

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 find 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)

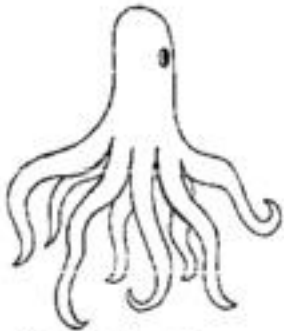
Examples of Aphasia Revealed by the Boston Naming Test

A

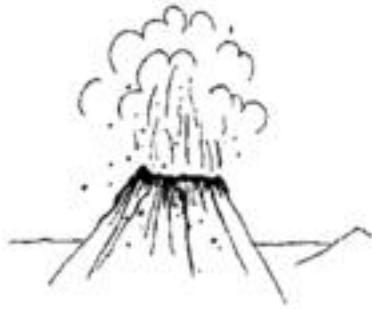
"coconut"



"cash register"

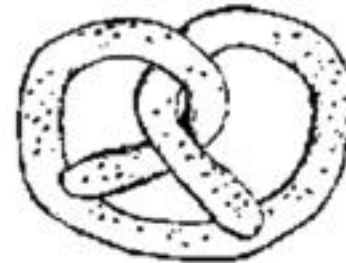


"spider"

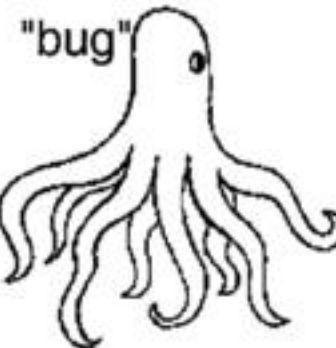


"don't know"

B



"snake"



"bug"



"stereo or
computer"



"lamp"

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

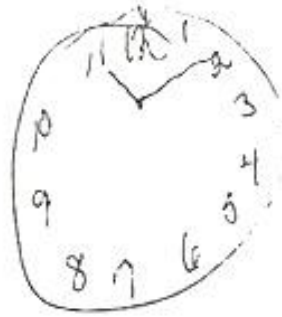
Diagnostic Test:

Clock Drawing Test (Draw a picture of an analog clock)

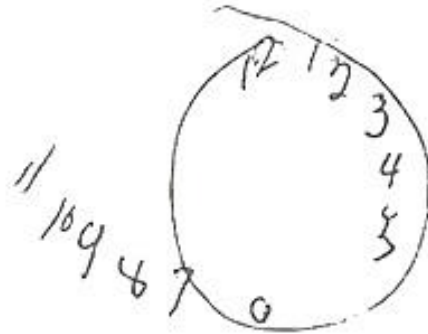
(see next slide)

Examples of Clock Drawing Test

Early Alzheimer's Disease



Moderate Alzheimer's Disease



Severe Alzheimer's Disease



Progressive Apraxia
As documented by the
Clock Drawing Test

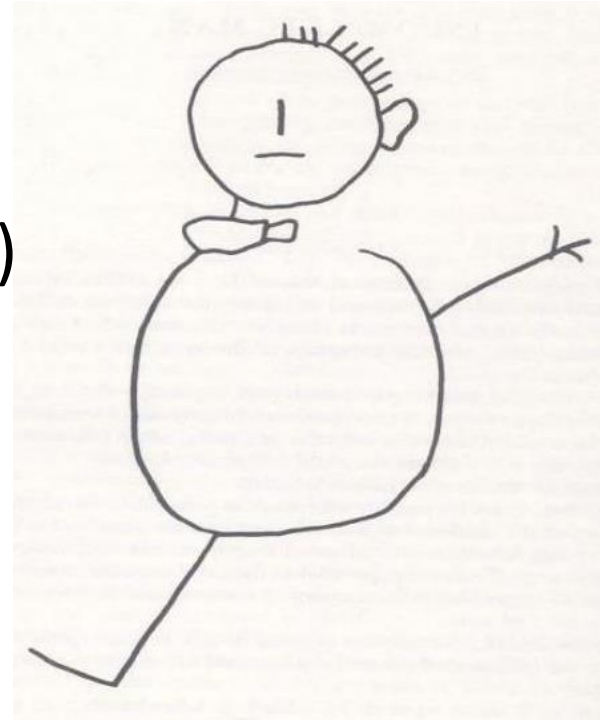
Agnosia

(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

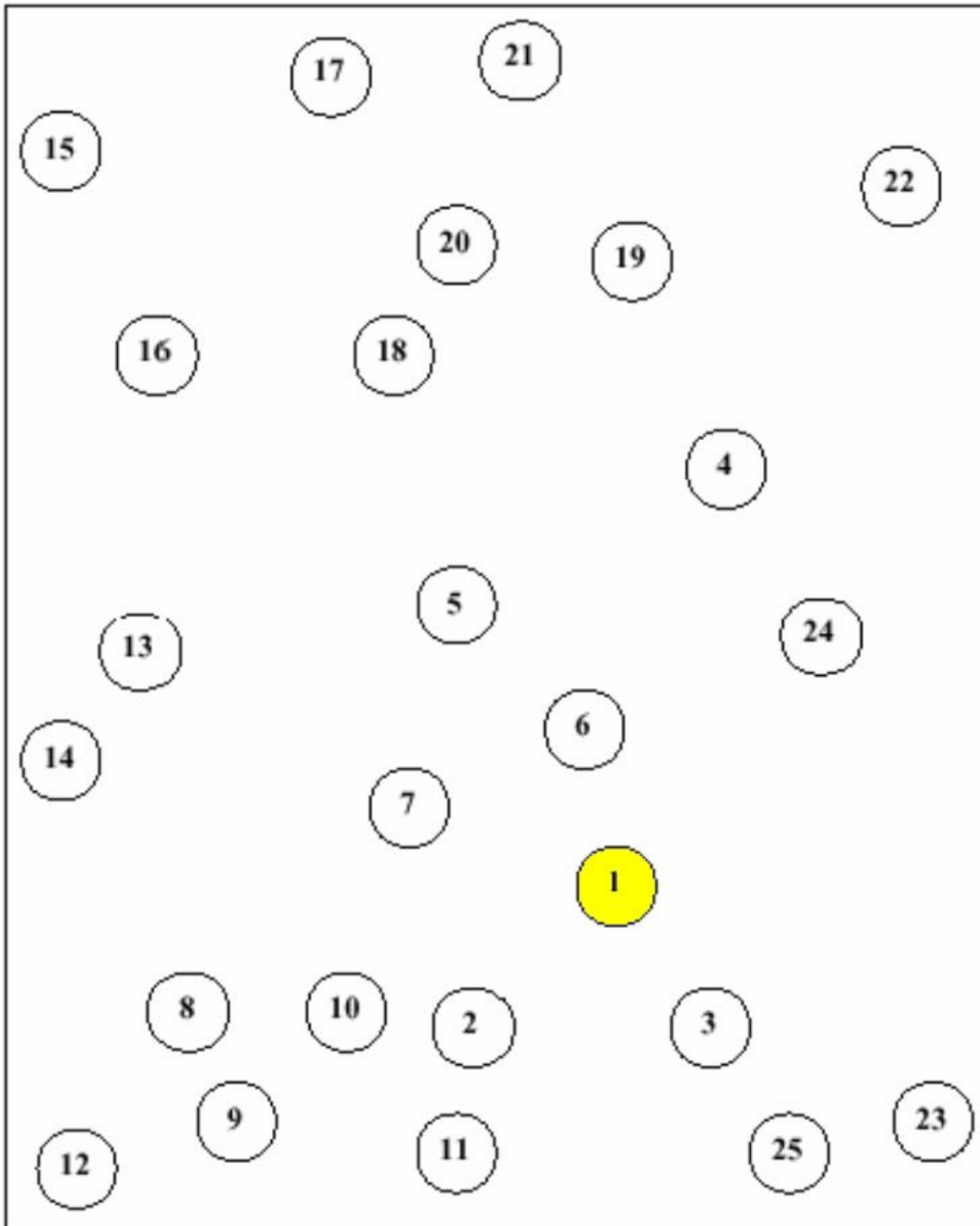
Diagnostic Tests:

Trail Making A & B

(Reitan, 1958)

Wisconsin Card Sorting Task

(Abstract concept formation)



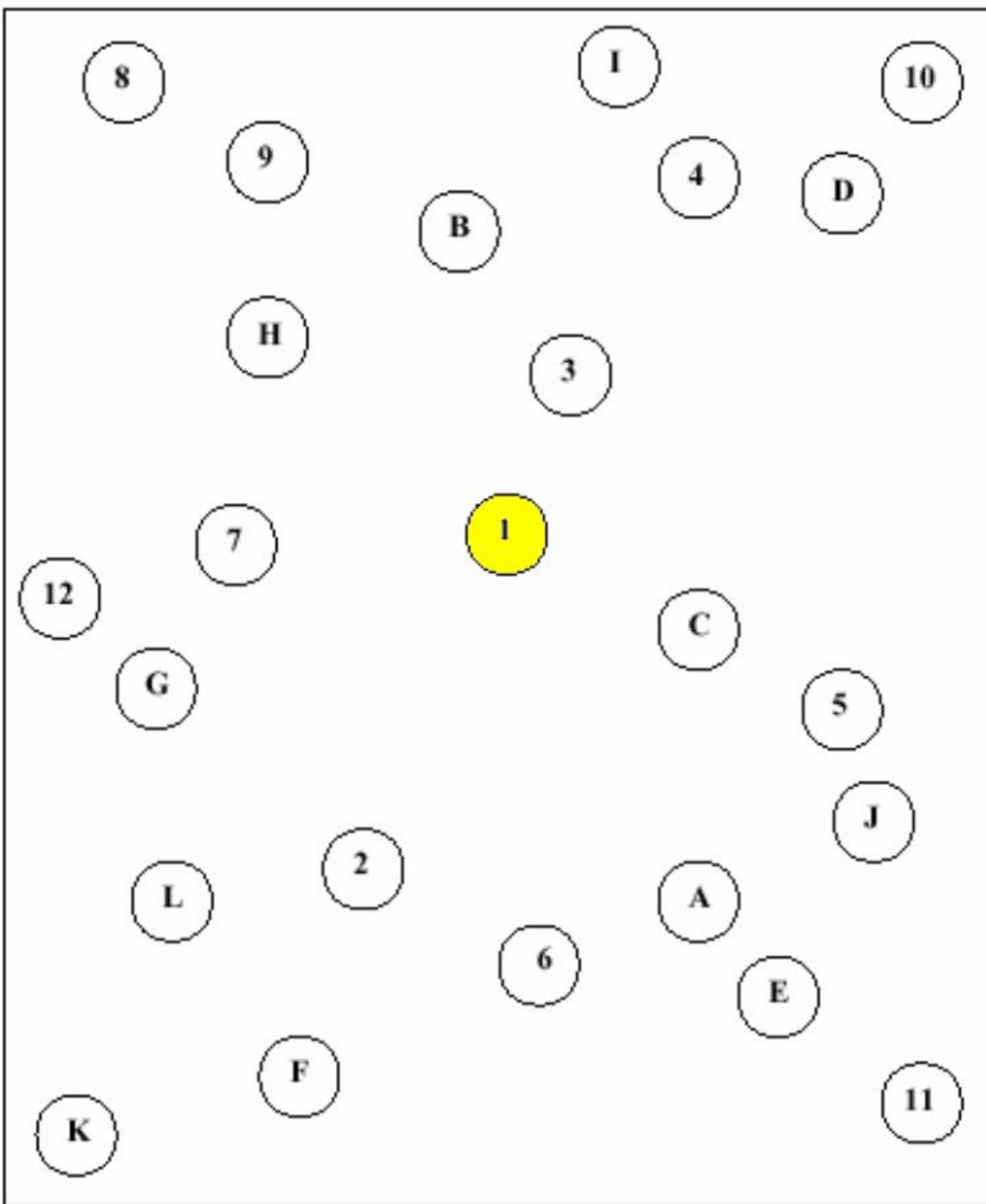
Trail Making A

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.

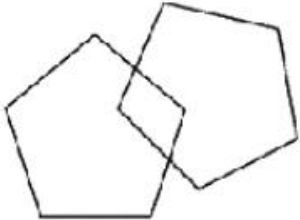
Mini-Mental Status Exam (MMSE)

(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?

Maximum Score	Score	
ORIENTATION		
5	()	What is the: (year) (season) (date) (day) (month)
5	()	Where are we: (state) (county) (town) (facility) (floor)
REGISTRATION		
3	()	Name three objects and have person repeat them back. Give one point for each correct answer on the first trial. 1. _____ 2. _____ 3. _____ Then repeat them (up to 6x) until all three are learned. [Number of trials ____]
ATTENTION AND CALCULATION		
5	()	Serial 7's. Count backwards from 100 by serial 7's. One point for each correct answer. Stop after 5 answers. [93 86 79 72 65] Alternatively spell "world" backwards. [D - L - R - O - W]
RECALL		
3	()	Ask for the names of the three objects learned above. Give one point for each correct answer.
LANGUAGE		
9	()	Name: a pen (1 point) and a watch (1 point) Repeat the following: "No ifs, ands, or buts" (1 point) Follow a three-stage command: "Take this paper in your [non-dominant] hand, fold it in half and put it on the floor". (3 points) [1 point for each part correctly performed] Read to self and then do: "Close your eyes" (1 point) Write a sentence [subject, verb and makes sense] (1 point) Copy design [5 sided geometric figure; 2 points must intersect] (1 point)
Score: ____/30		
Alert Overtly Anxious Concentration Difficulty		
Drowsy		
CLOSE YOUR EYES		
		
Sentence:		

Mini Mental Status Exam

Assesses the following cognitive domains:

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

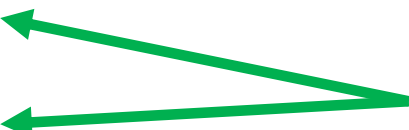
95% of community population scores ≥ 24

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

substance abuse

hypoglycemia

hypoglycemia

dehydration/electrolyte depletion

vitamin B12 deficiency

medication side effects

congestive heart failure

renal failure

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

Subcortical
Lesions

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

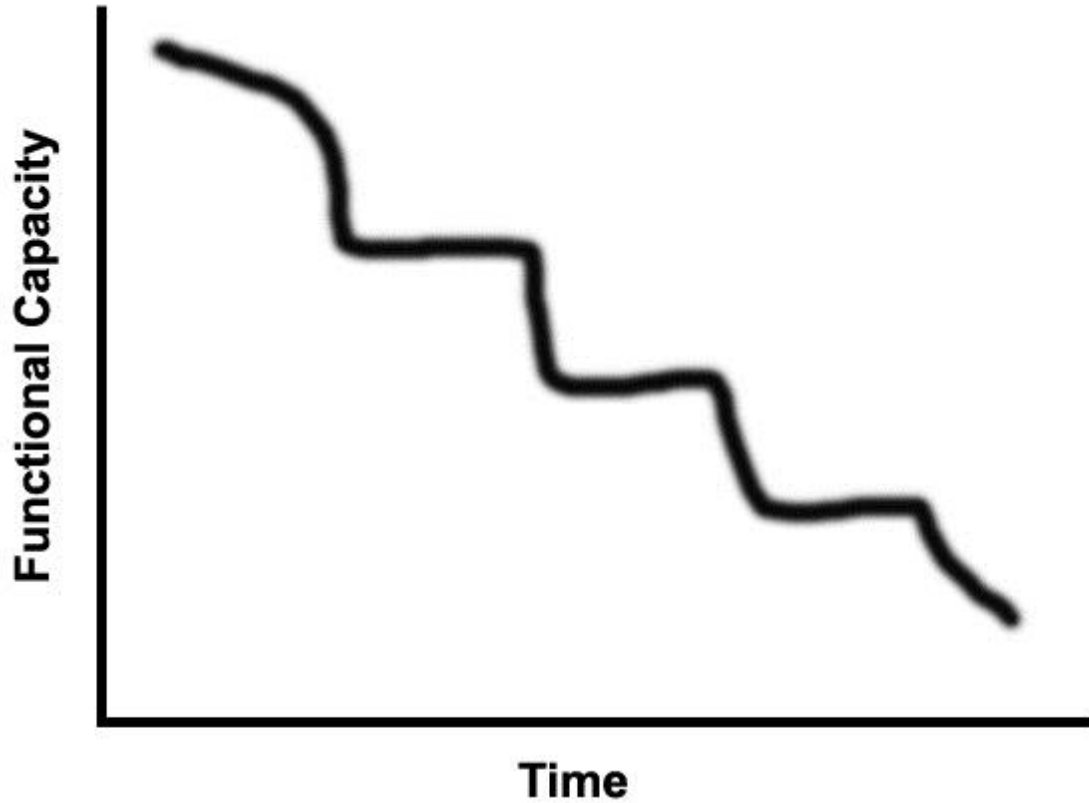
- (E) **Weakness in one or more extremities**

Vascular Dementia Dx

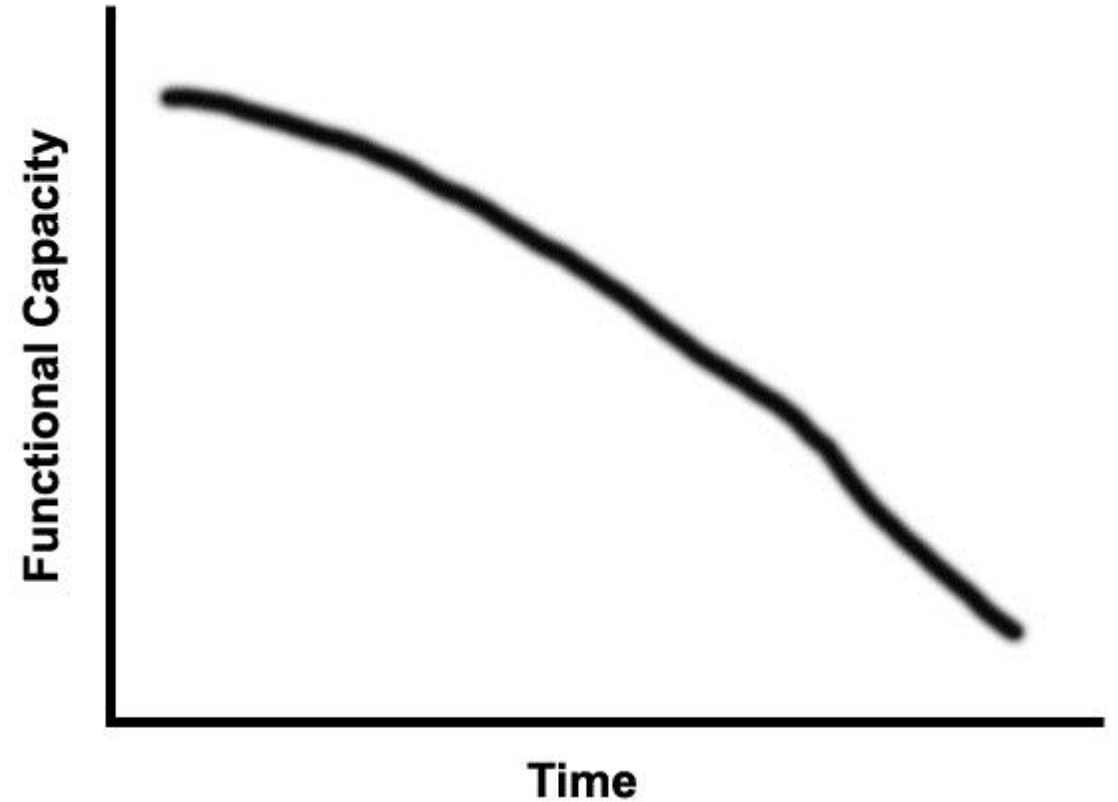
- **(5) Symptoms Persist in the Absence of Delirium**
(Chronic not transient states)
- **(6) Stereotypical Temporal Progression of Symptoms**
 - (A) Cognitive symptoms start within 3 months following stroke
 - (B) Abrupt onset of cognitive symptoms
 - (C) Stepwise progression as opposed to continuous 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

	Yes	No
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).	☐	☐
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 identify objects despite intact sensory function)	☐	☐
d. Disturbance in executive functioning (i.e., planning, organizing sequencing, abstracting)	☐	☐
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.	☐	☐
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..	☐	☐
D. The deficits do not occur exclusively during the course of delirium.	☐	☐

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

	Yes	No
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).	☐	☐
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 identify objects despite intact sensory function).	☐	☐
d. Disturbance in executive functioning (i.e., planning, organizing, sequencing, abstracting).	☐	☐
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.	☐	☐
C. The course is characterized by gradual onset and continuing cognitive decline.	☐	☐

Alzheimer's Disease

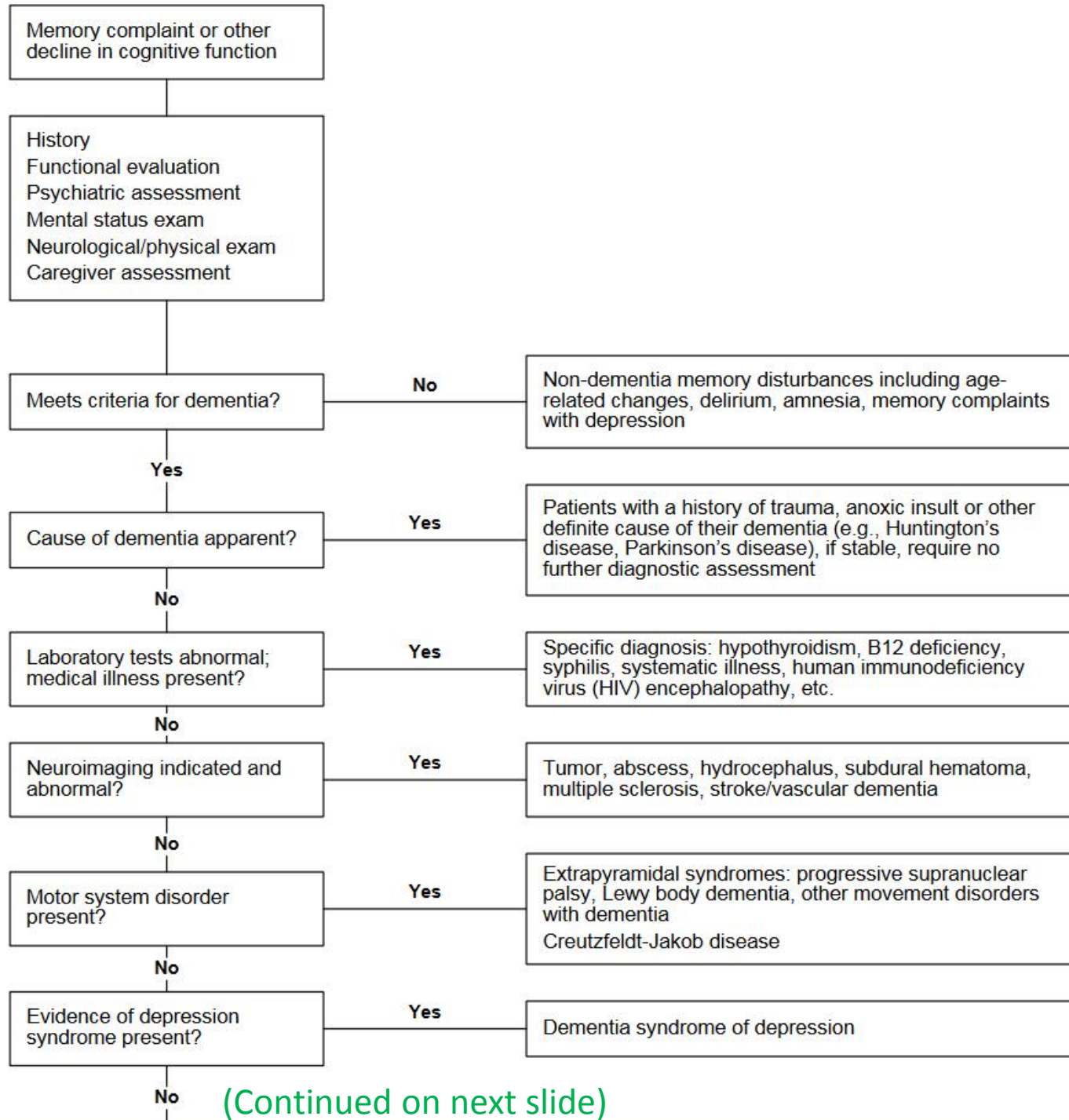
Diagnostic Checklist Part-1

Alzheimer's Disease

Diagnostic Checklist

Part-2

- | | | |
|---|--------------------------|--------------------------|
| 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 B ₁₂ 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"**

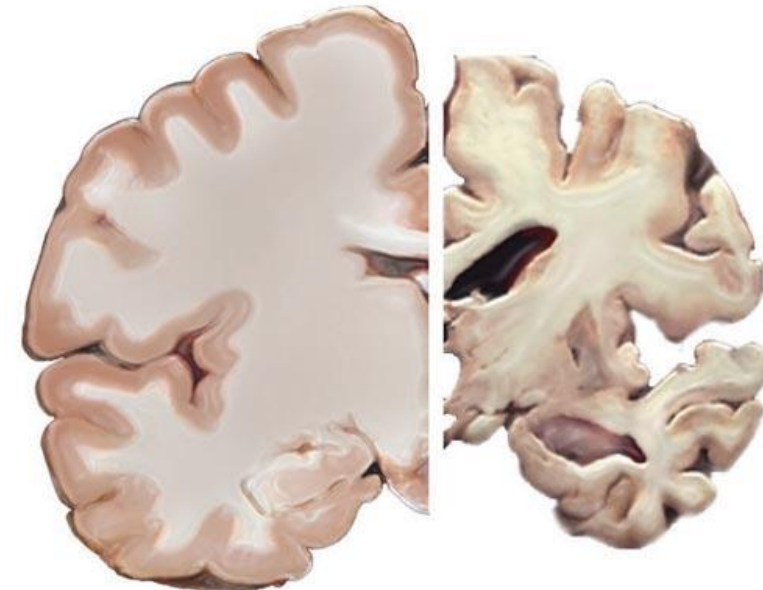
No

Alzheimer's disease	Memory, language and visuospatial disturbances; indifference, delusions, agitation
Frontotemporal dementia	Marked personality changes; relative preservation of visuospatial skills; executive dysfunction
Lewy body dementia	Marked visual hallucinations, delusions, fluctuating mental status, neuroleptic sensitivity

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

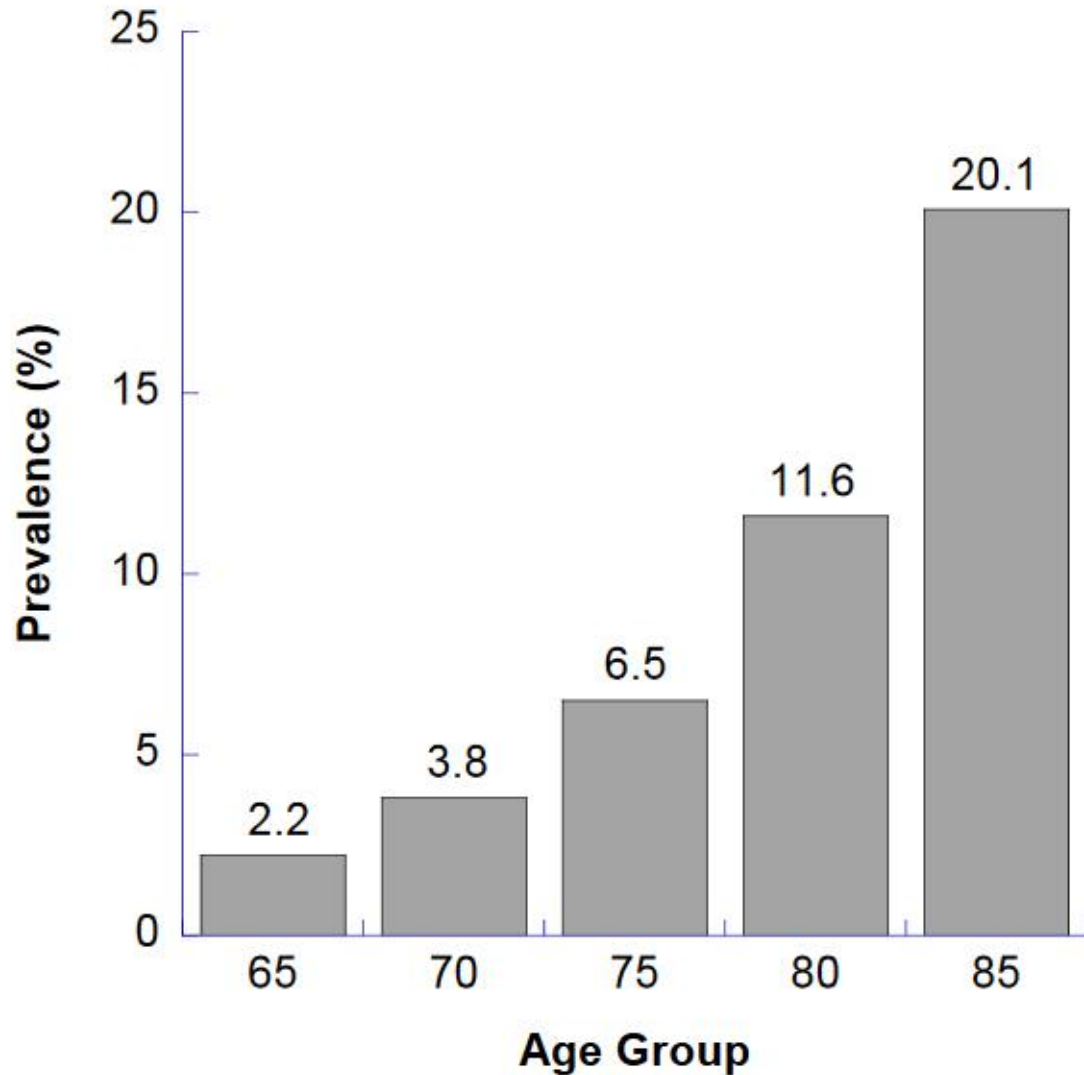
If no positive evidence for either of these varieties of dementia is found,
the default diagnosis is Alzheimer's disease

Healthy Brain Severe AD



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 (ADRD)

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 (ADRD)

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 (ADRD)

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.