2013 Webinar Series
State of the Science:
Dementia Evaluation and Management
Among Diverse Older Adults and Their Families

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Depression, Delirium and Dementia: Similarities and Differences

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2013 WEBINAR SERIES

“Depression, Delirium and Dementia: Similarities and Differences”

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About the Presenters

J. Wesson Ashford, M.D., Ph.D.

Dr. Ashford graduated from the University of California, Berkeley (1970) and completed his Medical Doctorate (1974) and Philosophy Doctorate (1984) degrees, and Psychiatry Training (1979) at UCLA. His Ph.D. dissertation was a finalist for the Lindsley Prize, for the best in Behavioral Neuroscience for the Society for Neuroscience, in 1984. He has been on the academic medical faculty of Southern Illinois University, the University of California, Davis, and the University of Kentucky, where he was vice-chair for research in psychiatry. Currently, Dr. Ashford is a Senior Research Scientist at the Stanford / VA Aging Clinical Research Center, the Director of the War Related Illness and Injury Study Center the VA Palo Alto Health Care System and Clinical Professor of Psychiatry & Behavioral Sciences at Stanford University (affiliated). He is Chair of the Memory Screening Advisory Board of the Alzheimer’s Foundation of America, a Senior Editor of the Journal of Alzheimer’s disease, and a recent member of the Scientific Advisory Board for the Northern California Chapter of the Alzheimer’s Association. He has authored or co-authored over 100 peer-reviewed publications.

Depression, Delirium, and Dementia

- Each condition has a discrete definition
- All 3 conditions have overlapping symptoms and signs
- All 3 can occur in the presence of another
- All 3 are more likely in older individuals
Dementia Definition

- **Multiple Cognitive Deficits:**
  - Memory dysfunction
    - especially new learning, a prominent early symptom
  - At least one additional cognitive deficit
    - aphasia, apraxia, agnosia, or executive dysfunction

- **Cognitive Disturbances:**
  - Sufficiently severe to cause impairment of occupational or social functioning, and
  - Must represent a decline from a previous level of functioning

Differential Diagnosis of Dementia

Top Ten

(commonly used mnemonic device: AVDEMENTIA)

1. Alzheimer Disease  (pure ~40%, + mixed~70%)
2. Vascular Disease, MID (5-20%)
3. Drugs, Depression, Delirium
4. Ethanol  (5-15%)
5. Medical / Metabolic Systems
6. Endocrine (thyroid, diabetes), Ears, Eyes, Environ.
7. Neurologic (other primary degenerations, etc.)
8. Tumor, Toxin, Trauma
9. Infection, Idiopathic, Immunologic
10. Amnesia, Autoimmune, Apnea, AAMI
Diagnostic Criteria For Dementia Of The Alzheimer Type
(DSM-IV, APA, 1994)

A. Multiple Cognitive Deficits
   1. Memory Impairment
   2. Other Cognitive Impairment
B. Deficits Impair Social/Occupational
C. Course Shows Gradual Onset And Decline
D. Deficits Are Not Due to:
   1. Other CNS Conditions
   2. Substance Induced Conditions
E. Do Not Occur Exclusively during Delirium
F. Not Due to Another Psychiatric Disorder

Delirium Definition
(often a problem in medical in-patients)

- Disturbance of consciousness
  - i.e., reduced clarity of awareness of the environment with reduced ability to focus, sustain, or shift attention
- Change in cognition (memory, orientation, language, perception)
- Development over a short period (hours to days), tends to fluctuate
- Evidence of medical etiology
Symptoms of a Major Depressive Episode

DSM-IV APA, 1994

- Depressed mood
- Markedly diminished interest or pleasure
- Significant weight change
- Changes in sleep patterns
- Psychomotor agitation or retardation
- Fatigue or energy loss
- Feelings of worthlessness, excessive or inappropriate guilt
- Diminished ability to think or concentrate
- Recurrent thoughts of death, suicidal ideation, or suicidal actions

Mental Disorders with prominent depressive symptoms

DSM-IV APA, 1994

- Major depressive disorder
- Dysthymic disorder
- Bipolar disorder (depressive episode)
- Mood disorders secondary to a general medical condition
- Mood disorders secondary to a substance (including medications)
- Adjustment disorder with depressed mood
- Bereavement
ALZHEIMER’S DISEASE – the major cause of dementia, develops over years

Estimate MMSE as a function of time

Estimated years into illness

MMSE score

AAMI / MCI      DEMENTIA

Alzheimer’s Disease versus Dementia

- 50 - 70% of dementias are AD
- Probable AD - 30% of cases, 90% correct
  - 20% have other contributing diagnoses
- Possible AD - 40% of cases, 70% correct
  - 40% have other contributing diagnoses
- Unlikely AD - 30% of cases, 30% are AD
  - 80% have other contributing diagnoses
Vascular Dementia – may start acutely
(DSM-IV - APA, 1994)

A. Multiple Cognitive Impairments
   1. Memory Impairment
   2. Other Cognitive Disturbances

B. Deficits Impair Social/Occupational

C. Focal Neurological Signs and Symptoms or Laboratory Evidence Indicating Cerebrovascular Disease Etiologically Related to the Deficits

D. Not Due to Delirium

Factors Associated with Multi-infarct Dementia

- History of stroke (especially in Nursing Home)
  - Followed by onset of dementia within 3 months
- Abrupt onset, Step-wise deterioration
- Cardiovascular disease - HTD, ASCVD, & Atrial Fib
- **Depression** (left anterior strokes), personality change
- More gait problems than in AD
- MRI evidence of T2 changes (??Binswanger’s disease)
  - Basal ganglia, putamen
  - Periventricular white matter
- SPECT / PET show focal areas of dysfunction
- Neuropsychological dysfunctions are patchy
**Post-Cardiac Surgery**

- 53% post-surgical confusion at discharge (delirium)
- 42% impaired 5 years later (dementia)
- May be related to anoxic brain injury, apnea
- May be related to narcotic/other medication
- May occur in those patients who would have developed dementia anyway (? genetic risk)
- Cardio-vascular disease and stress may start Alzheimer pathology
- Any surgery may have a similar effect related to peri-op or post-op anoxia or vascular stress

Newman et al., 2001, NEJM
Drug Interactions
Specific varieties of delirium, drug induced psychoses

• Anticholinergics: amitriptyline, atropine, benztropine, scopolamine, hyoscyamine, oxybutynin, diphenhydramine, chlorpheniramine, many anti-histaminics
  ◦ Cause delirium, may aggravate Alzheimer pathology
• GABA agonists: benzodiazepines, barbiturates, ethanol, anti-convulsants (impair memory, lead to depression)
• Beta-blockers: propranolol (problems: memory, depression)
• Dopaminergics: L-dopa, alpha-methyl-dopa
• Narcotics: may contribute to dementia (less depression)

Drug Toxicity (varieties of delirium)

• Anti-cholinergic
  ◦ Peripheral: blurred vision, dry mouth, constipation, urinary obstruction
  ◦ Central: confusion, memory encoding block
• Gaba-agonist:
  ◦ Muscle relaxant, anti-convulsant, sedative, anti-anxiety, amnesic, confusion (increased incidence of depression long-term)
• Medication induced electrolyte imbalance
  ◦ Confusion (watch for in nursing home)
Depression

- Onset: rapid (days to weeks)
- Precipitants: psycho-social (not organic)
- Duration: less than 3 months to presentation
- Mood: depressed, anxious
- Behavior: decreased activity or agitation
- Cognition: unimpaired or poor responses (classic neuropsych)
- Somatic symptoms: fatigue, lethargy, sleep, appetite disruption
- Course: rapid resolution with treatment
- But may precede cognitive impairment of Alzheimer’s disease

Delirium

- Susceptibility may be symptom of early dementia, or delirium may predispose to later dementia
- Predisposing factors - Age, infections, dementia
- Medical conditions
  - Infections:
    - G.U. - urinary
    - Respiratory (URI, pneumonia)
    - G.I.
  - Constipation
- Drug toxicity
- Fracture (especially related to hip fracture)
Ethanol
(presence may not be detectable without blood test)

- Possibly Neuroprotective
  - May not kill neurons directly (?Dietary recommendation – glass of wine?)
- Accidents, Head Injury
- Dietary Deficiency
  - Thiamine – Wernicke-Korsakoff syndrome
- Hepatic Encephalopathy
- Withdrawal Damage (seizures) Delayed Alcohol Withdrawal
  - Watch for in hospitalized patients
- Chronic Neurodegeneration
  - Cerebellum, gray matter nuclei
  - Cerebral atrophy (may be somewhat reversible)

Medical / Endocrine

- Thyroid dysfunction
  - Hypothyroidism – elevated TSH
    - Compensated hypothyroidism may have normal T4, FTI
  - Hyperthyroidism
    - Apathetic, with anorexia, fatigue, weight loss, increased T4
- Diabetes
- Hypoglycemia (loss of recent memory since episode)
- Hyperglycemia
- Hypercalcemia
- Nephropathy, Uremia
- Hepatic dysfunction (Wilson’s disease)
- Vitamin Deficiency (B12, thiamine, niacin, vitamin D)
  - Pernicious anemia – B12 deficiency, ?homocysteine elevated
Eyes, Ears, Nose, Mouth, Environment

- Must consider sensory deficits might contribute to the appearance of the patient being demented
- Visual problems are difficult to accommodate by a demented patient, ?To do cataract operation?, macular degeneration
- Central Auditory Processing Deficits (CAPD)
- Hearing problems are socially isolating
- Environmental stress factors can predispose to a variety of conditions
- Nutritional deficiencies (tea & toast syndrome)
  - Dental problems, impairment of olfaction

Neurological Conditions

- Primary Neurodegenerative Disease
  - Diffuse Lewy Body Dementia (? 7 - 50% of all dementias, may be common incidental finding)
    - Note relation to Parkinson’s disease, symptoms, increase incidence with age
    - Hallucinations, fluctuating course, neuroleptic hypersensitivity)
  - Fronto-temporal dementia (tau gene)
    - Impaired attention, behavioral dyscontrol
    - Decrease blood flow, hypometaboism on SPECT / PET
    - (Pick’s disease, Argyrophilic grain disease)

- Focal cortical atrophy
  - Primary progressive aphasia (many causes)
  - Unilateral atrophy, hypofunction on EEG, SPECT, PET

- Normal pressure hydrocephalus
  - Dementia with gait impairment, incontinence
  - Suggested on CT, MRI; need tap, ventriculography

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Other Neurologic Conditions

- Subdural hematoma
- Huntington’s disease
- Creutzfeldt-Jakob disease
  - Rapid progression
  - Characteristic EEG changes
- Multiple sclerosis
- Corticobasal degeneration
- Cerebellar degeneration
- Progressive supranuclear palsy

Tumor

- Primary brain tumor
  - Meningioma (treatable)
  - Glioma (usually not responsive to therapy)
- Metastatic brain tumor
- Remote effects of carcinoma

Toxins

- Heavy metal screen if considered
Trauma – acute (delirium) versus chronic (dementia)

Traumatic brain injury (mild, moderate, severe, complex)

- Concussion, Contusion
  - Occult head trauma if recent fall
- Subdural hematoma
- Hydrocephalus:
  - Normal pressure (late effect of bleed)
- Dementia pugilistica, chronic traumatic encephalopathy
  - Primarily a tauopathy, some relationship to APOE genotype
- Possible contributor to Alzheimer’s disease initiation and progression (? 4% of cases)
- Concern re: physical abuse by caretakers

Infectious Conditions Affecting the Brain

- HIV
- Neurosyphilis
- Viral encephalitis (herpes)
- Bacterial meningitis
- Fungal (cryptococcus)
- Prion (Creutzfeldt-Jakob disease); (mad cow disease)
AMNESIC DISORDER

A. Memory impairment
   - inability to learn new information, or
   - Inability to recall previously learned information

- Memory disturbance significantly impairs social, occupational function, deterioration from past
- Memory impairment not due to delirium, dementia
- Physiological basis or substance induced
   - Distinguish from dissociative disorders, dissociative amnesia, dissociative identity disorders
- Specify
   - Transient – less than 1 month
   - Chronic - more than 1 month

Causes of Amnesic Disorders

- Amnesia
  - Dissociative: localized, selective, generalized
  - Organic - damage to CA1 of hippocampus
    - thiamine deficiency (Wernicke-Korsakoff encephalopathy
      - (commonly due to an alcoholic binge over 1 week with no other nutrition),
    - hypoglycemia, hypoxia (including carbon-monoxide poisoning)
- Epileptic events
  - Partial complex seizures
- Specific brain diseases
  - Transient global amnesia
  - Multiple sclerosis
Age-Associated Memory Impairment vs Mild Cognitive Impairment (mild, amnestic, non-amnestic)

- Memory declines with age
- Age-related memory decline corresponds with atrophy of the hippocampus
- Older individuals remember more complex items and relationships
- Older individuals are slower to respond
- Memory problems precede development of dementia in Alzheimer’s disease

Dementia versus Depression

- Older individuals with depression are more likely to get dementia
- Alzheimer’s disease affects the brain systems which use norepinephrine and serotonin, two agents linked to depression through the medications used to treat depression
- Difficulty with remembering can be a stress leading to withdrawal and depression
- Depression is associated with increased stress (cortisol), which may accelerate the progression of the brain deterioration of Alzheimer’s disease

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Dementia versus Depression

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Dementia</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>General response</td>
<td>Lack of concern, denial, apathy</td>
<td>Amplification of and excessive preoccupations with deficits</td>
</tr>
<tr>
<td>Rate of progression</td>
<td>Mental decline happens slowly</td>
<td>Mental decline is relatively rapid</td>
</tr>
<tr>
<td>Primary cognitive change</td>
<td>Difficulty with short-term memory</td>
<td>Difficulty concentrating</td>
</tr>
<tr>
<td>Cognition</td>
<td>Confused and disoriented; becomes lost in familiar locations. Writing, speaking, and motor skills are impaired</td>
<td>Oriented to time, date, and place. Language and motor skills are slow, but normal</td>
</tr>
<tr>
<td>Awareness of condition</td>
<td>Doesn’t notice memory problems or underestimates their importance</td>
<td>Notices or worries about memory problems</td>
</tr>
</tbody>
</table>

Dementia versus Depression (continued)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Dementia</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mood</td>
<td>Normal most of the time. Unhappiness is reactive. Mood</td>
<td>Prolonged period (weeks) of pervasively ad mood, most of day, nearly every day. Little improvement with stimulation</td>
</tr>
<tr>
<td></td>
<td>brightens with stimulation</td>
<td></td>
</tr>
<tr>
<td>Interest</td>
<td>Lack of interest about things</td>
<td>Lack of interest in doing things</td>
</tr>
<tr>
<td>Initiative</td>
<td>Apathy, develops over years. No statements of sadness, tearfulness. Enjoys structured activities</td>
<td>Loss of interest, pleasure over weeks, with sad mood, guilt, hopelessness, thoughts of self-harm</td>
</tr>
<tr>
<td>Sleep</td>
<td>Gradual disruption of sleep-wake cycle (years), with night-time</td>
<td>Sleep changes, with increase of staying in bed, insomnia, early</td>
</tr>
<tr>
<td></td>
<td>wakening, daytime napping</td>
<td>morning awakening</td>
</tr>
<tr>
<td>Appetite, weight change</td>
<td>Increased appetite in spite of weight loss</td>
<td>Loss of appetite, weight likely to decrease</td>
</tr>
<tr>
<td>Psychomotor agitation</td>
<td>Gradual increase of agitation, related to confusion</td>
<td>Mentation and actions related to depression</td>
</tr>
</tbody>
</table>
On-line Assessment

- Brief Alzheimer Screen:
  - [www.medafiel.com/bas.htm](http://www.medafiel.com/bas.htm)

- Geriatric Depression Scale:
  - [www.medafiel.com/GDS15.htm](http://www.medafiel.com/GDS15.htm)

Brief Alzheimer Screen:
[www.medafiel.com/bas.htm](http://www.medafiel.com/bas.htm) (Mendiondo, Ashford, et al.)

- Repeat 3 words: "PEN", "TABLE", "ORANGE".
- What is the date today? (score for day of the month, +/-2 days is acceptable)
- NAMING - CATEGORY FLUENCY: In 30 seconds, name as many animals as you can,
- REVERSE SPELLING: "WORLD."
- RECALL:. "PEN", "TABLE", "ORANGE"
- Score is automatically calculated by computer.
Geriatric Depression Scale:

- Choose the best answer for how you have felt over the past week (Yes / No)
- 1. Are you basically satisfied with your life?
- 2. Have you dropped many of your activities and interests?
- 3. Do you feel that your life is empty?
- 4. Do you often get bored?
- 5. Are you in good spirits most of the time?
- 6. Are you afraid that something bad is going to happen to you?
- 7. Do you feel happy most of the time?
- 8. Do you often feel helpless?
- 9. Do you prefer to stay at home, rather than going out and doing new things?
- 10. Do you feel you have more problems with memory than most?
- 11. Do you think it is wonderful to be alive now
- 12. Do you feel pretty worthless the way you are now
- 13. Do you feel full of energy?
- 14. Do you feel that your situation is hopeless?
- 15. Do you think that most people are better off than you are?
- (score calculated automatically by computer)

Depression/Delirium/Dementia Management

- The first issue is to make the most accurate diagnosis possible.
- Often the diagnosis is difficult and more than one condition may be present.
- All medications and possible treatable conditions must be considered.
- If there is any consideration of depression, it should be treated, with or without dementia. First, consider an SSRI because this class of drug augments serotonin which can benefit depression and possibly dementia, particularly with agitation. Always avoid drugs with anticholinergic side-effects.
- Agitation may be associated with mood instability, and lithium in small doses may be helpful to stabilize mood, even in dementia.
Q & A – Please login to the Webex session

- The Q & A session will start at 12:45PM Pacific time on Wednesday Feb 6.
- The URL for the Q & A session is: https://stanford.webex.com/stanford/j.php?ED=17948553&UID=49446753&PW=NNDUwZGQ3MWUx&RT=Mm0 also available at http://sgec.stanford.edu/SGEC_Webinars.html
- Please use the “Chat” feature located on the right side of your screen to ask your questions. Please send your chat to everyone if possible.

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