Alzheimer’s Disease: New Criteria and Guidelines for Diagnosis, Early Recognition, Treatment, Behavioral Interventions, Prevention Strategies, Diverse Population Issues, and Resources

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Dementia

- Recognized since ancient times as consequence of aging
  - Today it is a major public health concern.
  - Approximately 5.2 million people in US with Alzheimer's Disease at all ages
  - One in nine individuals 65 and older (11 percent) have Alzheimer's Disease.
  - If no cure, 14 million will be affected by 2030.
Costs of Dementia

- Dementia costs this country $157 – $215 billion annually making the disease more costly than either heart disease or cancer. (Rand Corporation and University of Michigan, 2013)

- Greatest economic cost is providing institutional and home-based long-term care rather than medical services.

- If age-specific prevalence rates remain constant, with the growth of the aging population this cost will double by 2040.

New England Journal of Medicine, April 4, 2013 Funding by National Institute of Aging.

Average per Person Payments by Source for Healthcare Services provided to Medicare Beneficiaries Aged 65 and Older, with or without Alzheimer's Disease and other Dementias, 2004 Medicare Beneficiary Survey in 2010 Dollars

<table>
<thead>
<tr>
<th>Beneficiaries with Dementia</th>
<th>Beneficiaries without Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital</td>
<td>$9,768</td>
</tr>
<tr>
<td>Medical Provider</td>
<td>$5,551</td>
</tr>
<tr>
<td>Skilled Nursing Facility</td>
<td>$3,862</td>
</tr>
<tr>
<td>Home Health Care</td>
<td>$1,601</td>
</tr>
<tr>
<td>Prescription Meds</td>
<td>$3,198</td>
</tr>
</tbody>
</table>

*“Medical provider” includes physician, other medical provider and laboratory services, and medical equipment and supplies.

**Information on payments for prescription drugs is only available for people who were living in the community, that is, not in a nursing home or assisted living facility.

Created from data from Alzheimer’s Association, Characteristics, Costs and Health Service Use for Medicare Beneficiaries with a Dementia Diagnosis: Report 1: Medicare Current Beneficiary Survey, 2009.(125)
Costs of Dementia

- In 2010, 14.9 million family members and friends provided 17 billion hours of unpaid care to those with dementia.
- Economic value of unpaid care was $202.6 billion in 2010.

2011 Alzheimer's Disease Facts and Figures

Costs of Dementia

- More than 60% of caregivers rate the emotional stress of care-giving as high or very high; over 30% report symptoms of depression.
- The physical and emotional impact of care-giving is estimated to result in $7.9 billion in increased healthcare costs.

2011 Alzheimer’s Diseases Facts and Figures
Dementia Care Sites

• Nursing Home Care – 2008, 68% of all nursing home residents had some degree of cognitive impairment.

• Assisted Living Care – Estimates vary: 45–67% of residents of assisted living facilities have Alzheimer’s disease or other dementias.

• Adult Day Center Services – At least ½ of elderly participants in adult day centers have Alzheimer’s disease or other dementias.

• Home care – more than 1/3 (37%) of older people who receive primarily non-medical home care services have “cognitive impairment” consistent with dementia. (*Taken from State Home Care Programs from Connecticut, Florida and Michigan)

• 70 % of individuals with Alzheimer’s disease are taken care of at home.  

Alzheimer’s Disease

✓ Statistics – 5.2 million Americans
  ▪ The majority of those with the disease are women
    ▪ Age-specific incidence, however is the same for men and women
  ▪ People with lower levels of education appear to be at higher risk of Alzheimer’s and/or other dementias
  ▪ African-Americans are twice as likely to develop Alzheimer’s disease and/or other dementias
  ▪ Hispanic individuals are 1½ times more likely to develop Alzheimer’s disease and/or other dementias

2011 Alzheimer’s Diseases Facts and Figures

2013 Alzheimer’s Diseases Facts and Figures
Diversity and Rural Population Issues

• Alzheimer’s disease and other dementias are under-diagnosed in rural and minority populations more than in urban or white populations.
• Lack of diagnosis seriously reduces an individual’s access to available treatments and information.
• Active medical management, information and support, and coordination of medical and community services have been shown to improve quality and outcomes of care for people with dementia.

Issues of Rural Populations

• 65+ are 13.17% of USA population, but 20% of this age group live in non-metropolitan designated areas
• Most counties in PA are rural
• Limited access to health care and social services for prevention, diagnosis, management & treatment of chronic conditions
• Limited access to needed assistance with ADLs and IADLs, and long-term care options
• Increasing diversity: large concentrations of Hispanics (especially migrant labor areas) and African Americans (particularly in South)
Issues of Rural Populations

• Isolation issues
  – Social engagement can help in reducing risk for cognitive impairment
  – Need help in being connected to programs such as Adult Day Programs (which may not be available in many rural areas)
  – Lack of grocery stores: “food desert” issues
  – Mobility and transportation Issues
  – Younger family members may have moved to urban areas for jobs, so rural seniors may be even more alone
### Issues of Rural Populations

- Research (2012) found that rural living is associated with an increased risk of Alzheimer’s disease, with suggestion childhood rural residence increases risk.
- Research found over ½ of caregivers of rural patients with AD reported their patients experienced unmet service needs in 1 or more ADL and/or IADL (2013).
- Data show that nursing home use is more prevalent in rural communities than urban ones (2004).
- Video-telemedicine in memory disorders clinics: Being used for evaluation and management of rural elders with cognitive impairment

### Diversity Issues: African-Americans

- African-Americans are about 2 times more likely than white Americans to have Alzheimer’s and other dementias.
- However Medicare data show they were only 32% more likely to have a diagnosis (i.e., they were less likely than whites to have a diagnosis and less likely to say a doctor had told them they had a “memory-related disease”).
- Diagnosis is typically in the later stages of the disease, when they are more cognitively and physically impaired (so medical costs higher at that point).
Diversity Issues: African-Americans

• One of most promising areas of research is growing body of evidence that vascular disease may be a key mechanism in triggering the manifestation of Alzheimer’s disease.
• Persons with history of either high blood pressure or high cholesterol are 2X more likely to get AD; those with both risk factors are 4X more likely to get dementia.

Diversity Issues: African-Americans

• 65% of African-Americans have hypertension; higher risk of stroke; 60% higher risk of type 2 diabetes (contributes to vascular disease)
• Better management (or prevention) of these medical conditions, especially if treatment started in midlife, could reduce Alzheimer’s and other dementia risk.
• Ethnic and cultural bias in current screening and assessment tools lead to higher rates of false-positive results
New Research Finding

• Published April, 2013.
• Only large study to identify genetic risks of African Americans
  – African Americans with Alzheimer’s disease were more likely to have the gene ABCA7 which is thought to predispose carriers to the disease.
  – Increased risk by 80% - considered a modest increase.
  – The APOEε4 gene is present in the same proportion in African Americans as it is in people of European ancestry.

Diversity Issues: African-American Care-giving

• Most frequently documented cultural differences were:
  – Better psychosocial health of caregiver
  – More positive appraisals of caregiving
  – Greater spirituality or use of prayer
  – More social support for care-giver
  – Stronger beliefs about filial responsibility
  – Higher value placed on extended family networks
  – Greater aversion to institutionalization of relatives
Diversity Issues: Hispanics

- One and ½ times more likely than whites to have Alzheimer’s and/or other dementias
- Less likely to have a diagnosis of the condition
- When diagnosed typically in later stages of disease, so more impaired and need more medical care
- Hispanics with dementia are low users of formal service; less likely to see a physician and much less likely to receive services to help monitor and control their chronic conditions

Diversity Issues: Hispanic

- High incidence of diabetes – 64% higher than non-Hispanic white Americans; diabetes is one of the vascular risk factors related to risk of AD and other dementia in absence of stroke
- Study of older Mexican Americans found diabetes and hypertension contribute more to dementia in this ethnic group than in non-Hispanic whites
- Again, better management of these conditions (or prevention) beginning in midlife may reduce higher risk of AD and other dementia
Diversity Issues: Hispanic

• Hispanic community of USA represents people from over 17 Spanish-speaking countries, but culturally-based attitudes and behaviors unite them.
• Lack of Spanish-language abilities and cultural sensitivity in many health care systems:
  – Instills distrust
  – Limits access to care
  – Adversely affects quality of care they do receive
  – Imposes further burdens on extended family as interpreters

Diversity Issues: Hispanic

• Cultural biases in cognitive testing and inadequate translation of diagnostic tools may skew diagnosis of dementia in Hispanics
• Significant progress in developing culturally sensitive tools, but not standardized or normed across subgroups of Hispanics, and not widely used
• Older Hispanics have far less health insurance than non-Hispanic contemporaries
Diversity Issues: Hispanic Care-giving

- Strong cultural value of family responsibility
- High acceptance of cognitive impairment and dementia as a normal part of aging to be managed within the family
- Thus families provide more care, for longer periods, and at higher levels of impairment than non-Hispanic families.

Diversity Issues: Hispanic Care-giving

- Accept stress as a normal, expected part of the familial role
- Resistance to sharing familial problems with outsiders
- Reluctant to use formal services until overwhelmed
- Services must be provided in way that reinforces family values and overcomes cultural barriers
Alzheimer’s Disease

• Most prevalent kind of dementia (60 – 80% of all cases)

• Although there is an increased incidence with age, it is not consequential to the aging process
  • 13% population 65 years of age and older
  • Nearly half of the individuals (43%) over age 85

2011 Alzheimer’s Diseases Facts and Figures

Dementia

• Senility, Hardening of the Arteries, Organic Brain Syndrome (OBS)
Risk Factors for Alzheimer’s Disease

- Older age
- Genetics
- Head injury
- Ethnic background
- Rural background
- Lower social economic scale
- Lower education level
- Poor diet
- Lower levels of exercise
- Lower levels of cognitive engagement
- Lower levels of social engagement

Cognitive Reserve (CR) Hypothesis

✓ The concept of cognitive reserve provides an explanation for differences between individuals with susceptibility to age-related brain changes or pathology related to Alzheimer's disease, whereby some people can tolerate more of these changes than others and maintain function.

- Epidemiological studies suggest that lifelong experiences can increase this reserve:
  - Educational achievements - Higher IQ
  - Occupation attainment
  - Leisure activities in later years

Cognitive Reserve (CR) Hypothesis (cont.)

CR postulates that individual differences in how tasks are processed provide differential reserve against brain pathology or age-related changes.

• 2 Forms –
  » In neural reserve, preexisting brain networks that are more efficient or have greater capacity may be less susceptible to disruption.
  » In neural compensation, alternate networks may compensate for pathology's disruption of pre-existing networks (how tasks are performed that may allow some individuals to be more resilient).

✓ There is also the possibility that directly enhancing CR may help forestall the diagnosis of AD.


Dementia

• Not a disease, but a broader set of symptoms that accompanies certain diseases (Alzheimer’s Association) –

• Irreversible chronic brain failure
  – Structural damage to the brain
  – Loss of mental abilities
  – Involves memory, reasoning, learning and judgment
Dementia – DSM 5

- The term dementia is eliminated.
- Replaced with “major” or “minor” neurocognitive disorder.
- The definition focuses on the decline as opposed to deficit.
- Old definition required memory impairment, which is not always the first symptom.
- The presence of a “neurocognitive” disorder needs to be established, and then it is determined whether it is minor or major.

Minor Neurocognitive Disorder – DSM 5

- Modest cognitive decline from a previous level of functioning based on the concerns of the individual, knowledgeable informant or the clinician;
- Decline in neurocognitive performance in the range of one or two standard deviations below appropriate norms.
- The cognitive deficits are insufficient to interfere with independence (IADL’s), but more complex tasks require compensatory strategies or accommodation.
- The cognitive deficits do not occur in the context of a delirium.
- The cognitive deficits are not attributable to another mental disorder.
Major Neurocognitive Disorder – DSM 5

▪ There is evidence of a substantial cognitive decline from a previous level of performance in one or more of the domains based on the concerns of the individual, a knowledgeable informant, or the clinician;

▪ Decline in neurocognitive performance typically involving test performance in the range of two or more standard deviations below appropriate norms on formal testing or equivalent clinical evaluation.

Major Neurocognitive Disorder – DSM 5 (cont.)

▪ The cognitive deficits are sufficient to interfere with independence requiring minimal assistance with instrumental activities of daily living.
▪ The cognitive deficits do not occur in the context of a delirium.
▪ The cognitive deficits are not attributable to another mental disorder.
Changes in DSM 5

“The DSM IV terminology required the presence of memory impairment; often memory impairment is not always the first domain affected in dementia or neurocognitive disorders.”

Causes of Dementia

- Alzheimer’s Disease
- Vascular or Multi-infarct Dementia - strokes, mini-strokes, TIA’s
- Lewy Body Disease
- Pick’s Disease
- Jacob-Creutzfeldt Disease
- Parkinson’s Disease
- Substance abuse
Estimated Causes of Dementia

- Alzheimer’s disease
- Mixed causes
- Vascular Dementia
- Lewy Body Dementias
- Frontotemporal Dementia
- Unknown
- Other

Alzheimer’s Disease

- Slow and progressive; varies day to day
- Course of the disease is gradual, about 8-10 years.
- Causes?
- Diagnosis is one of inclusion.
- Presence of neurofibrillary tangles and senile plaques in brain matter
- Assessments make sure there are no other psychiatric illnesses or medical diseases causing the cognitive problems.
Normal Brain Function

How Neurons Communicate

Electrical impulses pass along the axon

Synapse

Vesicles containing neurotransmitter molecules

Receptors

Cellular Changes in AD

Neuritic plaques

Neurofibrillary tangles

Neuron
Alzheimer’s disease

Blue arrows: Amyloid plaques
Red arrows: Neurofibrillary tangles

Areas of brain affected

The Brain and Alzheimer’s Disease

Alzheimer’s disease attacks nerve cells (neurons) in several regions of the brain.

Cerebral cortex:
Involved in conscious thought and language

Basal forebrain:
Has large numbers of neurons containing acetylcholine, a chemical important in memory and learning.

Hippocampus:
Essential to memory storage. The earliest signs of Alzheimer’s are found in the nearby entorhinal cortex (not shown).
Alzheimer’s Disease: Complex Disorder

- Genetics
- Aging
- Amyloid deposits
- Inflammation
- Plaques and tangles
- Neuronal damage and loss
- Neurochemical changes
- Patient may have other dementias also.

Risk Factors for AD

- Age
- Family history/genetics
- Apolipoprotein E status
- Vascular risk factors:
  - Diabetes
  - Smoking
  - Midlife hypertension
  - Midlife hypercholesterolemia
  - Midlife obesity
- Alcohol intake
- Decreased physical activity
- Low “cognitive reserve”
- Head trauma
### Genetics of Alzheimer’s Disease

<table>
<thead>
<tr>
<th>Genetic cause</th>
<th>Percent of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosomal</td>
<td>Down syndrome</td>
</tr>
<tr>
<td>Early onset familial</td>
<td></td>
</tr>
<tr>
<td>Presenilin 1</td>
<td></td>
</tr>
<tr>
<td>Presenilin 2</td>
<td></td>
</tr>
<tr>
<td>Amyloid Precursor Protein</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>Late onset familial</td>
<td></td>
</tr>
<tr>
<td>Apolipoprotein E</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>Presumed genetic/environment interactions</td>
<td></td>
</tr>
</tbody>
</table>

Three alleles of apolipoprotein E: APOE\(\varepsilon\)2, APOE\(\varepsilon\)3, and APOE\(\varepsilon\)4.

- One \(\varepsilon\)4 allele increases risk of AD by ~2-3 times, two alleles increases risk of AD by ~10 times.
- But...frequency of APOE\(\varepsilon\)4 in late onset AD ~40%

### APOE\(\varepsilon\)4 is Risk-Factor Gene

- Increases risk of developing Alzheimer’s Disease (AD)
- But inheriting this allele does not mean definitely will develop AD
- Some with one or two of these alleles never get AD
- Some with AD do not have any of these alleles
Epigenetics: Nature Meets Nurture

• Expression of genes (when particular genes are “Switched” on or off) can be affected -- positively and negatively – by environmental factors, e.g.
  – Exercise
  – Diet
  – Chemicals
  – Smoking
  – Exposures in uterus

Epigenetics (cont.)

• Environmental and behavioral exposures during lifetime can alter a cell’s DNA and make people more or less susceptible to developing a disease later in life
• Emerging evidence the epigenetic mechanisms contribute to Alzheimer’s disease – can be protective, benign, or harmful
New Research Finding

• Announced by NIH April 25, 2013.
• Too much of a regulator protein called CD33 appears to promote late-onset AD by preventing support cells from clearing out toxic plaques (beta-amyloid)
• Now researchers are looking for agents that can cross the blood-brain barrier and block the CD33 activity

NIH Increases Funding for AD Research on Prevention & Novel Drug Targets

• Announced September 18, 2013
• $45 million in awards
• Test drugs aimed at preventing AD
• Identify and validate biological targets for novel therapies
Alzheimer’s Breakthrough Hailed as “Turning Point”

• Announced 10 October 2013 by British Medical Research Council
• Discovery of first chemical to prevent the death of brain tissue in a neurodegenerative disease
• Focused on the natural defense mechanisms built into brain cells
• When a virus hijacks a brain cell, it leads to build-up of viral proteins.


AD Breakthrough (cont.)

• Cells respond by shutting down nearly all protein production to halt the spread of virus.
• Many neurodegenerative diseases involve “misfolded”, faulty proteins, that linger and cause brain cells to shut down protein production – starve themselves to death.
• This process, repeated throughout brain, can destroy movement or memory or even kill.
• Researchers used a compound that prevented those defense mechanisms from kicking in.
AD Breakthrough (cont.)

- These results are from mice studies.
- Need to formulate a compound for humans and test it.
- Finding especially exciting because can apply to a wide range of neurodegenerative diseases.
- “Targeting a mechanism relevant to a number of neurodegenerative diseases could yield a single drug with wide-reaching benefits, but this compound is still at an early stage.”

Alzheimer’s Disease

- Higher prevalence with increasing age makes genetic association by chance more likely.

- Mode of inheritance is very difficult to determine.

- An older person has many potential other reasons for cognitive decline.
New Criteria for Alzheimer’s Disease

- Spearheaded by the Alzheimer’s Association and the National Institute on Aging (NIA) of the National Institutes of Health (NIH)
- Three expert workgroups from around the globe developed four articles including ready-to-use clinical diagnostic criteria for Alzheimer’s disease dementia and mild cognitive impairment (MCI) due to Alzheimer’s disease.
  

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New Criteria for Alzheimer’s Disease

“The National Institute on Aging/Alzheimer’s Association Diagnostic Guidelines for Alzheimer’s Disease” expand the definition of Alzheimer’s to include three phases of the disease (2 new pre-clinical):

1) Pre-symptomatic / pre-clinical
2) Mild Cognitive Impairment due to Alzheimer’s disease
3) Dementia caused by Alzheimer’s

New Criteria for Alzheimer’s Disease

• **Preclinical Alzheimer’s Disease** – measurable changes in biomarkers that can indicate the earliest signs of the disease, but before symptoms are noticeable. “Current thinking is Alzheimer’s begins creating measurable changes in the brain years, perhaps decades, before symptoms occur. This is leading to proposals for biomarker research to tell doctors what biomarker results confirm that a person is in what stage of the disease.”

http://www.alz.org/documents_custom/Alz_Diag_Criteria_FAQ.pdf

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New Criteria for Alzheimer’s Disease

• **Mild Cognitive Impairment (MCI)** – mild changes in memory and thinking abilities that are noticeable to the person and to family members and that can be measured, but do not affect one’s ability to carry out everyday activities. Many, but not all, individuals with MCI go on to develop dementia due to Alzheimer’s disease.

http://www.alz.org/documents_custom/Alz_Diag_Criteria_FAQ.pdf
**Mild Cognitive Impairment**

Prevalence is about 12-18% of population

Patients with MCI will convert from MCI to AD or other causes of dementia at a rate of about 5-16% per year as compared with 1-2% of the general population.

**MCI--New Criteria**

Core clinical criteria:
1. Concern regarding a change in cognition
2. Impairment in one or more cognitive domains
3. Preservation of independence in functional abilities
4. Not demented

Research criteria:

<table>
<thead>
<tr>
<th>MCI criteria incorporating biomarkers</th>
<th>Biomarker probability of AD etiology</th>
<th>Aβ (PET or CSF)</th>
<th>Neuronal injury (tau, FDG, sMRI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCI-core clinical criteria</td>
<td>Uninformative</td>
<td>Conflicting/indeterminant/untested</td>
<td>Conflicting/indeterminant/untested</td>
</tr>
<tr>
<td>MCI due to AD—intermediate likelihood</td>
<td>Intermediate</td>
<td>Positive</td>
<td>Untested</td>
</tr>
<tr>
<td>MCI due to AD—high likelihood</td>
<td>Highest</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>MCI—unlikely due to AD</td>
<td>Lowest</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>

Albert, et. al. Alzheimer's & Dementia. 2011
New Criteria for Alzheimer’s Disease

• Dementia due to Alzheimer’s disease – Memory, thinking and behavioral symptoms that impair a person’s ability to function in daily life.

http://www.alz.org/documents_custom/Alz_Diag_Criteria_FAQ.pdf

These New Criteria for Alzheimer’s Disease

☐ Will assist with:
  – Improving current diagnosis
  – Bringing the field closer to earlier detection and treatment
  – Leading to effective disease-modifying therapies

http://www.alz.org/news_and_events_diagnostic_criteria.asp
Early Recognition

• Improve the detection of Alzheimer's disease and related dementias in their early stages in persons exhibiting certain signs and behaviors.
• Educate health professionals, patients, and their families about symptoms that suggest the need for an initial assessment for a dementing disorder.
• Identify areas for further research on early recognition of dementia.

Early Recognition

• No current treatments that prevent the disease.
• Current treatments may “slow the progression”.
• Stigma issues?
• Some or many individuals don’t want to acknowledge that they may have the disease.
  – Since there is no treatment, it is understandable some individuals don’t want to acknowledge this.
Early Recognition

• Assist individuals and families in accessing knowledge, support and clinical trial information.
  – Support from professionals for knowledge and clinical strategies.
  – Support groups composed of others with early Alzheimer’s diagnosis.
  – Support groups for family members and other caregivers.

Alzheimer’s Disease and Cerebrovascular Disease

• Using current DSM-IV-TR criteria, cannot diagnose dementia due to Alzheimer’s in the presence of significant cerebrovascular disease
• Yet mixed dementia is more common than pure Alzheimer’s disease (in majority of people with AD, their brains have vascular microinfarcts, white matter lesions, or vessel wall alterations).
• Accumulating epidemiological, pathological, and imaging evidence have suggested a role for cerebrovascular disease in onset and progression of Alzheimer’s disease.
Alzheimer’s Disease and Cerebrovascular Disease (cont.)

- Vascular risk factors have been linked to risk for Alzheimer’s disease in many epidemiological studies:
  - High blood pressure and/or high cholesterol
  - Obesity
  - Elevated homocysteine
  - Atherosclerosis
  - Carotid stenosis
  - Atrial fibrillation
  - Diabetes
  - Coronary disease

Two Theories of Alzheimer’s Disease

**Amyloid Hypothesis**
- Abnormal amyloid protein precursor clevage ↓
- Aβ ↓
- Plaques/oligomers ↓
- Neurodegeneration ↓
- Alzheimer’s disease

**Vascular Hypothesis**
- Advanced aging and vascular risk factor ↓
- Brain hypoperfusion ↓
- Neuroglial energy crisis ↓
- Mild cognitive impairment ↓
- Neurodegeneration ↓
- Alzheimer’s disease
Alzheimer’s Disease and Cerebrovascular Disease (cont.)

- After testing hundreds of candidate treatments focusing mainly on the amyloid theory, researchers have found only several modestly effective symptomatic therapies but no treatment to slow Alzheimer’s disease progression or delay its onset.
- Failure of several leading anti-amyloid therapies (many of which made patients worse)

Alzheimer’s Disease and Cerebrovascular Disease (cont.)

- There are disagreements as to how to “integrate” the vascular risks into the “amyloid cascade”.
- Late-onset Alzheimer’s disease likely has a “multi-factorial” cause.
- Given the number of people worldwide who are affected by vascular risks, we must work on an integration of these factors.
- Could lead to early intervention efforts via education, lifestyle modification, and clinical trials of novel protective strategies.
Alzheimer’s Disease and Diabetes

- Individual with diabetes are twice as likely to develop Alzheimer’s disease.
  - Even individuals with impaired glucose tolerance (a level of poor glucose control that precedes diabetes) were 35% more likely to develop some type of dementia.
  - Theories
    - Vascular disease $\rightarrow$ Vascular dementia; diabetes can accelerate the disease.
    - Diabetes may play a role in that poor blood sugar control makes it harder for the body to clear away amyloid.
    - Or... high levels of glucose may create a toxicity-related or oxidative stress where harmful free radical molecules build up and damage tissue in the brain.

Alzheimer’s Disease, Vascular Disease and Diabetes

Treating diabetes and vascular risk factors such as hypertension and high cholesterol may help prevent dementia.
Vascular or Multi-Infarct Dementia

- The second most common type of dementia
- Affects more men than women, ages 55 – 75.
- Caused by a series of small strokes
- Different pattern than Alzheimer’s Disease (but can also be present in patients with AD).

### Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>Definition of dementia</th>
<th>Evidence of CVD</th>
<th>Causal relationship?</th>
<th>Sensitivity/ Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSM-IV (1994)</td>
<td>Decline in memory and one other cognitive domain that interferes with social or occupational function</td>
<td>Focal neurologic deficits or laboratory evidence of CVD</td>
<td>Clinician judgment that CVD is etiologically related cognitive impairment</td>
<td>0.50/0.84</td>
</tr>
<tr>
<td>ADDTC (Chui, 1992)</td>
<td>Probable Decline in intellectual function that interferes with customary affairs of life</td>
<td>Two or more strokes by history/examination or one by neuroimaging outside cerebellum OR one infarct temporally related to VCI</td>
<td></td>
<td>0.25/0.91</td>
</tr>
<tr>
<td></td>
<td>Possible</td>
<td>History of or evidence of one stroke or Binswanger’s syndrome</td>
<td>Not required</td>
<td>0.70/0.78</td>
</tr>
<tr>
<td>NINDS-AIREN (Roman, 1993)</td>
<td>Probable Decline in memory and two other cognitive domains severe enough to interfere with ADL’s</td>
<td>Focal signs on examination and imaging findings of CVD</td>
<td>Onset of dementia within 3 months of stroke or stepwise decline</td>
<td>0.20/0.93</td>
</tr>
<tr>
<td></td>
<td>Possible</td>
<td>Imaging findings or temporal relationship or stepwise decline</td>
<td></td>
<td>0.55/0.84</td>
</tr>
</tbody>
</table>
Vascular or Multi-infarct Dementia

• Risk factors:
  – Diabetes
  – Hardening of the arteries (atherosclerosis)
  – High blood pressure (hypertension)
  – Smoking
  – High Cholesterol
  – Heavy alcohol use
  – Stroke

Frontotemporal Dementia

• Uncommon form of dementia.
• Second or third most common cause of dementia in individuals under age 65.
• Damage to the frontal lobe and/or the temporal parts of the brain.
• A more rapid onset than in Alzheimer’s disease.
• May experience language difficulties, such as mutism, difficulty with word-finding, or aphasias.
Frontotemporal Dementia

• Common cause of dementia before the age of 65.
• Has presented as early as age 22.

Estimated primary cause of early versus late onset dementia

Frontotemporal Dementia

• Symptoms are more changes in personality and behavior:
  – Lack insight, and loss of ability to empathize with others, making them appear selfish and unfeeling
  – Behave inappropriately
  – Lose their inhibitions
  – Be easily distracted
  – Develop compulsive rituals
  – Become aggressive
Pick’s Disease

• Variant of Frontotemporal dementia
• Brain cells get larger and contain “Pick bodies”.
• Affects more men than women
• Onset of 40 – 60 years of age
• Produces changes in personality, judgment, language and memory
• Course of the disease is 6 – 12 years
• Cholinesterase inhibitors do NOT work

Dementia with Lewy Bodies

• One of the most common types of dementias
• Lewy body dementia exists either in pure form, or in conjunction with other brain changes, including those typically seen in Alzheimer's disease and Parkinson's disease.
• Presents as “cognitive decline” plus three defining characteristics
Dementia with Lewy Bodies

• Defining features:
  – “Fluctuations” in alertness and attention, such as frequent drowsiness, lethargy, lengthy periods of time spent staring into space, or disorganized speech;
  – Recurrent visual hallucinations,
  – Parkinsonian motor symptoms, such as rigidity and the loss of spontaneous movement.

Creutzfeldt-Jakob Disease

• Rare, fatal, rapid brain disease
• Death within 6 – 12 months of the diagnosis
• Thought to be caused by prions (protein in misfolded form) that change proteins into infectious proteins that cause brain death
Creutzfeldt-Jakob Disease

- Two types
  - Classic:
    - Sporadic – Most common (ages 45-75); Cause unknown
    - Familial (genetic) – abnormal gene
    - Iatrogenic – Less than 1% - acquired during medical procedure
  - Variant – Rare - Younger (ages 28–29) – eating meat from cows that have been contaminated

What have we learned?

- Diagnosis of AD is still clinical, but there are a number of tests that may be able to help confirm a diagnosis.
- Many of the steps in the pathologic cascade of AD have been identified and involve the production of Aβ, inflammation, excitotoxicity, synaptic degradation and cell death.
- Vascular risk factors have been linked to risk for AD and cerebrovascular events (even micro-) may be involved in some cases of AD.
- Protein deposition is a common feature in neurodegenerative disease and is seen in AD, DLB and FTD.
Current Treatment of Alzheimer’s disease

Medication Interventions for Dementia

• Cholinesterase Inhibitors
• NMDA Receptor Antagonist
• Antidepressant Medication
• Antianxiety Medication
• Antipsychotic Medication
• Mood Stabilizers
Cholinesterase Inhibitors

• Proposed to Increase Acetylcholine
• Target
  – Cognitive Symptoms of Alzheimer’s Disease
  – May Help Behavioral & Psych Symptoms of Dementia (BPSD)
    • Apathy
    • Delusions and Hallucinations

Cholinesterase Inhibitors

Benefits on Cognition:
  – Many trials have shown statistically significant improvement over placebo on measures of cognition and measures of overall improvement.
Secondary endpoints have shown:
  – Improved ADL’s in mild to moderate AD, unclear in severe AD
  – Fewer neuropsychiatric symptoms in mild to moderate AD (but not agitation)
  – Delayed placement to nursing homes
  – Less burden to caregivers
Cholinesterase Inhibitors

• Aricept - donepezil
  • Selective, reversible acetylcholinesterase inhibitor
• Exelon - rivastigmine
  • Dual inhibitor of both acetylcholinesterase and butyrylcholinesterase
• Razadyne - galantamine
  • Both an acetylcholinesterase inhibitor and a selective booster of nicotine action

Cholinesterase Inhibitors

• Aricept - donepezil
• Starting dose: 5 mg po q HS for 4 weeks, then 10 mg po q HS
• May take with or without food
• New Aricept 23 mg dosing
Cholinesterase Inhibitors

- Aricept - donepezil
- Common side effects:
  - Nausea and anorexia
  - Diarrhea
  - Insomnia
  - Fatigue
- May help cognition, behavior, ADLs, and delay Nursing Home placement

Cholinesterase Inhibitors

- Exelon - rivastigmine
- Starting dose: 1.5 mg twice a day for two weeks, then 3 mg twice a day for two weeks, then 4.5 mg twice a day for two weeks, then 6 mg twice a day (maximum).
- Should be taken with food in the morning and the evening
Cholinesterase Inhibitors

• Exelon - rivastigmine
• Common side effects:
  – Nausea and vomiting
  – Abdominal pain
  – Loss of appetite and weight
  – Dizziness
• May help cognition, behavior and function
• Now comes in a 24-hour Patch

Cholinesterase Inhibitors

• Razadyne - galantamine
• Starting dose: 4 mg po bid for 4 weeks, then 8 mg po bid for 4 weeks (usual dose), may give up to 12 mg po bid
• Given with morning and evening meals
• New - Extended release form
Cholinesterase Inhibitors

- Razadyne - galantamine
- Common side effects:
  - Nausea and vomiting
  - Diarrhea
  - Anorexia and weight loss
- May help general function, cognition, ADLs, and behavior

NMDA Receptor Antagonist

- Namenda - Memantine
  - N-methyl-D-aspartate (NMDA) receptor antagonist that protects against glutamate-mediated neurotoxicity.
  - For moderate to severe Alzheimer’s disease
  - Slows the progression
  - Start 5 mg po q day. Titrate to 10 mg po BID.
  - Side effects: dizziness, headache, confusion, constipation, incontinence, nausea, tiredness
Memantine

• Mechanism of action: NMDA receptor antagonist. Unknown reason for benefit.
• Evidence of efficacy with or without donepezil:
  – Improvement on measures of cognition, clinician global impression and ADL’s
  – Improvement on measure of neuropsychiatric symptoms
• Metabolism partially hepatic and renal excretion
• Common side effects: nausea, dizziness, tiredness

Reisberg, et. al. NEJM, 2003
Tariot, et. al. JAMA, 2004

Antidepressant Medications
Antidepressant Medications

- **Common Uses**
  - Major Depression
  - Obsessive Compulsive Disorder
  - Panic Disorder
  - BPSD (Behavioral and Psychological Symptoms of Dementia)
    - Emotionality and Irritability
    - Agitation and Aggression
    - Depressive Syndromes
    - Sleep-Wake Cycle Disturbance

- **“OLDER” TRICYCLIC Antidepressants**
  - Elavil - amitriptyline
  - Tofranil - imipramine
  - Norpramin - desipramine
  - Sinequan - doxepin
  - Pamelor - nortriptyline
  - Others

  Therapeutic Blood Levels Available
“OLDER” TRICYCLIC Antidepressants

- **Side Effect (SE) profile**:
  - Sedation
  - Anticholinergic
  - Dry mouth, constipation
  - Blurred vision, urinary problems
  - Orthostatic BP changes
  - Arrhythmias
  - Sexual dysfunction

Selective Serotonin Reuptake Inhibitors (SSRIs)

- Prozac - fluoxetine
- Zoloft - sertraline
- Paxil - paroxetine
- Celexa - citalopram
- Luvox - fluvoxamine
- Lexapro - escitalopram
Selective Serotonin Reuptake Inhibitors (SSRIs)

- **SE profile:**
  - GI Symptoms – Diarrhea, nausea, dry mouth
  - Weight Loss
  - Akathisia / Restlessness/ Nervousness
  - Headache
  - Insomnia
  - Hyponatremia (electrolyte disturbance with low sodium ion concentration)
  - Sexual Dysfunction

Dual Action Antidepressants

- **Effexor – venlafaxine**
  - Serotonin and noradrenaline reuptake inhibitor
  - Used to treat depression and anxiety disorders
  - Take with food
  - **SE profile:**
    - GI complaints
    - Sexual dysfunction
    - Insomnia
    - Dry mouth
    - Tiredness or weakness
    - Dose dependent elevation of BP
Dual Action Antidepressants

- Remeron – mirtazapine
  - Tetracyclic
  - Noradrenergic and specific sertonergic
- **SE profile:**
  - Sedation at low doses
  - Weight gain
  - Orthostatic changes
  - Dry mouth
  - Constipation
  - Anxiety
  - Confusion

Dual Action Antidepressants

- Cymbalta - duloxetine
  - Selective serotonin and norepinephrine reuptake inhibitor
  - Used to treat depression and generalize anxiety disorder
  - Also indicated for peripheral neuropathic pain and fibromyalgia
- **SE Profile:**
  - GI complaints
  - Insomnia
  - Dizziness
  - Weakness
  - Difficulty urinating
Other Antidepressants

- Wellbutrin - bupropion
  - Stimulates neurotransmission of norepinephrine and dopamine
  - Zyban – Same medication marketed to assist in smoking cessation.
    - Assists with following nicotine withdrawal symptoms: irritability, frustration, or anger; anxiety; difficulty concentrating; restlessness; and depressed mood or negative affect.
- SE Profile:
  - GI complaints
  - Agitation
  - Lowers seizure threshold
  - Sleep problems

Other Antidepressants

- Desyrel – trazodone
- SE Profile:
  - Sedation
  - Dry mouth
  - Nausea
  - Orthostatic changes
- Therapeutic Blood Levels Available
- May also be used for agitation
Serotonin Syndrome

• A rare but potentially life-threatening side effect of SSRIs
• Characterized by dangerously high levels of serotonin in the brain
• Can occur when an SSRI interacts with other Anti-depressants called monoamine oxidase inhibitors (MAOIs) or other medications such as tramadol (Ultram), migraine medications such as sumatriptan (Imitrex) and rizatriptan (Maxalt) or supplements that affect serotonin levels, such as St. John's wort

Serotonin Syndrome
REQUIRES IMMEDIATE MEDICAL ATTENTION!
Symptoms Include:

➢ Confusion
➢ Restlessness
➢ Hallucinations
➢ Extreme agitation
➢ Fluctuations in blood pressure
➢ Increased heart rate
➢ Nausea and vomiting
➢ Fever
➢ Seizures
➢ Coma
Anti-anxiety Medications

• Common Uses
  – Situational Anxiety
  – Panic Disorder
  – Insomnia
  – Behavioral and Psychological Symptoms of Dementia (BPSD)
    • Anxiety
    • Acute Agitation
    • Sleep Disturbance
Anti-anxiety Medications

• Short-acting
  – Serax - oxazepam
  – Ativan - lorazepam
• Intermediate-acting
  – Xanax - alprazolam
  – Librium - chlordiazepoxide
• Long-acting
  – Valium - diazepam
  – Tranxene - clorazepate
  – Klonopin - clonazepam

Anti-anxiety Medications
Benzodiazepines

SE Profile:
  – Drowsiness
  – Ataxia
  – Confusion
  – Slurred speech
  – Anterograde amnesia
  – Physical dependence
Anti-anxiety Medications

• BuSpar - buspirone
  • No physical dependence
  • Takes time to work

• SE profile:
  – Drowsiness
  – Light-headedness
  – Nausea

Antipsychotic Medications

• Common Uses
  – Schizophrenia
  – Delusional Disorders
  – Mood Disorders with Psychotic Features
  – Severe Personality Disorders
  – Behavioral and Psychological Symptoms of Dementia (BPSD)
    • Delusions, Hallucinations, Paranoia
    • Aggression and Violent Behavior
Antipsychotic Medications

Low Potency
• Thorazine - chlorpromazine
• Mellaril - thioridazine
  – Prolongs QT interval
  – Do not use with Prozac, Paxil or Luvox
  – Do not use!

  More anticholinergic / Less EPS

Antipsychotic Medications

Intermediate Potency

• Trilafon - perphenazine
• Loxitane - loxapine
• Moban - molindone

  Both anticholinergic and EPS
Antipsychotic Medications

High Potency

- Haldol - haloperidol
- Navane - thiothixene
- Prolixin - fluphenazine

Less anticholinergic / More EPS

Antipsychotic Medications

SE profile:
- Sedation
- Anticholinergic: dry mouth, blurred vision, constipation, urinary problems, orthostatic BP changes - especially low potency
- EPS (extrapyramidal):
  - Akathisia - motor restlessness
  - Parkinsonism - drooling, tremor, shuffling gait, rigidity
  - Tardive Dyskinesia (TD) - Involuntary movements - (Monitor with AIMS)
Atypical Antipsychotics

- Risperdal – risperidone
- Invega – paliperidone - metabolite of Risperdal

SE profile:
- Insomnia
- Agitation
- EPS (Extrapyramidal)
- Orthostatic hypotension
- Possibly no tardive dyskinesia (TD)

Atypical Antipsychotics

- Zyprexa – olanzapine

SE Profile:
- Orthostatics
- Mild anticholinergic
- Mild EPS
- Possibly no tardive dyskinesia
Atypical Antipsychotics

• Seroquel – quetiapine

SE Profile:
- Orthostatics
- Sedation
- GI upset
- Headache
- Low anticholinergic
- Low EPS
- Possible tardive dyskinesia

Atypical Antipsychotics

• Geodon – ziprasidone

SE Profile
- QT prolongation and risk of sudden death
- Orthostatic hypotension
- Somnolence
- EPS (Extrapyramidal)
- Rash
Atypical Antipsychotics

- Abilify – aripiprazole
  - Dopamine serotonin system stabilizer
  - Agonist and antagonist activity

SE Profile
- Headache, nausea, insomnia, somnolence, akathisia
- Low EPS
- Minimal weight gain
- Minimal glucose dysregulation

Antipsychotics and Dementia

- Black box warning: Elderly patients with dementia-related psychosis treated with atypical Antipsychotic are at an increased risk of death compared to placebo...over the course of a typical 10 week controlled trial, the rate of death in drug-treated patients was 4.5%, compared to a rate of about 2.5% in the placebo group...most of the deaths appeared to be either cardiovascular (heart failure; sudden death) or infectious (e.g. pneumonia) in nature.
Other Treatments

• Medical Food - Medical foods are defined in the 1988 amendment to the Orphan Drug Act as “a food which is formulated to be consumed or administered enterally (orally) under the supervision of a physician, and which is intended for specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.”


Other Treatments

• Medical foods are distinguished from supplements in that they address a specific identified metabolic condition, and they are typically available only by prescription. Supplements are part of one’s normal diet but may be taken in higher quantities.

• Axona is a medical food indicated for clinical dietary management of the metabolic processes associated with mild-to-moderate Alzheimer’s disease.
Other Treatments

• Axona is metabolized to BHB (b-hydroxybutyrate – keytone body) in the liver. BHB serves as an alternate energy for neuronal metabolism. BHB is a common metabolic substrate that is normally produced by the body for neurons in starvation states where glucose is less available.
  • One of the hallmarks of AD is hypo-metabolism
  • Hypo-metabolism precedes the occurrence of cognitive impairment and can be demonstrated in at-risk individuals prior to the onset of cognitive impairment.
  • Efficacy is only indicated in those individuals who do not carry the primary genetic risk factor of AD – APOE 4
  • Patients showed significant improvement in the Alzheimer’s Disease Assessment Scale—cognitive subscale (ADAS-cog) when Axona was administered for a minimum of 90 days.

Other Treatments

• In the 90-day study, 24.4% of patients taking Axona experienced diarrhea compared with 13.6% in the placebo group. Flatulence was noted in 17.4% of Axona-managed patients compared with 7.6% of those receiving placebo; dyspepsia was present in 9.3% of Axona-managed patients and 4.5% of those receiving placebo. Gastrointestinal side effects are reportedly reduced by administration of Axona with a meal or mixing it with a drink.
  • Axona contains caseinate (milk-derived protein), whey (milk), and lecithin (soy) and should not be used in patients allergic to these ingredients.
  • Axona induces a ketotic state and should be used with caution in patients at risk for ketoacidosis (eg, alcoholics or poorly controlled diabetics).
Other Treatments

• **Citocoline**: a brain chemical that occurs naturally in the brain, involved in the biosynthesis of brain phospholipids and acetylcholine

• Marketed as useful for AD and other types of dementia, head trauma, cerebrovascular disease, age-related memory loss, Parkinson’s diseases, ADHD, and glaucoma

• Prescription drug used in Europe and Japan for “thinking problems related to circulation problems in the brain.”

• In US, marketed as a dietary supplement

Other Treatments

• **Citocoline**: How does it work?

• Seems to increase a brain chemical called phosphatidylcholine, which is important for brain function.

• But research published in 2012 JAMA article found no improvement in functional and cognitive status in patients with traumatic brain injury in double-blind randomized clinical trial of 1213 patients.

• 1999 randomized trial found taking citicoline was ineffective in improving outcomes of stroke patients
Other Treatments

• **Citocoline**: Not approved as medication; marketed as supplement; be skeptical, since good research studies have not found it to be effective for specific brain disorders; good randomized double blind clinical trials need to be done with AD patients before this is recommended.

Future Treatments
Future Treatments

Reduce production of Amyloid β:
- β/γ-secretase inhibitors
- Selective anti-amyloid β_{1-42} agents
- Anti-amyloid β aggregation agents

Increase clearance of Amyloid β:
- Active and passive anti-amyloid β AB immunization
- IVIg
- Anti-inflammation agents

Other neurotransmitter modulation
- Tau protein modulation
- Link to diabetes (inhaled insulin)
- Vaccine
- Agents that can cross blood brain barrier and block action of CD33

2012 New Investigator Research Grant

Beta-amyloid (also known as Abeta) is a protein fragment that aggregates into toxic clusters as well as amyloid plaques, one of the hallmarks of Alzheimer's disease in the brain. Most studies of beta-amyloid have focused on two forms of the molecule, which have 40 or 42 chemical units (amino acids). However, recent studies have identified shorter versions of beta-amyloid that are highly toxic to nerve cells. One of these shorter versions is also modified by the addition of a pyroglutamate chemical group.
2012 New Investigator Research Grant (Cont.)

Vitaly Vasilevko, Ph.D., and colleagues have performed extensive studies of pyroglutamate-modified beta-amyloid and shown that it is highly toxic and forms aggregates in the brain. Furthermore, its levels in different parts of the brain correspond to levels of neurodegeneration. **Dr. Vasilevko's team has proposed to develop a vaccine that directs the immune system to recognize and remove pyroglutamate-modified beta-amyloid from the brain.** The researchers will test this vaccine in mice that have been genetically modified to have Alzheimer's-like brain degeneration. This study represents a new approach to the development of vaccines against beta-amyloid, and may be the first step toward the development of a vaccine that can be tested in humans.

Future Treatments

- **Einar M. Sigurdsson, Ph.D., and colleagues have been working to develop a vaccine treatment that targets another hallmark of Alzheimer's disease, the neurofibrillary tangle.** This structure is composed mainly of abnormally altered tau protein. In preliminary studies with mice engineered to develop abnormal tau, Dr. Sigurdsson's team has developed antibodies that bind to such tau and slow the protein's accumulation in the brain.
- For this proposed grant, the researchers will conduct further studies with mice to refine their antibody treatments. At the same time, they will also test the antibodies' effectiveness on cultured cells. The researchers hope to acquire a better understanding of how the antibodies reduce abnormal tau levels. They also hope to determine which vaccines have the fewest side effects.
Future Treatments (Cont.)

• In a follow-up investigation, Dr. Sigurdsson's team will study the nerve cells of mice that receive the most effective tau vaccine treatments. The researchers hope to learn how mouse nerve cells are affected by both tau accumulation and the removal of accumulated tau. For this purpose, they will use a newly developed imaging technique called manganese-enhanced magnetic resonance imaging (MEMRI).

• Results of this study could lead to more effective and safer vaccine trials. Dr. Sigurdsson's team believes that an optimal vaccination treatment would combine vaccines for tau with improved vaccines for beta-amyloid.

Behavioral Interventions
Behavioral and Psychological Symptoms of Dementia (BPSD)

• Symptoms of disturbed perception, thought content, mood or behavior that frequently occur in persons with Dementia
• BPSD are treatable!
• BPSD can result in:
  • Suffering
  • Premature Institutionalization
  • Increased Costs of Care
  • Loss of quality of life for the person and caregivers

Finkel et al 1996

Behavioral and Psychological Symptoms of Dementia

• Hallucinations (Usually visual)
• Delusions
  • People are stealing things
  • Abandonment
  • This is not my house
  • You are not my spouse
  • Infidelity
Behavioral and Psychological Symptoms of Dementia

• Misidentifications
  • People are in the house
  • People are not who they are
  • Talk to self in the mirror as if another person
  • Events on television

Behavioral and Psychological Symptoms of Dementia

• Depressed Mood
• Anxiety
• Apathy
  • Decreased social interaction
  • Decreased facial expression
  • Decreased initiative
  • Decreased emotional responsiveness
Behavioral and Psychological Symptoms of Dementia

• Wandering
  • Checking
  • Attempts to leave
  • Aimless walking
  • Night-time walking
  • Trailing
  • Excessive activity

Behavioral and Psychological Symptoms of Dementia

• Verbal Agitation
  • Negativism
  • Constant requests for attention
  • Verbal bossiness
  • Complaining
  • Relevant interruptions
  • Irrelevant interruptions
  • Repetitive sentences
Behavioral and Psychological Symptoms of Dementia

• Verbal Aggression
  • Screaming
  • Cursing
  • Temper Outbursts

• Physical Agitation
  • General Restlessness
  • Repetitive Mannerisms
  • Pacing
  • Trying to Get to a Different Place
  • Handling Things Inappropriately
  • Hiding Things
  • Inappropriate Dressing or Undressing
Behavioral and Psychological Symptoms of Dementia

• Physical Aggression
  • Hitting
  • Pushing
  • Scratching
  • Grabbing Things
  • Grabbing People
  • Kicking and Biting

Behavioral and Psychological Symptoms of Dementia

• Disinhibition
  • Poor Insight and Judgment
  • Emotionally Labile
  • Euphoria
  • Impulsive
  • Intrusiveness
  • Sexual Disinhibition
Dementia Assaulrs the Person’s Identity and Self-Esteem

Behavioral Management is the key in taking care of anyone with a Dementia!
Causes of Behavioral Problems in Older Adults

• “Mental Health” Issues
  ✓ Behavioral and psychological symptoms of dementia
  ✓ Delirium
  ✓ Depressive illness
  ✓ Anxiety
  ✓ Regressive symptoms of psychiatric illness

• Personality “issues”

• Institutional causes of problem behaviors

Causes of Behavioral Problems in Older Adults

Psychiatric symptoms are common among individuals who live in nursing homes and other “care facilities”, with prevalence rates ranging from 51 percent to 94 percent.
Communication
10 Keys of Communication

• Set a positive mood for interaction
• Get the person’s attention
• State your message clearly
• Ask simple, answerable questions
• Listen with your ears, eyes and heart

Fact Sheet: Caregiver’s Guide to Understanding Dementia Behaviors, Family Caregiver Alliance

Communication (Cont.)
10 Keys of Communication

• Break down activities into a series of steps
• When the going gets tough, distract and redirect
• Respond with affection and reassurance
• Remember the good old days
• Maintain your sense of humor

Fact Sheet: Caregiver’s Guide to Understanding Dementia Behaviors, Family Caregiver Alliance
Handling Troubling Behaviors

• Check with the doctor first!
• We cannot change the person
  – Try to accommodate the behavior, not control the behavior.
  – Remember that we can change our behavior or the physical environment.

Fact Sheet: Caregiver’s Guide to Understanding Dementia Behaviors, Family Caregiver Alliance

Handling Troubling Behaviors (Cont.)

• Behavior has purpose.
• Behavior is triggered.
• What works today may not work tomorrow.
• Get support from others!

Fact Sheet: Caregiver’s Guide to Understanding Dementia Behaviors, Family Caregiver Alliance
### Three Steps in Identifying Causes of Behaviors

1. Identify and examine the behavior:
   - Could it be related to medication or illness?
   - What was the behavior? Could it be considered harmful?
   - What happened before the behavior?
   - What was the trigger?
   - What happened immediately after the behavior occurred? How did individuals react?

   *Alzheimer’s Association* – “How to respond when dementia causes unpredictable behaviors.”

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### Three Steps in Identifying Causes of Behaviors (Cont.)

2. Explore potential solutions:
   - What are the individual’s needs? Are they being met?
   - Can adapting the surroundings comfort the person?
   - How can you change your reaction or your approach to the behavior? Are you responding in a calm and supportive way?

   *Alzheimer’s Association* – “How to respond when dementia causes unpredictable behaviors.”
Three Steps in Identifying Causes of Behaviors (Cont.)

3. Explore different responses:
   ✓ Did your new response help?
   ✓ Do you need to re-evaluate for other potential causes and solutions?
   ✓ What could you do differently?

   Alzheimer’s Association – “How to respond when dementia causes unpredictable behaviors.”

Remember Behaviors may be related to:

• Physical discomfort – illness or medication
• Overstimulation – loud noises or a “busy” environment
• Unfamiliar surroundings – new places or the inability to recognize home
• Complicated tasks – difficulty with activities or chores or even simple requests
• Frustrating interactions – inability to communicate effectively

   Alzheimer’s Association – “How to respond when dementia causes unpredictable behaviors.”
Delirium

- Delirium is a sudden, severe confusional state with rapid changes in brain function that occur with physical or mental illness
- Fluctuating level of consciousness
- Reversible/ treatable

Delirium

• Symptoms:
  ✓ Changes in alertness
  ✓ Changes in feeling (sensation) and perception
  ✓ Changes in level of consciousness or awareness
  ✓ Changes in movement
  ✓ Changes in sleep patterns, drowsiness
  ✓ Confusion (disorientation)
Delirium

• Symptoms:
  ✓ Decrease in short-term memory and recall
  ✓ Disrupted or wandering attention
  ✓ Disorganized thinking
  ✓ Emotional or personality changes
  ✓ Incontinence
  ✓ Psychomotor restlessness

Delirium

• Causes:
  ✓ Medications
  ✓ Infections
  ✓ Metabolic/ endocrine
  ✓ Vitamin Deficiency
  ✓ Anesthesia
  ✓ Trauma
  ✓ Alcohol or sedative drug withdrawal
Risk Factors for Delirium

- Pre-existing cognitive problems
- Advanced age
- Hospitalization
- Multiple medical conditions
- Depression
- Use of multiple medications, especially those with anticholinergic properties
- General anesthesia
- Visual problems
- Male gender
- Abnormal serum sodium

Behaviors are a form of communication!

Understanding, flexibility, and creativity are the keys to effective behavior management!
The Case for Individualized Care

Non-drug treatments

Collaborative care
• Can improve quality of care and improve behavioral and psychological symptoms of patients and caregivers.\textsuperscript{1}

Exercise plus caregiver training
• Can improve physical health and depression in patients with AD.\textsuperscript{2}

Cognitive training and memory rehabilitation
• Can improve cognition function\textsuperscript{4}

Enhanced counseling and support for caregivers
• Can reduce nursing home placement\textsuperscript{5}

Prevention Strategies; or How can we Maintain our Brain?

Studies on Prevention Strategies

• Studies have not demonstrated that health or lifestyle factors can prevent or slow Alzheimer’s disease or cognitive declines. (National Institute on Aging, September 2012)

• Clinical trial results do not support the use of a medication or dietary supplement to prevent these conditions. (National Institute on Aging, September 2012)
Studies on Prevention Strategies

• Several clinical and observational studies have shown that associated factors such as physical activity, blood pressure and diabetes control change risk. (National Institute on Aging)
  ➢ Exercise – epidemiological studies and some intervention studies suggest that physical exercise may play a role in reducing risk of AD and age-related cognitive decline.
    • Increases the number of small blood vessels and number of connections between nerve cells in mice.
    • Exercise raises the level of a nerve growth factor (a protein key to brain health) in the area of the brain that is important to memory and learning.
      (National Institute on Aging, September 2012)

Studies on Prevention Strategies

➢ Diet – A number of studies suggest that eating certain foods may help keep the brain healthy, while others may be detrimental to cognitive health.
  • A diet that includes lots of fruits, vegetables and whole grains and one that is low in fat and added sugar can reduce the risk of many chronic diseases.
  • Studies have found a diet rich in green leafy vegetables and cruciferous vegetable like broccoli and cabbage is associated with a reduced rate of cognitive decline.
  • One study documented that individuals who ate a “Mediterranean Diet” had a 28% lower risk of developing MCI and 48% lower risk of progressing to AD.
    (National Institute on Aging, September 2012)
Studies on Prevention Strategies

- Chronic Diseases – Age related diseases such as vascular disease, high blood pressure, heart disease and type 2 diabetes may increase the risk of Alzheimer’s disease.
  - Many studies are looking at whether preventing or controlling these conditions by medications, diet or exercise can reduce the risk.

- An active brain!
  - Staying cognitively active throughout life through social engagement or intellectual stimulation is associated with lower rates of Alzheimer’s disease.
    (National Institute on Aging, September 2012)

Keep Medically Healthy

Stop smoking
- Ongoing smoking is related to a faster decline of thinking ability
- Current smokers have an increased risk of dementia
- Not as clear about former smokers

Treat high blood pressure
- People who have high blood pressure are more likely to develop mild cognitive impairment; midlife high blood pressure is related to dementia; certain high blood pressure drugs may help reduce risk of cognitive decline.

Lose weight
- Being overweight in mid-life is associated with worse cognition and an increased risk of dementia in later life.
- In particular, truncal obesity increases risk of dementia
- But, an unintended late life weight loss is a bad sign
Diet

Following a Mediterranean diet is related to slower loss of thinking ability and may lower the risk of developing dementia.

• Keep unhealthy fats to a minimum (no more than 20 percent of calories); eat lots of fresh fruits and vegetables, a minimum of red meat, and plenty of fish.

Increased fish consumption (one or more meal per week) is associated with a 10-13% reduced rate of cognitive decline.

Eating vegetables, especially leafy green vegetables is associated with slower cognitive decline. Fruit may not be protective.

• A study of 13,388 nurses found that women who ate more cruciferous and leafy vegetables in their 60's had a lower rate of cognitive decline. The more of these vegetables they ate, the better.
What about fats?
Increased intake of polyunsaturated & monounsaturated fatty acids decreases risk of cognitive decline, but may not protect against dementia.

How might unsaturated fatty acids work?
– Omega-3 fatty acids, specifically “DHA”, are an essential component of neural cell membranes that help to transmit information into and out of brain cells.
– Or, fatty acids may work by counteracting free radicals that cause oxidative damage to brain cells
– Or, some research suggests they may help improve the efficiency of nerve signal transmission at synapses.

In particular, some fish are high in omega-3 fatty acids: Salmon, mackerel, tuna, sardines and herring.

Which fish are safe?

<table>
<thead>
<tr>
<th>WILD</th>
<th>FARMED</th>
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<tbody>
<tr>
<td>ANCHOVIES</td>
<td>CARP</td>
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<tr>
<td>ARCTIC CHAR, color added</td>
<td>CATFISH (domestic)</td>
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<tr>
<td>ATLANTIC BUTTERFISH</td>
<td>STRIPED BASS (rockfish)</td>
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<tr>
<td>BLACK COD (Sable, Butterfish on West Coast)</td>
<td>TILAPIA</td>
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<tr>
<td>BLACK SEA BASS</td>
<td>TROUT (rainbow and steelhead)</td>
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<tr>
<td>HADDOCK</td>
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<td>HAKE (white, silver and red-Chilean, Cape and Argentine)</td>
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<tr>
<td>HALIBUT (Pacific only)</td>
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<td>HERRING</td>
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<td>MACKEREL (Atlantic or Boston only)</td>
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<tr>
<td>MAHI-MAHI</td>
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<tr>
<td>PACIFIC COD</td>
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<tr>
<td>PACIFIC SAND DAB (yellowtail flounder)</td>
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<tr>
<td>PACIFIC WHITING</td>
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<tr>
<td>PLAICE</td>
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<td>PORGIES</td>
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<tr>
<td>SALMON (Pacific)</td>
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<td>SARDINES</td>
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<td>SHAD</td>
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<td>SMELT</td>
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<tr>
<td>SOLE (gray, petrale, rex, yellowfin)</td>
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<tr>
<td>WHITEFISH</td>
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</tbody>
</table>
## Supplements

**Vitamin E:**
- Amount of dietary intake has been associated with slower cognitive decline.
- It is not clear if there is any benefit from supplement forms of Vitamin E and high doses have been related to increased risk of death and heart attack.

**Folate:**
- In America, no benefit to supplementation (foods have been fortified with Folate since 1996).
- In areas where it is not fortified, there is a benefit to Folate in reducing cognitive decline.

## Supplements

**Caffeine:** 3 or more cups a day may slow cognitive decline in women (no evidence in men).

**Fish oil** supplements may not be protective against cognitive decline.

**Ginkgo biloba** likely does not slow cognitive decline or prevent dementia.

**Low vitamin D** levels are associated with more cognitive decline.
**Foods high in Vitamin E**

- Wheat germ oil
- Almonds
- Sunflower seeds
- Safflower oil
- Peanuts
- Corn oil
- Spinach
- Broccoli
- Soybean oil
- Kiwi
- Mango
- Spinach

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**Alcohol**

Moderate use of alcohol (any type) is associated with a decreased rate of cognitive decline.

But... Alcohol can kill brain cells, and the more you drink the more brain cells are destroyed.

Limit: Two drinks per day for a man or one drink for a woman.
Can drugs prevent dementia?

**Aspirin or other NSAIDs (ibuprofen, naproxen):**
- These do not prevent cognitive decline or dementia when started after age of 65
- Due to side effects, not recommended presently
- Conflicting studies of people who started using these drugs at a younger age

**Hormone replacement therapy:**
- No. This may worsen cognition and increase risk of dementia.

**“Statins” (cholesterol medication):**
- Not clear because of conflicting evidence. Several trials are ongoing.
- One recent trial did not show that statin medications protect against AD or decline in cognition

Social Engagement

- Greater social networks and social engagement decrease cognitive decline.

- Many, but not all studies show social interaction is associated with less cognitive decline.
  - A large study reported in the *New England Journal of Medicine* found that people who engaged in leisure activities such as learning to play a musical instrument or dancing were less likely to develop dementia.

- A feeling of loneliness is associated with an increased risk for Alzheimer’s disease.
Ideas for Staying Socially Connected

• Volunteer at a charity, school, museum or organization
• Join a book club, bowling league, or any group dedicated to being actively engaged
• Get a pet. Animal shelters are full of potential companions looking for good homes. (They can also be great places to volunteer.)

Ideas for Staying Socially Connected (Cont.)

• Join a group in your religious organization
• Maintain a network of friends and family with whom you regularly interact
• Pursue social activities, like wine tastings, lecture programs, or traveling with friends
• Get involved in projects that require you to have regular contact with others: planning a gathering for a club, organizing a card- or game-playing night with friends
Ideas for Staying Socially Connected (Cont.)

• Get connected while you improve your health: Join a walking or biking club or your local fitness center, go out golfing, or take yoga or cooking classes
• Take an adult-education or college course

Physical Activity

Key points:
• Better physical fitness at age 11 is associated with higher IQ at age 79.
• Physical “frailty” in old age is associated with more brain changes of Alzheimer’s disease.
• Physical exercise stimulates the production of new brain cells in the hippocampus. The hippocampus is vital for learning and memory.
Exercise

Many, but not all studies show that physical exercise can slow cognitive decline.

• A study reported in the *Journal of the American Medical Association* of over 18,000 women showed that even easy walking for 1.5 hours/week was associated with better cognition and slower decline of their thinking ability.

• Another study in the same journal showed that in people who noticed memory problems, physical activity three times/week modestly improved their thinking ability.

Continued Learning

Staying mentally active
• Many studies show activities that engage your brain like reading, playing board games, playing musical instruments, and dancing were associated with less mental decline.

Purposeful training
• In depth cognitive training can have effects that last over 10 years (see ACTIVE study funded by NIH). Cognitive "training sessions" improved concentration and problem-solving skills in healthy adults ages 65 and older for over 20 years, and memory for over 10 years.

Anything that expands your knowledge may be effective; Ideas:
• Learning a new language
• Take dance lessons
• Learn a new sport
• Read a new book
• Do crossword or Sudoku puzzles
Conclusions

• Keep medically healthy.
• Follow a healthy diet.
• Remain physically and mentally active.
• Relationships are a good thing.

Multidisciplinary Needs for Individuals with Alzheimer’s disease

• Social needs for both caregivers and patients.
• Cognitive difficulties and behavioral manifestations
• Psychiatric symptoms
• Complicated medical needs
• Changing communication and ADL needs
• Normal age related changes may cause iatrogenic illness
Multidisciplinary Approach

• History and Physical
• Laboratory tests - CBC with Differential, Thyroid studies, B12, Folate, Chemistry Profile, RPR, UA, Sedimentation Rate
• Psychiatric Assessment
• Psychological testing
• Evaluation of functional abilities
• Social factors

Resources for Professionals and Family Caregivers
Assessment Scales

- Montreal Cognitive Assessment – MOCA
- St. Louis University Mental Status Examination - SLUMS
- Mini-Mental Status Examination MMSE-(Folstein - Copyrighted)
- Clock Drawing
- Blessed Dementia Scale
- BEHAVE-AD: Behavioral Pathology in Alzheimer’s Rating Scale
- Cornell Scale for Depression in Dementia

Resources

- Confusion Assessment Method – (CAM) -
- Mini-Cog -
- American Geriatric Society BEERS Criteria -
Resources

• Alzheimer’s Association – www.alz.org
• ADEAR – adead@alzheimers.org
• Family Caregiver Alliance – www.caregiver.org
• Geriatric Mental Health Foundation – www.gmhfonline.org
• Older Women’s League - http://www.owl-national.org

Resources

• National Institutes of Health Medline Plus – www.medlineplus.gov

• Centers for Disease Control and Prevention Health Aging - www.cdc.gov/aging

• Pennsylvania Department of Aging - http://www.aging.state.pa.us

• Pennsylvania Department of Long Term Living - www.dpw.state.pa.us/about/OLTL/
Alzheimer’s Association Resources


Alzheimer’s Association Hispanic Resources

- [http://www.alz.org/espanol/about/que_es_la_enfermedad_de_alzheimer.asp](http://www.alz.org/espanol/about/que_es_la_enfermedad_de_alzheimer.asp)
Alzheimer’s Association Hispanic Resources

- [http://www.alz.org/espanol/signs_and_symptoms/comportamientos.asp#intro](http://www.alz.org/espanol/signs_and_symptoms/comportamientos.asp#intro)

Early Onset Dementia and Disability Resources

- Individuals with early onset dementia can apply for Social Security Disability and Supplemental Security Income Benefits
- (Effective February 27, 2010)
Resources for Families


• Still Alice, Lisa Genova. (2009)

• Contented Dementia, Oliver James. (2008)

• Dementia Reconsidered: the Person Comes First, Thomas Kitwood. (1997)

Resources for Families

• The Caregiver Helpbook: Powerful Tools for Caregiving by Vicki Schmall, Marilyn Cleland and Marilyn Sturdevant. Published by Legacy Health System. Accompanies a class by the same name. Class information and the book are available by contacting Legacy Caregiver Services, 1015 NW 22nd Ave., Ste. N300, Portland, OR 97210, (503) 413-7706.


• Caring for Yourself While Caring for Your Aging Parents, Third Edition: How to Help, How to Survive by Claire Berman. Published by Henry Holt and Company, Inc. 115 West 18th Street, New York, NY 10011, (212) 886-9200.
PLEASE fill out the evaluation forms that were in your packet and turn them in at the back table in order to receive your certificate of attendance.

Registered Nurses will be given your PSNA Certificate awarding you 4 contact hours when you hand in your evaluation.

Other professionals who qualify for CEUs must also hand in your evaluations; your certificates will be mailed to you.

THANK YOU for your attention and quest for knowledge to help you in your work with older adults who may have cognitive issues!