ALZHEIMER’S DEMENTIA

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Importance of Early Diagnosis

- Family understanding: pt is ill, not willful
- Patient safety: driving walking, cooking
- Financial and legal planning while pt still competent
- Pt often needs to know dx
- R/O reversible causes of cognitive decline
- Initiate AD TX

Early Signs Suggesting a Dementing Process

- Inability to remember recent conversations: asking the same questions repeatedly
- Difficulty paying bills, balancing bank statements or completing business forms
- Difficulty handling problems at home or at work
- Using words incorrectly or trouble finding the right words to express a thought
- Becoming more irritable or more passive and withdrawn than usual

Three (3) critical questions
- Speed of onset
- Duration of symptoms
- Progression of symptoms

Clinical Features of Dementia Syndrome (1)

- Multiple cognitive deficits including memory impairment and at least one of the following
  - Aphasia
  - Apraxia
  - Agnosia
  - Disturbed executive functioning (eg planning, organizing, abstracting)

- Severe enough to impair occupational or social functioning
- Representing a decline from previously higher functioning
- Not occurring exclusively during the course of delirium

Aphasia: loss of speech
Apraxia: disorder of voluntary movement or proper use of an object

DISORDER OF VOLUNTARY MOVEMENT
Disorder of voluntary movement consisting in partial or complete inability to execute purposeful movement in ability to perform purposeful movements (in absence of sensory/motor loss)

OBJECT BLINDNESS
Inability to carry out proper use of an object although it can be named and its uses described

Examples: apraxia algera, cortical apraxia, ideational apraxia, ideokinetic apraxia, innervation apraxia, limb-kinetic apraxia, motor apraxia, ocular motor apraxia, transcortical apraxia

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Agnosia: lack of ability to recognize or perceive sensory stimuli

Examples: auditory agnosia, finger agnosia, ideational agnosia, localization agnosia, optic agnosia, position agnosia, tactile agnosia, visual-spatial agnosia

Disturbed executive functioning (e.g., planning, organizing, abstracting)

DIAGNOSING ALZHEIMER’S DISEASE

COMPONENTS OF THE DIAGNOSIS OF AD

- Two discreet disease account for the majority of individuals w progressive dementia
  - **Alzheimer's Disease**: most common form (70% of all dementias and becoming even more prominent in the oldest old)

- **Vascular dementia** (VaD): 20%
  - MID (multinfarct dementia)
  - subcortical dementia
  - Binswanger’s disease

- Valid criteria for confirming or ruling out vascular dementia
  - Step-wise course
  - History of one or more strokes
  - Early development of gait disorder
  - Asymmetric neurologic findings on P/E
  - Multiple strokes
  - Significant small vessel disease on CT scan

- Several sets of criteria developed to diagnose Alzheimer’s disease (AD)
  - Diagnostic and Statistical Manual of Mental Disorders, 4th ed (DSM IV)
    - Multiple cognitive deficits
    - Insidious onset
    - Progressive deterioration

- NINCDS/ADRDA*: more detailed - see below
  - "Definite AD" when cases verified via biopsy or autopsy
  - "Probably AD" the most stringent level of certainty w/o pathologic confirmation
  - "Possible AD" where less certainty e.g., several concurrent etiologies

NINCDS-ADRDA: National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer’s Disease and Related Disorders Association

- Careful history indicated
  - Medical/neurological
  - Medication history
  - Psychiatric history
  - Family history
  - Social/cultural history
- DSM IV Criteria
  - Characteristic history
  - Objective demonstration of cognitive impairment on mental status
  - Testing with validated tool
  - Demonstration of history of steady deterioration over time with exclusion of
    - Possible causative
    - Contributory conditions

DIAGNOSTIC CRITERIA FOR DEMENTIA OF THE ALZHEIMER'S TYPE

DSM-IV

A. The development of multiple cognitive deficits manifested by both
   1. Memory impairment (impaired ability to learn new info or recall previously learned info) and
   2. One (or more) of the following cognitive disturbances
      a. Aphasia (language disturbance)
      b. Apraxia impaired ability to carry out motor activities despite intact motor function
      c. Agnosia (failure to recognize or ID objects despite intact sensory function)
      d. Disturbance in executive functioning (planning, organizing, sequencing, abstracting)

B. The cognitive deficits each cause significant impairment in social or occupational functioning and
   represent a significant decline from previous level of functioning

C. The course is characterized by gradual onset and continuing cognitive decline

D. The cognitive deficits are not due to any of the following:
   1. Other CNS conditions that cause progressive deficits in memory and cognition (CVA, Parkinson's
disease, Huntington's disease, subdural hematoma, normal-pressure hydrocephalus, brain tumor)
   2. Systemic conditions that are known to cause dementia (hypothyroidism, B12 or folic acid deficiency,
niacin deficiency, hypercalcemia, neurosyphilis, HIV infection
   3. Substance-induced conditions

E. The deficits do not occur exclusively during the course of delirium

F. The disturbance is not better accounted for by another Axis I disorder (eg Major depressive episode,
schizophrenia, bereavement, etc.)

American Psychiatric Association Diagnostic and Statistician Manual of Mental Disorders, 4th ed. Washington, DC:
American Psychiatric Association; 1994: 126, 139, 140. 142, 143.
DIFFERENTIAL DIAGNOSIS OF DEMENTIA

- Alzheimer’s disease
- Dementia with Lewy bodies (DLB) aka diffuse Lewy body disease
- Vascular dementia: multi-infarct dementia (MID)
- Alzheimer’s disease combo with DLB or MID
- Depression aka pseudodementia
- Frontotemporal dementias
  - Pick’s disease
  - Familial progressive subcortical gliosis
  - Idiopathic
  - Progressive aphasia with dementia
  - Frontal lobe dementia with motor neuron disease
- Frontotemporal dementia and parkinsonism linked to chromosome 17

- Infectious etiologies
  - General paresis (neurosyphilis)
  - Cryptococcal meningitis
  - HIV-related dementia
  - Creutzfeldt-Jakob disease
  - Norma- pressure hydrocephalus
  - Chronic subdural hematomata
  - Partial complex status epilepticus
  - Progressive supranuclear palsy
  - Huntington’s chorea
  - Hypothyroidism
  - Vitamin B12 deficiency

DIAGNOSTIC CATEGORIZATION OF ALZHEIMER’S DISEASE

DEFINITE

- Clinical evidence of dementia
- Supportive evidence by standardized mental status assessment
- Corroboration of cognitive deficits in 2 or more areas including memory decline
- Decline of other cognitive functions (in the absence of delirium)
- Age onset between 40 and 90 years
- Absence of systemic illness or brain disease which could account for progressive deficits in memory and other cognitive functions
- Supportive but not mandatory features include the following
  - Progressive deficits in specific cognitive functions eg aphasia, apraxia, perceptual recognition
  - Impaired activities of daily living
  - Family history of Alzheimer’s-type disease esp if confirmed histologically
  - Normal or nonspecific findings on CSF exam, MRI or CT brain scan and EEG
- The presence of features consistent with the diagnosis including
  - Psychiatric and behavioral abnormalities
  - Weight loss
  - In advance stages: myoclonus, increased muscle tone, gait disturbance, seizure
- Histopathologic confirmation by autopsy or brain biopsy

PROBABLE

- The above features of a neurodegenerative disease of insidious onset
  - Gradually progressive
  - Without histologic confirmation
POSSIBLE

- Typical features of dementia but with
  - Variations in onset, presentation or clinical course
  - Coexistent systemic or brain disease that is not considered to be the primary explanation of cognitive decline
  - The presence of a single, gradual progressive cognitive deficit without an alternative identifiable explanation.

UNLIKELY

- Sudden onset
- Focal neurologic deficits
- Seizures early in the course of the disease
- Gait disturbance early in the course of the disease


IMPORTANCE OF EARLY DIAGNOSIS: IMPLICATIONS FOR PRIMARY CARE*

- AD is under-reported and often unrecognized in primary care setting
  - AD is the most common cause of dementia in older patients
  - Early symptoms of AD are often mistaken for normal aging
- Primary care providers are often first to see most early state AD
  - Patients usually do not seek medical attention for cognitive difficulties
  - Patient concerns re: cognitive decline should lead to mental status assessment
- Informant interview and office-based assessment are the two most important diagnostic tools
- Early and accurate diagnosis may provide to prepare
  - Medical care
  - Financial and legal challenges
- Depression and delirium may complicate diagnosis of delirium
- Diagnosis of AD is primarily one of inclusion not exclusion; standardized criteria exist

* Highlights from Consensus Statement (JAMA, 1997; 278: 1368-1371)
  American Association for Geriatric Psychiatry (AAGP) - American Geriatric Society (AGS)
DIAGNOSING ALZHEIMER'S DISEASE

COGNITIVE ASSESSMENT (see “Cognitive Assessment Tools”)

- Mini-Mental Status Exam
- Cognitive Clock
- Physical Self-Maintenance Scale

PHYSICAL EXAM: SPECIFIC ASPECTS OF DEMENTIA FOCUSED PHYSICAL EXAM

| Localizing and lateralizing CNS signs | - Cranial nerves, power and coordination of extremities
|                                      | - Balance and gait, presence of primitive reflexes,
|                                      |   - Increased tone, brisk reflexes
| Signs of Parkinson’s disease         | - Cogwheel rigidity
|                                      | - Bradykinesia
|                                      | - Facies, tremor
| Contributory factors                 | - Vision, hearing
|                                      | - Cardiovascular, chronic lung disease, CA
| Other aspects                        | - Personal hygiene
|                                      | - Urinary incontinence, bowel difficulties
|                                      | - ROM, signs of painfulness or dysmotility
|                                      | - Signs of abuse or neglect

DIAGNOSTICS TO R/O OTHER CAUSES OF DEMENTIA

Laboratory/Diagnostic Tests: Assessment of Dementia in the Elderly

- CBC
- ESR (screen for inflammatory processes)
- Blood chemistry panel (incl LFT and renal function)
- Serum electrolytes (incl zinc and Mg)
- Thyroid function testing
- Vit B1 and folic acid levels
- Serologic test for syphilis and HIV
- U/A
- CT: especially if history is that of less than two (2) yrs cognitive decline
- Other Tests*
  - Neuropsychologic testing esp in difficulty to evaluate patients
  - SPECT scans: shows characteristic function patterns in AD and can help differentiate Pick’s and vascular causes
  - EEG
  - LP * Useful if diagnosis is uncertain and increased certainty will influence management; Role of biological markers is unclear (ApoE, etc.)
<table>
<thead>
<tr>
<th>HISTORY WHICH EXCLUDES ALZHEIMER’S DISEASE (AD)</th>
<th>PHYSICAL FINDINGS WHICH EXCLUDE AD DISEASE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FINDING</strong></td>
<td><strong>EXPLANATION</strong></td>
</tr>
<tr>
<td>Sudden onset of dementia</td>
<td>Consider systemic disease, drug effect, CVD, infection or brain tumor</td>
</tr>
<tr>
<td>Normal memory</td>
<td>Consider psychiatric disease, CVD, or early frontal lobe dementia</td>
</tr>
<tr>
<td>Plateaus in course</td>
<td>Alzheimer’s disease (AD) is usually relentlessly progressive; consider stroke; amnestic syndrome</td>
</tr>
<tr>
<td>Depression</td>
<td>Consider pseudodementia secondary to depression</td>
</tr>
<tr>
<td>Personality change</td>
<td>If change is an early sign with memory loss consider frontal lobe dementia</td>
</tr>
<tr>
<td>Seizures</td>
<td>Uncommon in early AD but do occur in late disease; consider stroke, mass lesions</td>
</tr>
</tbody>
</table>
DISTINGUISHING DEMENTIA FROM DELIRIUM OR DEPRESSION

DEMENTIA vs DELIRIUM

**Distinction is critical** - REMEMBER DELIRIUM IS MEDICAL EMERGENCY
- Consider if history is more acute (e.g. infections, MI, pneumonia, sepsis)
- Delirium can reflect life-threatening etiologies
- Requires urgent care if delirium is suspected

### DELIRIUM VS DEMENTIA

<table>
<thead>
<tr>
<th>DELIRIUM</th>
<th>DEMENTIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Abrupt precise onset with identifiable cause</td>
<td>- Gradual onset that cannot be identified</td>
</tr>
<tr>
<td>- Acute illness, generally days to weeks; rarely more than one month</td>
<td>- Characteristically progressing over years</td>
</tr>
<tr>
<td>- Usually reversible; often completely</td>
<td>- Generally irreversible, often chronically progressive</td>
</tr>
<tr>
<td>- Disorientation early</td>
<td>- Disorientation later in the illness; often after months or years</td>
</tr>
<tr>
<td>- Variable moment to moment - hour to hour - throughout day</td>
<td>- Much more stable (unless delirium develops)</td>
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<tr>
<td>- Prominent physiologic changes</td>
<td>- Less prominent physiologic changes</td>
</tr>
<tr>
<td>- Clouded, altered and changing level of consciousness</td>
<td>- Consciousness not clouded until terminal</td>
</tr>
<tr>
<td>- Strikingly short attention span</td>
<td>- Attention span not characteristically reduced</td>
</tr>
<tr>
<td>- Disturbed sleep-wake cycle with hour variation</td>
<td>- Disturbed sleep wake cycle with day-night reversal, not hour to hour variation</td>
</tr>
<tr>
<td>- Parked psychomotor changes (hyperactive or hypoactive)</td>
<td>- Psychomotor changes characteristically late (unless depression develops)</td>
</tr>
</tbody>
</table>

Ham, RJ (1997). The Diagnosis and Assessment of Alzheimer's Disease by Primary Care Physicians from the Continuing Education Home Study Program For Physicians sponsored by The School of Medicine of The University of North Carolina at Chapel Hill.

**SYNDROMES WHICH MIMIC DEMENTIA OR WORSENING PREEXISTING DEMENTIA**

D - Drugs
E - Emotional illness, including depression
M - Metabolic/endocrine disorders
E - Eye (visual problems, ear (hearing difficulty), environment (inappropriate or changed)
N - Nutrition neurological problems
T - Tumors, trauma, toxins
I - Infection
A - Alcoholism
DEMENTIA vs DEPRESSION

DEPRESSION

- Occurrence of five or more of the following symptoms
- Duration must be for at least two weeks
- Represents a change from prior function
- At least one symptom must be either depressed mood or loss of interest/pleasure

SYMPTOMS

- Depressed mood
- Diminished interest or pleasure in most activities
- Wt loss/gain or a marked change in appetite
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feelings of worthlessness or excess guilt
- Diminished ability to concentrate or make decisions
- Recurrent thoughts of death or suicidal ideation, attempts or plans

- Symptoms cause significant distress in function
- Symptoms not attributable to substance abuse or general medical condition
- Symptoms not better accounted for by bereavement


DEPRESSION VS DEMENTIA

<table>
<thead>
<tr>
<th>DEPRESSION</th>
<th>DEPRESSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Abrupt onset</td>
<td>- Insidious onset</td>
</tr>
<tr>
<td>- Short duration</td>
<td>- Long duration</td>
</tr>
<tr>
<td>- Previous psychiatric history (including undiagnosed depressive episodes)</td>
<td>- No previous psychiatric history</td>
</tr>
<tr>
<td>- Complaints of memory loss</td>
<td>- Often unaware of memory loss</td>
</tr>
<tr>
<td>- “I don’t know answers”</td>
<td>- Near-miss answers</td>
</tr>
<tr>
<td>- Fluctuating cognitive loss</td>
<td>- Stable cognitive loss (although loss is progressive over time)</td>
</tr>
<tr>
<td>- Equal memory loss for recent and remote events</td>
<td>- Memory loss is greatest for recent events</td>
</tr>
<tr>
<td>- Depressed mood (if present) occurs first</td>
<td>- Memory loss occurs first</td>
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COGNITIVE ASSESSMENT TOOLS

- Pt often has good social skills therefore questioning may be unable to penetrate this misleading social facade
- Use objective validated tests with numeric scores
- Sensitive to change over time
- Tests do not measure two major components of dementia: function and behavior
- Tests have cultural bias and reduced validity in presence of poor vision, varying educational levels, different primary language, tremor or other motor components

Mini-Mental State Examination (MMSE)

- One of most widely used screening tests for cognitive function
- Questions evaluating: orientation, memory, attention, ability to name objects, follow verbal and written commands, write a sentence spontaneously, copy a complex polygon figure
- Maximum score is 30 - test not timed
- Brief/easy to administer at home or office/clinic
- Assessment of dementia not complete w/o test
- Best performed separately from interview after informing the pt that you are going to test his/her memory

ADMINISTRATION

- Face patient, assuring eye contact, communication and minimal distractions; establish rapport
- Inform pt that you will ask a standardized set of questions to assess memory
- Ask in order listed and score immediately
- Partial credit cannot be given
- Encourage subject to chose one answer

INTERPRETATION OF RESULTS

- Normal: score 26 or greater
- 20-26 consistent w mild dementia
- Teens: moderate dementia
- Below 10: severe dementia
- MMSE findings of memory impairments and at least one cognitive area suggests dementia but a finding of impairment only in memory does not necessarily exclude dementia
- Some patients with early dementia may score in normal range on MMSE
- Reassess in 6 months if no cognitive impairment and history is not especially strong
- If history is strong and test is normal -> second opinion or further testing
Mini-Mental State Examination (MMSE)

<table>
<thead>
<tr>
<th>ORIENTATION</th>
<th>Score</th>
<th>Max Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is the (year)(season)(date)(day)(month)</td>
<td>( )</td>
<td>5</td>
</tr>
<tr>
<td>Where are we (state)(county)(town/city)(hospital)(floor)</td>
<td>( )</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>REGISTRATION</th>
<th>Score</th>
<th>Max Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Name 3 common objects (eg “apple,” “table,” “penny”)</td>
<td>( )</td>
<td>3</td>
</tr>
<tr>
<td>- Take 1 second to say each. Then ask the patient to repeat all three after you have said them.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Give one point for each correct answer</td>
<td></td>
<td></td>
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<tr>
<td>- Then repeat them until he/she learns all 3</td>
<td></td>
<td></td>
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<tr>
<td>- Count trials and record</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trials:</td>
<td>________</td>
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</tr>
</tbody>
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<table>
<thead>
<tr>
<th>ATTENTION AND CALCULATION</th>
<th>Score</th>
<th>Max Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spell “world” backwards. The score is the number of letters in correct order (D___ L ___ R ___ O___ W___)</td>
<td>( )</td>
<td>5</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>RECALL</th>
<th>Score</th>
<th>Max Score</th>
</tr>
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<tbody>
<tr>
<td>Ask for the 3 objects repeated above. Give 1 point for each correct answer. (Note: Recall cannot be tested if all 3 objects were not remembered during registration)</td>
<td>( )</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LANGUAGE</th>
<th>Score</th>
<th>Max Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name a “pencil” and “watch”</td>
<td>( )</td>
<td>2</td>
</tr>
<tr>
<td>Repeat the following: “No if ands or buts”</td>
<td>( )</td>
<td>1</td>
</tr>
<tr>
<td>Follow a 3 stage command:</td>
<td>( )</td>
<td>3</td>
</tr>
<tr>
<td>“Take a paper in your hand, fold it in half, and put it on the floor”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Read and obey the following: “Close your eyes”</td>
<td>( )</td>
<td>1</td>
</tr>
<tr>
<td>Write a sentence</td>
<td>( )</td>
<td></td>
</tr>
<tr>
<td>Copy the following design</td>
<td>( )</td>
<td>1</td>
</tr>
<tr>
<td>Total Score</td>
<td>______</td>
<td></td>
</tr>
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Clock Drawing Test (CDT) a.k.a. “Cognitive Clock”

- Freehand clock drawing is complex task
- Requires abilities in addition to constructional skills
  - Visuospatial as well as conceptual capacity are tested
- Testing is qualitative not quantitative
- Demonstrated to be sensitive measure of constructional apraxia
- May also reflect general deficits in conception of time
- Particularly useful as screening tool to differentiate normal elderly vs cognitively impaired
- Especially useful for screening for Alzheimer’s disease (75% of all dementias)
- Note that test not establish diagnosis of dementia but screens needs for further testing*
- Test is sensitive to change over time.


INSTRUCTIONS

- Ask the person to draw the face of a clock, putting the numbers in the correct positions
- After patient draws clock ask him to draw hands indicating either of following
  - Ten (10) minutes after eleven (11)
  - Twenty (20) minutes after eight (8)

SCORING CLOCK DRAW

- Various methods have been described
- Sensitive, brief and easy to apply is the 0-4 point method *
  - Draws closed circle: Score 1 point
  - Places numbers in correct positions Score 1 point
  - Includes all 12 correct numbers Score 1 point
  - Places hands in correct positions Score 1 point


INTERPRETATION

- Certain errors rarely produced by cognitively intact persons
  - Grossly distorted contour
  - Extraneous markings
  - Unlikely that perfectly drawn clock will be created by cognitively impaired person

- Low score indicates need for further evaluation
  - Cut-off score is subjective and arbitrary
  - Classification errors may occur
  - Must use clinical judgment in interpreting test
  - When in doubt - multiple source of evidence should be examined
  - Mini-Mental Status Exam* (MMSE), a standardized assessment tool, should follow
Other Cognitive Tests (nonqualitative)

- Ability to access long term memory: recall names of 4-legged animals - at least 10 should be recalled in 30 seconds
- Abstract capacity: proverb interpretation
- Proverbs are culturally specific
- Same info via ask how arm and leg are similar or more advanced how laughing and crying or eating and sleeping are similar

Observation over time is part of the diagnostic technique

"Alzheimer's disease is not diagnosed 'by exclusion'; therefore there may be a period of diagnostic uncertainty but the diagnosis confirms itself over time, provided that an accurate history and objective scored mental status test, sometimes repeated at intervals, are obtained."
PHYSICAL SELF-MAINTENANCE SCALE (PSME)

Patient's Name ________________________________________ Date ___________________

Numbers one through five in each category represent worsening states of function. Choose the number that best describes the patient’s functional status. Scores in all six categories should then be totaled. The higher the final score, the greater the degree of impairment.

A. Toileting
1. Cares for self at toilet completely, no incontinence
2. Needs to be reminded or needs help in clean self or has rare (Weekly at most) accidents
3. Soiling or wetting while asleep more than once a week
4. Soiling or wetting while awake more than once a week
5. No control over bowel or bladder

B. Feeding
1. Eats without assistance
2. Eats with minor assistance at mealtimes and/or with special preparation of food, or help in cleaning up after meals
3. Feeds self with moderate assistance and is untidy
4. Requires extensive assistance for all meals
5. Does not feed self at all and resists efforts of others to feed him/her

C. Dressing
1. Dresses, undresses, and selects clothes from own wardrobe.
2. Dresses and undresses self with minor assistance
3. Needs moderate assistance in dressing or selection of clothes
4. Needs major assistance in dressing, cooperates with efforts of others to help
5. Completely unable to dress self and resists efforts of others to help

D. Grooming
1. Always neatly dressed, well groomed, without assistance
2. Grooms self adequately with occasional minor assistance e.g. shaving
3. Needs moderate and regular assistance or supervision in grooming
4. Needs total grooming care, but can remain well groomed after help from others
5. Actively negates all efforts of others to maintain grooming

E. Physical Ambulation
1. Goes about grounds or city
2. Ambulates within residence or about one block distance
3. Ambulates with assistance of (check one)
   a. (  ) another person  b. (  ) railing  c. (  ) cane  d. (  ) walker
   e. (  ) wheelchair - gets in and out without help
   f. (  ) wheelchair - needs help getting in, out
4. Sits unsupported in chair or wheelchair but cannot propel self without help
5. Bedridden more than half the time

F. Bathing
1. Bathes self (tub, shower, sponge bath) without help.
2. Bathes self with help in getting in and out of tub
3. Washes face and hands only, but cannot bath rest of body
4. Does not wash self but is cooperative with those who bath him/her
5. Does not try to wash self and resists efforts to keep him/her clean

MANAGEMENT OF ALZHEIMER’S DISEASE

OBJECTIVES IN THE MANAGEMENT OF PROGRESSIVE DEMENTIAS

- Preserve function, including physical, social and self-care skills, for as long as possible
- Discuss the patient’s preferences for recessitation and high technology maintenance while still cognitively able
- Appoint a healthcare proxy or write advance directive while still able
- Access preserved long-term memory for enjoyment and validation
- Appropriately and actively use the behavior mgt techniques and psychotropic medications
- Maintain pts in the security and familiarity of their own homes for as long as possible
- Carefully plan all relocations, whether temporary or long-term.

PRACTICAL TIPS FOR COGNITIVE FEATURES

- **Indecisiveness:** reduce choices available
  Example: “Let’s have lunch” vs “What do you want for lunch?”

- **Disorientation:**
  - Provide cues “here’s your room at the end of the hall”
  - Avoid relocation but, if necessary, bring familiar items e.g. photographs

- **Hallucinations:**
  - Do not be overly concerned if they are not distressing to patient
  - Where treatment is necessary, antipsychotic agent is first choice
    “Start low -> go slow”

- **Delusions:**
  - Usually derived from misinterpretation of actual events and objects
  - Use of antipsychotic drugs may help
  - Neither confront pt with reality which could result in argument, nor reinforce delusion
  - Redirect and distract the patient.

BEHAVIORAL FEATURES

- **Repetitiveness:** caused by memory loss and insecurity. Answer decisively, then distract

- **Lack of motivation:**
  - Caused by indecisiveness and being overwhelmed.
  - Organize fulfilling activities; start projects which patient can complete

- **Personality changes:**
  - Neurochemical changes in the brain, rather than deliberate wilfulness
  - May cause disinhibition, inappropriate sexuality, or other personality changes.
  - Maintaining a sense of humor is helpful
  - Distraction and changing the situation may sometimes help.
- **Communication difficulties:**
  - Word finding difficulties and anxiety contribute to difficulty expressing ideas
  - Check for impaired hearing
  - Comprehension may be somewhat preserved
  - Avoid talking about dementia in front of patients unless you actively include them in the conversation.

- **Speech impairment:**
  - Expressive aphasia frequently present
  - It may relieve frustration for the family to "fill in" for the patient.

- **Wandering:**
  - Register pt in Alzheimer’s Association Safe Return Program (800-272-3900)
  - Secure the environment (eg complex handles, alert neighbors, etc.)

- **Emotionality:**
  - Outbursts and catastrophic reactions sometimes avoided with appropriate management
  - Weeping may be indication of depression
  - Avoid overwhelming situations, reduce interfering stimuli
  - Medications may be helpful
    - Low does of neuroleptics (for delusions or to the psychotic symptoms)
    - Antidepressants (for clinical depression)
    - Short-acting minor tranquilizers (for anxiety)

**TREATMENT**

- Investigational - potentially neuroprotective
  - Estrogen
  - Anti-inflammatory RX (prednisone and NSAIDs)
  - Antioxidants (vit E)
  - Monoamine inhibitors: selegiline (Eldepryl)
  - Vit E
    - Shown to delay progression/dependency of moderately severe Alzheimer’ pts
    - "Moderate" doses reasonable albeit efficacy not known for certain

- FDA approved: cholinesterase inhibitors
  - Tacrine HCL (Cognex): qid dosing and hepatotoxic
  - Donepezil HCL (Aricept): qd dosing and not toxic

**CHOLINOMIMETIC THERAPY**

- Neurophysiologic processes contributing to memory loss in AD
  - Atrophy of cholinergic ventral forebrain neurons
  - Partial deafferentation of the hippocampus

- Therapies are designed to enhance cholinergic pathways
  - Two (2) cholinesterase-inhibitors available; one may be available shortly
    - tacrine (Cognex)
    - donepezil (Aricept)
    - metrifonate

- Both tacrine and donepezil indicated for mild to moderate
- Only 1/3 patients have clinically significant response
- Therapeutic trial of 1-2 months is recommended on maintenance dosing
  - D/C after 1-2 months if no observable improvement occurs *
  - If patient is more impaired following D/C then can resume **

* Memory, orientation, reasoning, language
** Affect may be quite subtle and only detected in retrospect

TACRINE (Cognex)
- First FDA approved agent
- S/E and short half-life (qid dosing) limits use
  - Most common is GI upset
  - Most serious is potential for hepatotoxicity
  - Requires periodic monitoring of serum transaminase
- Dosing
  - 10 mg/qid with 10 mg qid
  - 10 mg qid increments q 4 weeks pending response and LFTs
  - Max dosing 40 mg qid

DONEPEZIL (Aricept)
- Greater specificity for brain tissue; longer half-life
- Not shown to be hepatotoxic
- Higher dosing may result in cholinergic S/E
  - Nausea, diarrhea
  - Insomnia
- Dosing
  - Initial dose: 5 mg PO hs;
  - Maintenance dose after 1 month: 10 mg PO hs

RIVASTIGMINE (Exelon) - newest agent - introduced 2000

ANTIDEPRESSANT THERAPY
- AD patients have significant component of depression
- May respond to antidepressants
- SSRI have become first-line choices because well tolerated
- Tricyclic agents have become less favored
  - Cardiotoxicity
  - Orthostatic hypotension

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)
- Inflammation plays key role in pathogenesis of AD
- Neuritic (senile) plagues are a hallmark of AD
  - Immunoglobulins
  - Complement factors
  - Specific agents
    - Amyloid proteins, activated microglia, cytokines
    - Acute phase reactants, protease inhibitors
- Longitudinal study suggests ASA/NSAIDs decrease relative risk of AD
  - Effect not seen with acetaminophen
  - Relative risk AD observed in study
    - 0.40 for those with 2 or more years use of NSAID
    - 0.65 for those with less than 2 years use
    - 0.74 for ASA users
  - Study supports previous studies which indicate protective role with chronic use

ESTROGEN USE (ERT)
- Numerous studies indicate inverse relationship re ERT and RR of AD
- Meta-analysis of postmenopausal ERT and risk of dementia
  - 29% risk reduction with ERT
- Therapy does not necessarily improve cognition - 5 yr study ERT in elderly women
  - Estradiol did not correlate with cognitive function
  - Estrone levels had inverse relationship with performance of certain task

VITAMIN E AND SELEGILINE
- Vitamin E, an antioxidant, may protect vs free radical damage in brain
- Selegiline (Eldepryl) is selective monamine oxidase B inhibitor
  - Increases levels of brain catecholamines
  - May have antioxidant neuroprotective effect
- Both agents appear to slow down progression of AD
  - Greatest effect in vitamin E group
  - Selegiline group was second
  - Combo therapy had least effect

GINGKO BILOBA
- Thought to have antioxidant properties
- Free radicals thought to play role in AD (excessive lipid peroxidation -> cell damage)
- Controlled trials: Pts receiving therapy had better overall performance scores
  - 6-12 month study period; effect seen with both AD and vascular dementia
  - No serious adverse effects; dosing was 40 mg tid
REFERENCES:


2. Ham, RJ (1997). The Diagnosis and Assessment of Alzheimer's Disease by Primary Care Physicians from the Continuing Education Home Study Program For Physicians sponsored by The School of Medicine of The University of North Carolina at Chapel Hill.


