Dementia

“De—mentia” - the taking of the mind (Latin)
Dementia is a syndrome – a group of symptoms – that can have a number of causes

**Major Symptoms:**

• Memory impairment
• Cognitive impairment(s)
• Impairments cause significant decrements in social and/or occupational functioning

**Sometimes accompanied by:**

- Depression
- Anxiety
- Delirium

Transient reductions in clarity and environmental awareness (i.e., confusion) with impaired selective attention
Memory Impairment

• Especially “recent” memory
  (Events occurring in the immediate past)

• **Diagnosis:**
  Delayed (5 minute) Recall Task
  (see MMSE)
Cognitive Impairments

One or more of the following:

- **Aphasia**
  Impairment of speech/language

- **Apraxia**
  Difficulty executing skilled motor behaviors

- **Agnosia**
  Visual object recognition

- **Executive Function**
  Planning, organizing and sequencing activities (frontal lobe)
Aphasia
(Impairment of Language/Speech)

• Difficulty finding the right word (Anomia) (e.g., “hand clock” instead of “watch”)
• Pausing; articulatory groping; phrase repetition
• Difficulty writing and performing simple arithmetic calculations

Diagnostic Tests:

**Word Fluency Test** (Name as many animals as you can in 2 min) (Mean = 27 versus 7 in SDAT)

**Boston Naming Test**
Name 60 line-drawings; 20 seconds each
(see next slide for example)
Examples of Aphasia Revealed by the Boston Naming Test
Apraxia
(Difficulty Executing Skilled Motor Behavior)

• Difficulty is due to central nervous system (as peripheral nervous disorders have previously been ruled-out)
• Difficulties stem from inability to mentally represent the necessary motor control sequences
• Examples:
  Buttoning a shirt; Using familiar utensils and tools

Diagnostic Test:
Clock Drawing Test  (Draw a picture of an analog clock)
(see next slide)
### Examples of Clock Drawing Test

<table>
<thead>
<tr>
<th>Disease</th>
<th>Clock Drawing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Alzheimer's Disease</td>
<td><img src="image1" alt="Example" /></td>
</tr>
<tr>
<td>Moderate Alzheimer's Disease</td>
<td><img src="image2" alt="Example" /></td>
</tr>
<tr>
<td>Severe Alzheimer's Disease</td>
<td><img src="image3" alt="Example" /></td>
</tr>
</tbody>
</table>

**Progressive Apraxia**

As documented by the Clock Drawing Test
Agnosia
(Problems with Visual Object Recognition)

• Visual object recognition problems occur despite intact visual acuity and color vision

• Patients can describe “features” of objects but cannot integrate them into a whole (as needed to achieve object recognition)

Diagnostic Tests:
- Picture Sorting Task(s)  (Sort into predefined categories)
- Incomplete Picture/Occluded Object Test(s)
Executive Function
(Planning, organizing and sequencing activities)

• The most basic levels of executive function involve maintaining goal states while simultaneously planning and sequencing behaviors designed to achieve those goals
• Executive functions are primarily mediated by frontal lobe mechanisms

Diagnostic Tests:
- **Trail Making A & B** (Reitan, 1958)
- **Wisconsin Card Sorting Task** (Abstract concept formation)
Trail Making A

Connect the circles from #1 to #20 in the correct numerical sequence.

Perform the task as quickly as you can while maintaining accuracy.

Typical Completion Times

Normal Older Adults: 29 seconds
Dementia Patients: 78+ seconds
Trail Making B

Alternating between two parallel goal sequences.

Connect the labelled “dots” in sequence while alternating between numerals and letters (i.e., 1-A-2-B-3-C, etc.).

Typical Completion Times

Normal Older Adults: 95 seconds
Dementia Patients: 275+ seconds
Wisconsin Card Sorting Task

• Abstract concept formation test
• Participants must assign card to a category based upon stimulus shape, color or numerosity. However, they are not told the rule. They must discover it through a trial & error process in which “correct” versus “wrong” feedback is provided
• Individuals with frontal lobe impairment make many errors on this task, including persistently using an old rule that is no longer valid

Let’s explore the WCST via a computer-administered demonstration.
**Mini-Mental Status Exam (MMSE)**
(Quick & Dirty Cognitive Assessment in Dementia)

- Most commonly used instrument for monitoring cognitive function in dementia patients
- Simple to administer
- Free to use
  Public domain; *Merck Manual of Geriatrics*

- Let’s explore the MMSE
  How does it capture the criteria for dementia Rx?
  What does it tell us about the profound effects of dementia?
Mini Mental Status Exam

Assesses the following cognitive domains:

- Orientation (Time; Place)
- Attention
- Recent Memory
- Working Memory/Executive Function
- Aphasia
- Apraxia

95% of community population scores ≥ 24

Dementia Patients

- ≤ 9    Severe
- 10-20  Moderate
- 21-24  Mild
Major Types of Dementia

- **Alzheimer’s Disease**  (70 %)
- **Vascular Dementia**  (10%)
- **Miscellaneous**  (11%)
  - Lewy-Body Dementia
  - Frontotemporal Dementia
  - Parkinson’s Disease
  - Normal-Pressure Hydrocephalus
- **Acute Disorders**  (9%)
  (Dementia “mimics”)

We will focus upon these two varieties of dementia.

Try to discover the features used to differentially diagnose these disorders.
Acute vs. Chronic Disease Dx

• Many **reversible medical conditions** can produce symptoms very similar to dementia

• A diagnosis of dementia should not be made until this acute conditions are ruled-out via examination and lab tests

**Some Acute Dementia Mimics**

- hypothyroidism
- vitamin B12 deficiency
- substance abuse
- medication side effects
- hypoglycemia
- congestive heart failure
- hypoglycemia
- renal failure
- dehydration/electrolyte depletion
- etc...
Vascular Dementia
Vascular Dementia Dx

• (1) Memory Impairment
• (2) Cognitive Impairment
  (Aphasia; Apraxia; Agnosia; Executive Function)
• (3) Significant Social and/or Occupational Impact
• (4) Documented Cerebrovascular disease

(See next 2 slides)
Vascular Dementia Dx

• **Evidence from Brain Imaging Studies** (MRI; PET)
  - cortical infarctions
  - white matter tract thinning
  - focal subcortical lesions

• **Positive Neurological Indicators:**

  (A) **Exaggerated Deep Tendon Reflexes**
  - No top-down CNS inhibitory modulation

  (B) **Extensor-Plantar Response**  (Babinski Reflex)
  - Abnormal reflex to stimulation of soles of the feet
    - dorsal flexion of the big toe (lifts way up)
    - abduction (fanning out) of the remaining toes
Vascular Dementia Dx

• **Positive Neurological Indicators of Cerebrovascular Disease** (continued)

(C) **Pseudobulbar Palsy**
- Dysphagia (difficulty swallowing or chewing)
- slow and indistinct speech
- stiff and spastic tongue
  (Results from lesions in the corticobulbar pathway)

(D) **Gait Abnormalities**
- Bent over posture; shuffling of the feet

(E) **Weakness in one or more extremities**
Vascular Dementia Dx

• (5) **Symptoms Persist in the Absence of Delirium**
  (Chronic not transient states)

• (6) **Stereotypical Temporal Progression of Symptoms**
  
  (A) Cognitive symptoms start within 3 months **following stroke**
  (B) **Abrupt onset** of cognitive symptoms
  (C) **Stepwise progression** as opposed to continuous rate of cognitive decline

(See examples on next slide)
Vascular Dementia Dx

Stepwise progression thought to be characteristic of Vascular Dementia

Continuous progression thought to be characteristic of Alzheimer’s Disease
Vascular Dementia Characteristics

• Chronic and irreversible disease resulting from brain cell death

• **Mechanism of brain deterioration**
  multiple subcortical infarctions
  focal cerebral lesions
  and/or
  diffuse small vessel disease

• **Age of Onset:** 50-70 (mean = 66)
  earlier than Alzheimer’s disease
  small vessel disease peaks in 7th decade of life
  (80% have a history of hypertension)
Vascular Dementia Diagnostic Checklist

A. The development of multiple cognitive deficits manifested by both:

1. Memory impairment (impaired ability to learn new information or to recall previously learned information).
   - Yes ☐ No ☐

2. One or more of the following cognitive disturbances:
   a. Aphasia (language disturbance)
   - Yes ☐ No ☐
   b. Apraxia (impaired ability to carry out motor activities despite intact motor function)
   - Yes ☐ No ☐
   c. Agnosia (failure to recognize or identify objects despite intact sensory function)
   - Yes ☐ No ☐
   d. Disturbance in executive functioning (i.e., planning, organizing, sequencing, abstracting)
   - Yes ☐ No ☐

B. The cognitive deficits in criteria A1 and A2 each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning.
   - Yes ☐ No ☐

C. Focal neurological signs and symptoms (e.g., exaggeration of deep tendon reflexes, extensor plantar response, pseudobulbar palsy, gait abnormalities, weakness of an extremity) or neuroimaging evidence indicative of cerebrovascular disease (e.g., multiple infarctions involving cortex and underlying white matter) that are judged to be etiologically related to the disturbance.
   - Yes ☐ No ☐

D. The deficits do not occur exclusively during the course of delirium.
   - Yes ☐ No ☐
Vascular Dementia Characteristics

• **Gender Distribution:** Twice as likely in men

• **Brain damage often highly localized** (especially in earlier stages) rather than broad and diffuse as in Alzheimer’s disease

Hence, loss of cognitive functions tend to be “patchy” rather than universal...i.e., some cognitive skill can be spared while others are significantly diminished
Vascular Dementia Clinical Progression

• **Earliest symptoms:**
  - dizziness
  - headaches
  - decreased physical/mental vigor
  - vague physical complaints

• **Sudden onset** of the significant symptoms is typical

• **Small vessel disease symptoms often precede cognitive symptoms**
  (gait apraxia; pseudobulbar palsy; urinary incontinence)

• **Erratic/patchy loss of cognitive skills**

• **Stepwise progression of illness**
Vascular Dementia Clinical Progression

• General apathy
  (early in vascular dementia; later in Alzheimer’s disease)

• Free recall maintained better than Alzheimer’s disease

• “Good judgment” often maintained in some domains of behavior

• Hallucinations and delirium sometimes present

• Confusion tends to worsen at night
  (so-called “sundowning” effect)
Vascular Dementia
Prognosis and Treatment

• During later phases of the disease institutionalization or round-the-clock home care become necessary
• **Survival duration following institutionalization is typically 3-4 years**
• **Many other physiological symptoms of cardiovascular disease** are often manifest in vascular dementia patients requiring pharmacological or surgical intervention
• **Patients become bedridden in the terminal phase of the disease**
• **Death is usually incited by a cardiovascular event or persistent pneumonia**
Vascular Dementia
Risk Factors

• Fatty diet
• Lipid metabolism disease (high cholesterol & triglycerides)
• Smoking
• Environmental pollution
• Poor aerobic fitness
• Hypertension (80%)
• Hereditary heart disease

Same Risk Factors As Heart Disease
Alzheimer’s Disease
Alzheimer’s Disease

• Chronic, incurable and deadly brain wasting disease (It is the **most common variety of Dementia**)

• First chronicled by **Alois Alzheimer in 1906**
(Formerly known as “presenile dementia” and considered rare)

• **Definitive diagnosis only upon autopsy**
(amyloid plaque; tau-protein **neurofibrillary tangles**)

• Given its high prevalence, it is usually the **“default diagnosis”** once the general criteria for dementia are established
### Alzheimer’s Disease Diagnostic Checklist Part-1

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. The development of multiple cognitive deficits manifested by both:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Memory impairment (impaired ability to learn new information or to</td>
<td></td>
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</tr>
<tr>
<td>recall previously learned information).</td>
<td></td>
<td></td>
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<tr>
<td>c. Agnosia (failure to recognize or identify objects despite intact</td>
<td></td>
<td></td>
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<tr>
<td>sensory function).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Disturbance in executive functioning (i.e., planning, organizing,</td>
<td></td>
<td></td>
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<tr>
<td>sequencing, abstracting).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B. The cognitive deficits in Criteria A1 and A2 each cause significant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>impairment in social or occupational functioning and represent a</td>
<td></td>
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<tr>
<td>significant decline from a previous level of functioning.</td>
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<tr>
<td>C. The course is characterized by gradual onset and continuing cognitive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>decline.</td>
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</tr>
</tbody>
</table>
D. The cognitive deficits in Criteria A1 and A2 are not due to any of the following:
   1. Other central nervous systems, conditions that cause progressive deficits in memory and cognition (e.g., cerebrovascular disease, Parkinson’s disease, Huntington’s disease, subdural hematoma, normal-pressure hydrocephalus, brain tumor).

   2. Systemic conditions that are known to cause dementia (e.g., hypothyroidism, vitamin B₁₂ or folic acid deficiency, neurosyphilis, HIV infection).

   3. Substance-induced conditions.

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

F. The disturbance is not better accounted for by another disorder (e.g., major depressive disorder, schizophrenia).
Dementia Criteria Established

No Evidence to Indicate Other Varieties of Dementia

Alzheimer’s Disease

By “default”
Frontotemporal and Lewy-body dementias can be diagnosed with positive evidence from brain imaging studies.

If no positive evidence for either or these varieties of dementia is found, the default diagnosis is Alzheimer’s disease.
Alzheimer’s Disease

• 4th Leading Cause of Death among Adults in the U.S.A. (Heart disease; Cancer; Stroke)

• 1-in-10 Persons over the Age of 65 (5.5 Million Americans)

• Age of Onset:
  Vast majority of victims over the age of 65
  Probability of diagnosis increases exponentially beyond age 65
Prevalence of Alzheimer’s Disease

5.5 Million Americans (projected to double by 2040)

17K in South Dakota

82% of those diagnosed with Alzheimer’s are 75 or older

Majority of all nursing home residents
Alzheimer’s Disease

• Gender Distribution
  2.0 Million Men
  3.5 Million Women

  **Lifetime Risk:**
  10% Men
  20% Women  (2x More Likely than Men)
  (Opposite of Vascular Dementia)

Q: Why are women 2X more likely to develop Alzheimer’s Disease?

A: Because they live much longer...and the risk increases exponentially for every year lived beyond age 65
Alzheimer’s Disease

• **Gradual onset of symptoms**  
  (unlike Vascular dementia with 50% “sudden” onset)

• **Brain damage is pervasive rather than localized**  
  (All cognitive functions decline together)

• **Steady, continuous decline** of memory and cognitive functions  
  (as opposed to stepwise progression)
Alzheimer’s Disease

• **Duration of survival following diagnosis**

  4-8 years is typical  (20 years has been documented on occasion)

  Reflects slow, insidious deterioration of the brain
  (Which likely begins many years before first sign of symptoms)

  40% of time post-diagnosis is spent in the terminal phase
  (requiring 24/7 continuous nursing care)

  @ age 80 – 75% of Alzheimer’s patients are institutionalized

  2/3’s die in a nursing home
Alzheimer’s Disease Prognosis
Three Stages of Progression (ADRDA)

First Stage

• Forgetfulness
• Impairment of judgment
• Increasing inability to handle routine tasks
• Lack of spontaneity
• Loss of initiative
• Disorientation for time and places
• Depression and terror
Alzheimer’s Disease Prognosis
Three Stages of Progression (ADRDA)

Second Stage

• Wandering and perseveration
• Increasing disorientation
• Increasing forgetfulness
• Agitation and restlessness
• Inability to attach meaning to sensory perceptions
• Inability to think abstractly
• Muscle twitching may develop
• Convulsive seizures may develop
Alzheimer’s Disease Prognosis
Three Stages of Progression (ADRSA)

Third (Terminal) Stage

- Complete dependence for all ADL’s
- Disorientation for people and ultimately for self
- Severe speech impairment (including complete muteness)
- Develop a morbid need to put everything into their mouths (Psychoanalytic regression to “oral” stage of development?)
- Develop a necessity to touch everything in sight
- Body becomes physically emaciated
- Complete loss of control of all bodily functions
Alzheimer’s Disease
Risk Factors

- **Advanced Age** (by far the most powerful predictor)
- **Sex** (twice as likely in women)
- **Familial Inheritance** (parent, brother, sister)
- **Sleep Disorders**
- **Excessive Alcohol Consumption**
- **Genetics**
  - Inherit a copy of the **APOE/e4 gene** from BOTH parents
  - (2% of population but 11% of Alzheimer’s patients)
Alzheimer’s Disease
Treatment

• There is no cure for Alzheimer’s disease (Recent tests of promising drugs have been very disappointing)

• Aerobic exercise programs may slow the rate of progression

• Currently there are 5 FDA-approved drugs
  Very small improvements in cognition
  Improvements quickly nullified by continued progressive declines

  Acetylcholine esterase inhibitors (Acetylcholine Mechanism):
  Aricept®, Exelon®, Razadyne®

  NMDA agonists (Glutamate Toxicity Mechanism):
  Namenda®, Namzaric® (Namenda+Aricept)

Between 2002-2012 there were FDA-approved clinical trials of 244 drugs for treating Alzheimer’s disease. Only one was successful and ultimately given FDA approval.