallucinations
- Feelings of persecution
- Incoherence
- Overexcitability

- Emotional withdrawal or isolation
- Apathy
- Social withdrawal
- Lack of feelings or inappropriate emotion (e.g., laughing at the death of a loved one)
How Do You Diagnose Alzheimer’s Disease?

- Clinical diagnosis – no one test can confirm the disease
- Constellation of:
  - History from patient and family
  - Cognitive testing
  - Physical exam
  - Lab tests (to rule out other conditions)
  - CT scan or MRI scan of the brain (test for amyloid deposition and if any concern for mini-strokes, etc.)
  - Genetic evaluation
Memory task
  ◦ “What were the 3 items I gave you to remember a few minutes ago?”

Other areas of thinking assessed
  ◦ Language
  ◦ Judgment
  ◦ Comprehension
  ◦ Attention
  ◦ Visual-spatial
Mini-Mental Status Exam (MMSE)

- 30 point scale published in 1975
- Quick, universal, easy to give
- Sensitive and specific
- Must be consistent with asking, scoring
- Tests orientation, registration, attention/calculation, recall, language, and praxis
- Generally 24 or lower think possible dementia
- Mild cognitive impairment 20-24
- Moderate impairment 10-20
- Severe impairment <10
- With Alzheimer's, typically lose 2-4 points/year
Simple but informative
Tests memory, language comprehension, executive function, visuospatial, visuomotor, concentration, fine motor skills, math, visual fields.
Ask to draw face, place numbers, draw hands to read either 11:10 or 8:20
Either score as correct/incorrect or give one point each for drawing complete circle, numbered correctly positioned, all 12 numbers present, hands correct
Other Causes of Dementia

- Alzheimer’s disease
- Lewy Body disease
- Vascular dementia
- Fronto-temporal dementia
- Parkinson’s disease
Lewy Body Disease

- Characterized by:
  - Fluctuating cognition, attention, and alertness
  - Recurrent visual hallucinations
  - Parkinsonism
  - Recurrent falls
  - Syncope (fainting spells)
  - Increased sensitivity to medicines used to control agitation (Haldol)
  - Delusions
  - Medications for Parkinson’s may worsen hallucinations and delusions
Vascular Dementia

- Quick-onset of memory problems
- Risk factors for stroke (high blood pressure, diabetes, high cholesterol, etc.)
- "Step-wise" progression
- Commonly seen together with AD
- Will often see focal neurological signs
- Group of disorders affecting the frontal and temporal lobes (includes Pick’s disease)
- Early findings may include apathy, anger, loss of inhibitions, rudeness, lack of empathy, changes in sexual behavior, and/or poor hygiene
- Memory loss occurs later in disease
- Patients lack awareness or concern that their behavior has changed

**Frontotemporal Dementia (FTD)**
Characterized by:

- Tremors
- Limb stiffness
- Difficulty with speech
- Difficulty initiating movement

Late in the disease may develop memory problems

If Parkinson’s symptoms develop at the same time as memory loss, it most likely is Lewy Body disease
Huntington’s Disease

- Autosomal dominant
- 5 to 7/100,000 prevalence
- Average age onset 40 yr. with progression and death in 17 years.
- Subcortical dementia with atrophy of caudate nucleus
- Triad
  - Dementia
  - Chorea (intermittent jerking lumbs, trunk)
  - Positive family history
- Personality changes - irritability, apathy, typically prior to chorea
- Depression common in up to 50%
Normal Pressure Hydrocephalus

- Less than 2%, onset 60-70 yr. old
- Triad
  - Progressive dementia
  - Gait apraxia (fail to alternate legs)
  - Urinary incontinence
- Caused by impaired CSF circulation with ventricular dilation
- HCT/MRI - ventricular dilation with minimal atrophy
- CSF pressure, EEG, lab tests - normal
- Series of LPs monitoring for gait improvement
Creutzfeldt-Jakob Dementia (CJD)

- Prion - proteinaceous infective agent lacking DNA, RNA
- 1/1,000,000 annual incidence
- Rapidly progressive neurodegenerative disorder, fatal average 6 months
- Clinically - early fatigue, insomnia, anorexia, progression to dementia, behavioral disturbances, myoclonus
- Transmitted by corneal transplant, intracerebral EEG electrodes, tainted human growth hormone
Cognitive impairment in 50% chronic alcoholics
Direct toxic effects of alcohol and secondary vitamin deficiencies
See confusion, gaze palsy, nystagmus, ataxia, retrograde and anterograde amnesia, peripheral neuropathies
Chronic thiamine deficiency
HCT/MRI - may be normal or show cerebral atrophy, hemorrhages in mammillary bodies
EEG - normal
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Current research

Overview
- Education and emotional support to the patient and their families
- Safety review
- Caregiver support
- Behavioral interventions
- Medical therapy

Treatment of Alzheimer’s Disease
Medical Therapy for AD

- Medications used to treat Alzheimer’s disease
- Medications used to treat behavioral symptoms (such as wandering and agitation)
- Medications used to treat depression and anxiety in Alzheimer’s patients
- Potential preventive therapies
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Medications used to treat Alzheimer’s disease

FDA Approved Medications

◦ Acetylcholinesterase inhibitors (Mild to Mod AD)
  ◦ Tacrine (Cognex)
  ◦ Donepezil (Aricept)
  ◦ Rivastigmine (Exelon)
  ◦ Galantamine (Reminyl)

◦ NMDA receptor antagonist (Mod to Severe AD)
  ◦ Memantine (Namenda)
Acetylcholinesterase inhibitors block an enzyme which breaks down acetylcholine in the space between nerve cells.
Stages of Alzheimer’s Disease

Normal

MCI

Mild

Moderate

Severe

Begin cholinesterase inhibitor therapy

AD
Stages of Alzheimer’s Disease

- Normal
- MCI
- Mild
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- Severe

Begin cholinesterase inhibitor therapy

Stop cholinesterase inhibitor therapy
Cholinergic drugs
- Delay the progression of memory loss
- Delay time to nursing home placement
- Improve behavioral symptoms
- Help relieve some caregiver burden
Memantine (Namenda)
- Works by protecting cells from too much glutamate, a chemical released in excess by damaged brain cells in Alzheimer’s disease
- Approved by FDA in January 2004
- Useful in combination with cholinesterase inhibitors
- Indicated for moderate to severe AD (MMSE score <14)
Stages of Alzheimer’s Disease

- Normal
- MCI
- Mild
- Moderate
- Severe

- Begin cholinesterase inhibitor therapy
- Add memantine

The diagram illustrates the progression of Alzheimer's Disease stages from Normal to Severe, with interventions indicated for MCI and Moderate stages.
Treatment of Alzheimer’s Disease

- Medications used to treat Alzheimer’s disease
- Medications used to treat behavioral symptoms (such as wandering and agitation)
- Medications used to treat depression and anxiety in Alzheimer’s patients
- Potential preventive therapies
Medications used to treat behavioral symptoms

- **Agitation**
  - Risperidone (Risperdal)
  - Olanzapine (Zyprexa)
  - Quetiapine (Seroquel)
  - Haloperidol (Haldol) – avoid in persons with Lewy Body disease

- **Insomnia**
  - Trazodone
  - AVOID BENEDRYL (INCLUDED IN TYLENOL P.M.) AND SEDATIVES LIKE VALIUM!
Medications used to treat Alzheimer’s disease

Medications used to treat behavioral symptoms (such as wandering and agitation)

Medications used to treat depression and anxiety in Alzheimer’s patients

Potential preventive therapies

Treatment of Alzheimer’s Disease
Medications used to treat depression and anxiety

- **Depression**
  - Fluoxetine (Prozac)
  - Paroxetine (Paxil)
  - Sertraline (Zoloft)
  - Citalopram (Celexa)
  - Venlafaxine (Effexor)

- **Anxiety (use with caution! may worsen symptoms)**
  - Lorazepam (Ativan)
  - Alprazolam (Xanax)
  - Buspirone (Buspar)
Mood and anxiety symptoms may improve with cholinergic drugs.

Some medications used for anxiety (like Ativan) may actually lead to increased agitation.

Increased socialization may help with some depression and anxiety symptoms.

Medications used to treat depression and anxiety.
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Alzheimer’s Association research link
  ◦ http://www.alz.org

Alzheimer Research Forum
  ◦ http://www.alzforum.org/home.asp

Alzheimer’s Disease Education & Referral (ADEAR) Center (National Institute on Aging)
  ◦ http://www.alzheimers.org/nianews/nianews.html

Current AD Research – International and National
- UW Medical School and Madison VA GRECC Wisconsin Comprehensive Memory Program
  - Clinical trials for:
    - Women and men with AD
    - Adult children of persons with AD (Wisconsin Registry for Alzheimer’s Prevention [WRAP])
    - Persons with Mild Cognitive Impairment (MCI)
    - Healthy adults without memory complaints
Current areas under investigation at Wisconsin Comprehensive Memory Program:

- Functional MRI
- Hormone therapy (women and men)
- Isoflavonoids
- Statin therapy (AD prevention and treatment)

(608) 263-2582 or toll free 1-866-MEM-PROG

Current AD Research – Local
There is hope...