

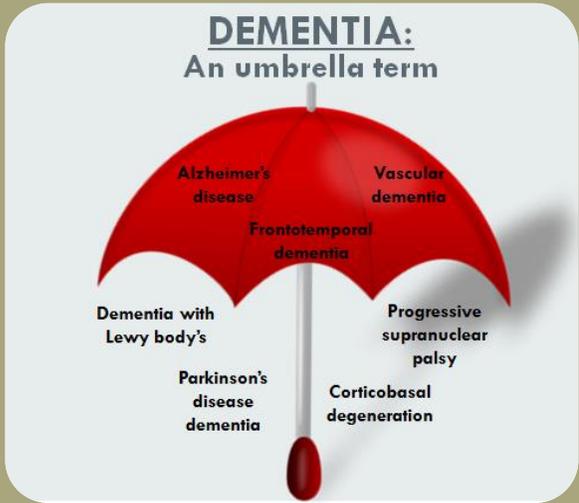
So You Think It's Dementia

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Objectives

- At the end of the presentation, the participant should be able to:
- Differentiate between the two structural groups of Dementia
- Name the top 3 types of Dementia
- Understand the management and treatment of certain types of Dementia
- Explain the consequences of Stereotype threats
- Acknowledge new treatments for Dementia in the pipeline



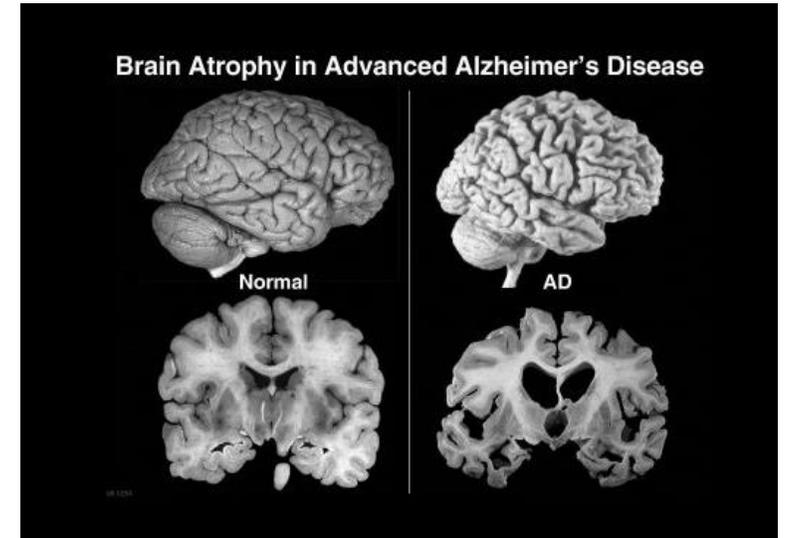
Definition

- “a syndrome occurring as a result of disease of the brain, which is usually chronic or progressive in nature. It consists of impairment of several higher cortical functions, which include memory, thinking, comprehension, calculation, learning, language and judgement. These impairments often occur alongside changes in emotional control, social behavior or motivation.....
- The causes of dementia are not fully understood, but the result is always structural and chemical changes in the brain, leading to neuronal loss and shrinkage of brain volume.....it is a clinical syndrome”

Dening T, Sandilyan MB (2015) Dementia: definitions and types. *Nursing Standard*. 29, 37, 37-42.

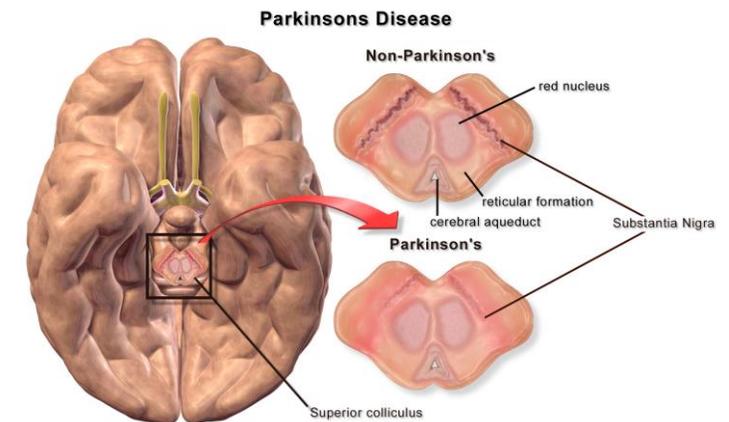
Two Groups of Dementias

- Cortical dementias - happen because of problems in the cerebral cortex, the outer layer of the brain. They play a critical role in memory and language. Example: Alzheimer's Disease



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- Sub-cortical dementias - happen because of problems in the parts of the brain beneath the cortex. People with subcortical dementias tend to show changes in their speed of thinking and ability to start activities. Example: Parkinson's disease

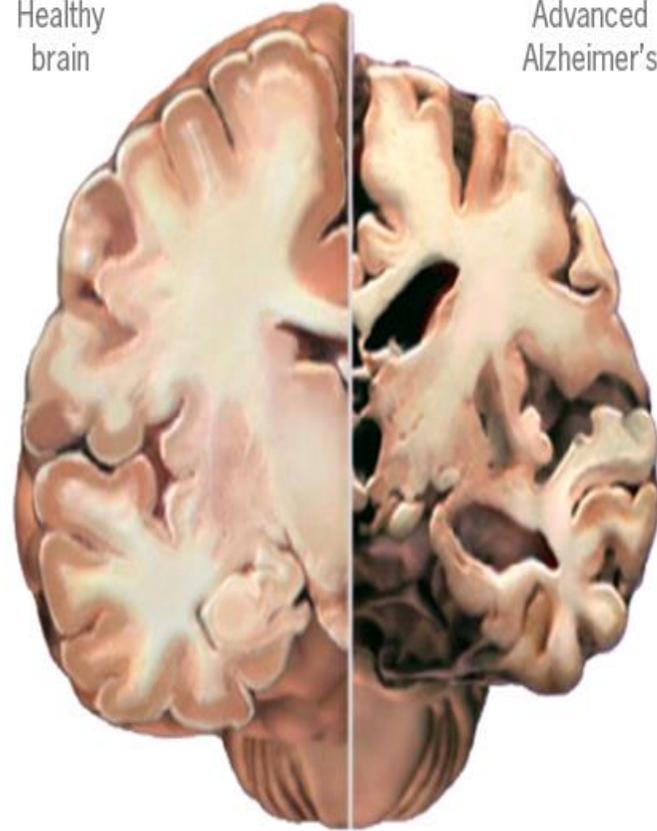


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Three most common types

- Alzheimer's disease - abnormal deposition of insoluble 'plaques' of a fibrous protein called amyloid and twisted fibers called 'neurofibrillary tangles' in the brain; slow onset, several stages
- Vascular disease - It occurs when blood supply to the brain is compromised by arterial disease, which results in reduced neuronal function and eventually the death of brain cells
 - HTN, CVA, Diabetes
 - May be slow or gradual
- Dementia with Lewy bodies – closely associated with Alzheimer's and Parkinson's diseases; small aggregations of a protein called alpha-synuclein that occur in cells in various areas of the brain, including the cerebral cortex in dementia with Lewy bodies; falls and visual hallucinations, paradoxical response to psychotropic drugs

Healthy
brain



Advanced
Alzheimer's

Source: Modified from http://www.alz.org/braintour/healthy_vs_alzheimers.asp

Alzheimer's Disease Definition

- Alzheimer's disease is a progressive disease that destroys memory and other important mental functions. At first, someone with Alzheimer's disease may notice mild confusion and difficulty remembering. Eventually, people with the disease may even forget important people in their lives and undergo dramatic personality changes.

Symptoms

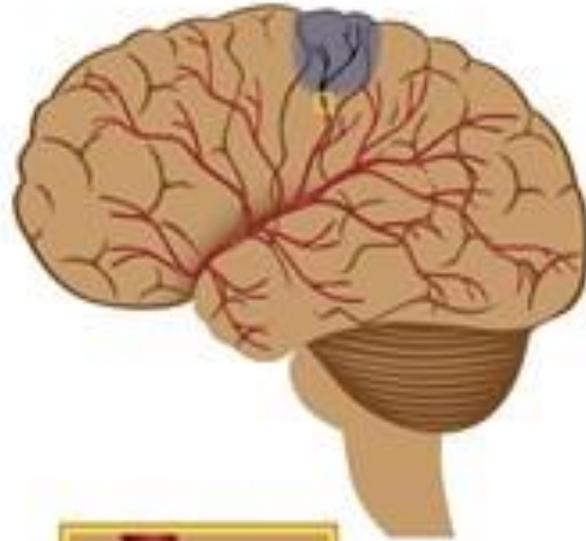
- **Memory**
- Everyone has occasional memory lapses. It's normal to lose track of where you put your keys or forget the name of an acquaintance. But the memory loss associated with Alzheimer's disease persists and worsens, affecting the patient's ability to function at work and at home.
- **Thinking and reasoning**
- Alzheimer's disease causes difficulty concentrating and thinking, especially about abstract concepts like numbers.
- Multitasking is especially difficult
- **Making judgments and decisions**
- Responding effectively to everyday problems, such as food burning on the stove or unexpected driving situations, becomes increasingly challenging.
- **Planning and performing familiar tasks**
- Once-routine activities that require sequential steps, such as planning and cooking a meal or playing a favorite game, become a struggle as the disease progresses. Eventually, people with advanced Alzheimer's may forget how to perform basic tasks such as dressing and bathing.
- **Changes in personality and behavior**

Stages of Alzheimer's Disease

- There are five stages associated with Alzheimer's disease:
 - preclinical Alzheimer's disease
 - mild cognitive impairment due to Alzheimer's disease
 - mild dementia due to Alzheimer's
 - moderate dementia due to Alzheimer's
 - severe dementia due to Alzheimer's

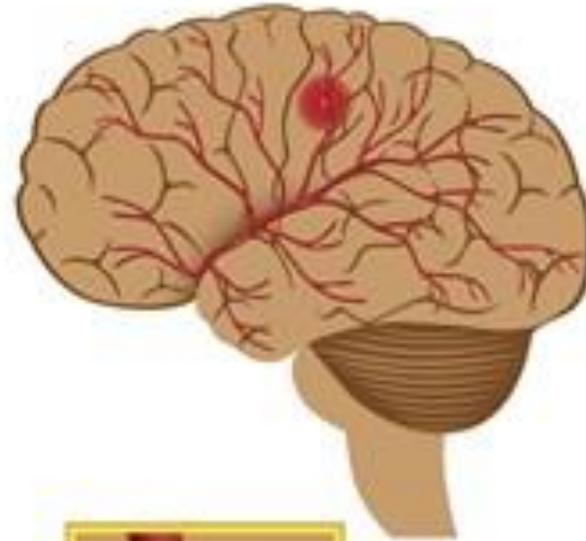
Brain Stroke

Ischemic Stroke



Blockage of blood vessels; lack of blood flow to affected area

Hemorrhagic Stroke



Rupture of blood vessels; leakage of blood

Vascular Dementia Definition

- Vascular dementia is a general term describing problems with reasoning, planning, judgment, memory and other thought processes caused by brain damage from impaired blood flow to the brain.
- Vascular dementia can develop after a stroke blocks an artery in the brain, but strokes don't always cause vascular dementia. Whether a stroke affects thinking and reasoning depends on the stroke's severity and location. Vascular dementia can also result from other conditions that damage blood vessels and reduce circulation, depriving the brain of vital oxygen and nutrients.

• <https://www.mayoclinic.org/diseases-conditions/vascular-dementia/symptoms-causes/syc-20378793>

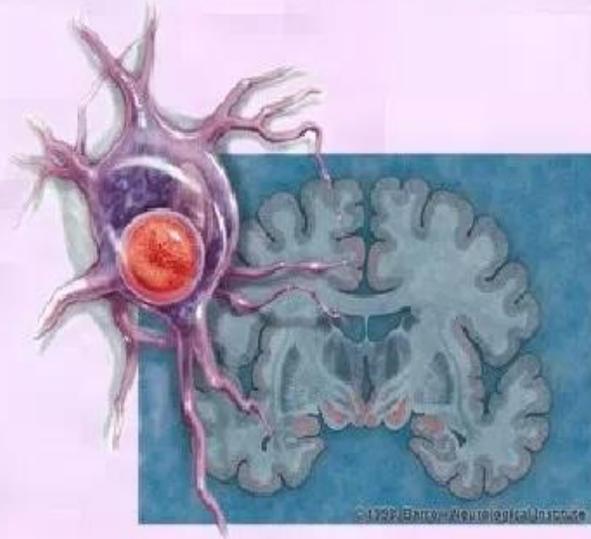
Vascular Dementia Risk Factors

- In general, the risk factors for vascular dementia are the same as those for heart disease and stroke.
- Risk factors for vascular dementia include:
 - Increasing age. The disorder is rare before age 65, and the risk rises substantially by age 90
 - History of heart attack, strokes or ministrokes.
 - Abnormal aging of blood vessels (atherosclerosis).
 - High cholesterol - elevated levels of low-density lipoprotein (LDL), the "bad" cholesterol, are associated with an increased risk of vascular dementia.
 - High blood pressure
 - Diabetes
 - Smoking
 - Obesity
 - Atrial fibrillation

Vascular Dementia Symptoms

- Can have quick onset (post-stroke) or slow
- Confusion
- Trouble paying attention and concentrating
- Reduced ability to organize thoughts or actions
- Decline in ability to analyze a situation, develop an effective plan and communicate that plan to others
- Difficulty deciding what to do next
- Problems with memory
- Restlessness and agitation
- Unsteady gait
- Sudden or frequent urge to urinate or inability to control passing urine
- Depression or apathy

**Lewy bodies are:
Very tiny abnormal protein structures.**



**Lewy body in neuron of
brain.**

Red areas: where Lewy
bodies are found in brain.

**The kind of symptoms (and the disease)
depends on where the bodies reside in the brain**

Lewy Body Dementia

- Factors that increase the risk of developing Lewy body dementia, include:
 - Age > than 60
 - Male gender
 - Family history of Lewy body dementia or Parkinson's disease
 - History of depression
- Complications
- Lewy body dementia is progressive. Signs and symptoms worsen, causing:
 - Severe dementia
 - Aggressive behavior
 - Depression
 - Increased risk of falling and injury
 - Worsening of parkinsonian symptoms, such as tremors
 - Death, on average about eight years after symptoms start

Symptoms Common to Most Dementias

- Amnesia
- Expressive aphasia
- Receptive aphasia
- Agnosia
- Apraxia

Common Behaviors

- Wandering
- Pacing
- Repetition
- Rummaging
- Inappropriate Sexual Behavior

Common Conditions

- Hallucinations
- Delusions
- Agitation
- Catastrophic Reaction
- Sun-downing

Diagnostics

- Alzheimer's – rule out other diseases
- Vascular – CT/MRI
- Lewy Body's – rule out; CT/MRI
- Atypical – depends on presentation

Other Types of Dementia

- Parkinson's Dementia
- Huntington's Dementia
- Early Onset Dementia
- Frontotemporal Dementia
- Normal Pressure Hydrocephalus

Type of Daily Needs for Demented Persons

- Physical
- Creative
- Social
- Sensory
- Productive
- ADL's

Treatments

NONPHARMACOLOGIC THERAPY AND SUPPORTIVE CARE	MEDICATION RECOMMENDATIONS	DRUGS WITH UNPROVEN BENEFIT
<p>Behavioral disturbance — Recognition and treatment of delusions, hallucinations, depression, agitation, aggression, and sleep disturbances are important aspects of the care of patients with dementia</p>	<p>A treatment trial with a cholinesterase inhibitor for patients with mild to moderate dementia (MMSE 10-26)</p> <p>The choice between donepezil, rivastigmine, and galantamine can be based upon cost, individual patient tolerance, and physician experience, as efficacy appears to be similar</p>	<p>Estrogen replacement – A meta-analysis found that women who had menopause symptoms had improvements in verbal memory, vigilance, reasoning, and motor speed with estrogen replacement, but no enhancement of other cognitive functions</p>

Treatments, continued

NONPHARMACOLOGIC THERAPY AND SUPPORTIVE CARE	MEDICATION RECOMMENDATIONS	DRUGS WITH UNPROVEN BENEFIT
<p>Nutrition — Inadequate nutrition is common in patients with Alzheimer disease (AD) and is associated with increased morbidity and mortality. A systematic review found that provision of high calorie supplements can help with weight gain in patients with dementia; however, the limited available data did not support a benefit in regard to functional and survival outcomes</p>	<p>In patients with mild to moderate Alzheimer dementia (AD) who are interested in seeking therapy with vitamins, supplementation with vitamin E (2000 IU daily) suggested</p> <p>The benefits of vitamin E are likely to be modest and could be offset by combination therapy with memantine. Vitamin E is not recommended for other forms of dementia or for the prevention of AD.</p>	<p>Antiinflammatory drugs – Except for one small clinical trial of indomethacin, randomized trials of antiinflammatory medications including, naproxen, hydroxychloroquine, diclofenac, rofecoxib, and aspirin have not found a benefit for these agents in slowing cognitive decline in patients with AD</p>

Treatments, continued

NONPHARMACOLOGIC THERAPY AND SUPPORTIVE CARE	MEDICATION RECOMMENDATIONS	DRUGS WITH UNPROVEN BENEFIT
<p>Exercise programs — Several studies have demonstrated that formal exercise programs may improve physical functioning or at least slow the progression of functional decline in patients with AD; by contrast, exercise programs do not appear to improve cognitive functioning in adults with dementia</p>	<p>In patients with severe dementia (MMSE <10), continuing memantine, given the possibility that memantine may be disease-modifying; in some patients with advanced dementia it may make sense to discontinue administration of medications to maximize quality of life and patient comfort</p>	<p>Statins — While there have been investigations in a potential role of statin therapy in the prevention and treatment of Alzheimer disease, there is as yet, no established role for statins for these indications.</p>

Treatments, continued

NONPHARMACOLOGIC THERAPY AND SUPPORTIVE CARE	MEDICATION RECOMMENDATIONS	DRUGS WITH UNPROVEN BENEFIT
<p>Alcohol — Alcohol can exacerbate cognitive dysfunction and behavioral disturbance in patients with dementia. Patients with dementia, particularly those with mild AD, can sometimes drink to excess because they lose track of how many drinks have been consumed. Limit alcohol consumption to low amounts</p>	<p>Behavioral disturbances are common in individuals with dementia and may respond to symptomatic treatment.</p>	<p>Vitamin B - Supplementation with B vitamins, in particular those that are involved in homocysteine metabolism, have been studied in patients with AD in hopes that they may demonstrate efficacy in preventing or slowing the progression of AD. An 18-month randomized trial of high-dose vitamin B-complex supplementation (folate, B6, B12) in 340 patients with mild to moderate AD found no beneficial effect on cognitive measures</p>

Treatments, continued

NONPHARMACOLOGIC THERAPY AND SUPPORTIVE CARE	MEDICATION RECOMMENDATIONS	DRUGS WITH UNPROVEN BENEFIT
Survival — Dementia shortens life expectancy, although actual survival estimates have varied in different reports.		Omega-3 fatty acids - clinical trials have not supported a therapeutic role for omega-3 fatty acid supplementation in the treatment of AD
Patient education materials - Basics topics (see " Patient education: Dementia (including Alzheimer disease) (The Basics) ") • Beyond the Basics topics (see " Patient education: Dementia (including Alzheimer disease) (Beyond the Basics) ")		

https://www.uptodate.com/contents/treatment-of-dementia?source=search_result&search=dementia&selectedTitle=2~150#H1

MMSE

- https://compendiumapp.com/post_4xQlen-Ly

Coping Tips

- **Monitor personal comfort.** Check for pain, hunger, thirst, constipation, full bladder, fatigue, infections and skin irritation. Maintain a comfortable room temperature.
- **Avoid being confrontational** or arguing about facts. For example, if a person expresses a wish to go visit a parent who died years ago, don't point out that the parent is dead. Instead, say, "Your mother is a wonderful person. I would like to see her too."
- **Redirect the person's attention.** Try to remain flexible, patient and supportive by responding to the emotion, not the behavior.
- **Create a calm environment.** Avoid noise, glare, insecure space and too much background distraction, including television.
- **Allow adequate rest** between stimulating events.
- **Provide a security object.**
- **Acknowledge requests**, and respond to them.
- **Look for reasons behind each behavior.** Consult a physician to identify any causes related to medications or illness.
- **Explore various solutions.**
- **Don't take the behavior personally**, and share your experiences with others.

Case Study #1

- Name: Jamie Bartholomew
- DOB: 3/15/55
- CC: His wife thinks he is getting more forgetful lately. He complains of occasional dizziness

Subjective

- HPI: Last week, his wife says he could not find his way home from work. He wants to know if there is some kind of test you can do to find out if he is going crazy. His wife thinks he is overly worried for nothing. He has not had any seizures since the one he had after his operation in 2014. He has not seen a neurologist in the past 2 years.
- PMH: glioblastoma of the right frontal lobe 2014; CVA of R MCA 2014 & seizure disorder 2014 post-op.
- PSH: brain tumor resection 2014 - Unfortunately, it was wrapped around an artery, so they did not get it all.
- FH: father – deceased at age 82– MI; mother deceased at age 85 – COPD
- SH: married, quit smoking 10 years ago, occasional wine at bedtime; 2 children; he works part-time as a librarian
- Allergies: Sulfa – rash
- Medications: Keppra 500 mg. p.o. BID; ASA 325mg. p.o. Qday
- Immunizations: up to date

What Questions Would You Ask?

- O – onset of the symptoms?
- S – any other symptoms?
- Any falls?
- Incontinency?
- Aggressive?

Answers to Questions

- He has no pain, no headache, no change in vision. Occasional dizziness; no other symptoms
- No recent falls
- He does not use any device to ambulate
- He is occasionally incontinent
- He sleeps well at night
- He does not think he has a memory problem
- His wife says he forgets where he put the keys to the car, and sometimes can't find his way back home
- He sometimes gets upset with her and calls her names, but no physical abuse

Objective

- PE: vital signs are stable; wt. 100 kg.; height 182 cm., BMI – 29 kg/m²
- General physical examination is normal

What is the
next step?

- Assess gait, memory, and do blood work. If blood work negative, consider CT or MRI

DDXs

- Vascular Dementia
- Recurrent brain tumor
- Normal pressure hydrocephalus
- Infection
- Seizure disorder
- Brain injury
- CVA
- Alzheimer's Dementia
- Metabolic abnormalities

Management

- Safety measures
- Behavioral interventions – reminder notes, toileting, familiar objects, adequate lighting, duplicates of important objects made in case they get lost; redirection
- Possible shunt
- Medications
 - Donepezil – mild to moderate disease; SE – GI
 - Galantamine – mild to moderate disease; SE – arrhythmias, bradycardia, urinary obstruction
 - Rivastigmine – mild to moderate disease; SE - GI
 - N-methyl-d-aspartate – moderate to severe disease; SE comparable to placebo
 - Herbal medications – Ginkgo biloba and huperzine A – inconsistent evidence for efficacy, safe alternatives?
- Support group for family
- Respite stay

Case Study #2

- Mrs. SJ is an 80 year-old woman who is brought to the clinic by her husband who is concerned about her memory problems. He first noticed some memory decline a few years ago, but the onset was subtle and did not interfere with her day-to-day activities
- She used to be very active with a ladies' group, but lately has preferred to stay home. She shows little interest in keeping the house clean and tidy, which is unusual for her
- She asks you if you think she has Alzheimer's disease

Subjective

- PMH: Osteoporosis; breast cancer 1998
- PSH: mastectomy secondary to breast cancer
- FH: father – died from alcohol related causes; mother – deceased due to CVA
- SH: married x 60 years; no tobacco use; 1 – 2 glasses of wine daily
- Allergies: none
- Medications: Calcium supplement
- Immunizations and screenings: up to date

What Questions Would You Like to Ask?

- 1.
- 2.
- 3.
- 4.
- 5.

Answers to Questions

- No pain, no recent falls. Does not need help with medication administration, banking or transportation – not interested in driving anymore
- Independent with activities of daily living
- She is worried she has Alzheimer's disease
- She feels low at times, and misses her daughter who died 2 years ago
- Sleeps during the night and sometimes during the day

Objective

- PE: Vital signs are within normal limits
- General physical examination is normal, CN exam – wnl

What Diagnostics Would You Do?

- MMSE, Clock test, CBC, electrolytes, glucose, calcium, liver function tests, folate, vitamin B₁₂, TSH, ESR. Consider syphilis screening if there is a risk factor or evidence of prior infection
- Noncontrast Head CT or MRI
- What other test might you do based on her answers?

Test results

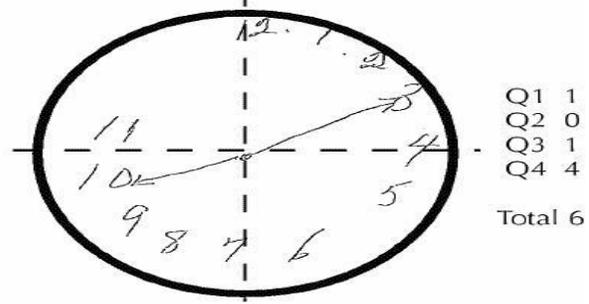
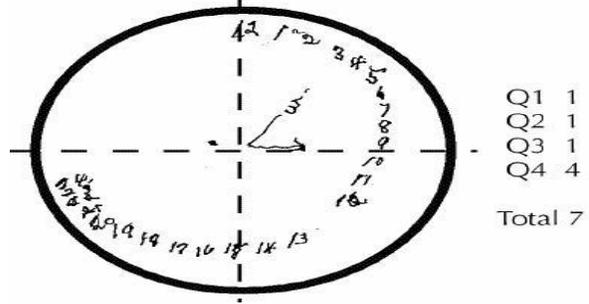
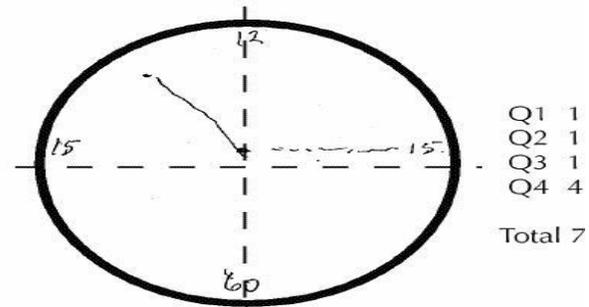
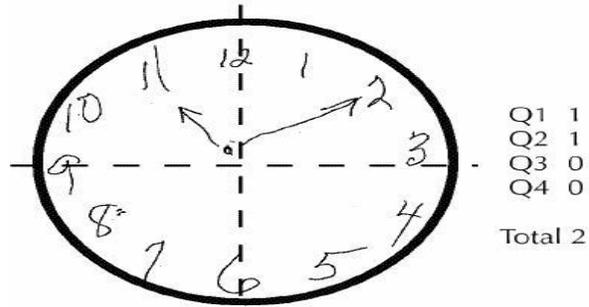
- MMSE 26/30
- Clock test – 2 pts.
- PHQ-9 - 10

MMSE

- https://compendiumapp.com/post_4xQlen-Ly

Method for evaluating clock drawings described by Watson and colleagues¹³

1. Divide the circle into 4 equal quadrants by drawing one line through the centre of the circle and the number 12 (or a mark that best corresponds to the 12) and a second line perpendicular to and bisecting the first.
2. Count the number of digits in each quadrant in the clockwise direction, beginning with the digit corresponding to the number 12. Each digit is counted only once. If a digit falls on one of the reference lines, it is included in the quadrant that is clockwise to the line. A total of 3 digits in a quadrant is considered to be correct.
3. For any error in the number of digits in the first, second or third quadrants assign a score of 1. For any error in the number of digits in the fourth quadrant assign a score of 4.
4. Normal range of score is 0–3. Abnormal (demented) range of score is 4–7.



Differential Diagnoses

- Dementia of Alzheimer type
- Vascular Dementia
- Infection
- Other Types of Dementia
- Depression
- Dementia worry

Management

- Safety measures, determine SI
- Behavioral interventions – increase exercise, re-introduce hobbies, social support, nutrition, counseling for grief therapy
- Medications if behavioral interventions not working
 - SSRI
- Reassurance that to her and her husband that she does not have Alzheimer's disease

Dementia Worry

- AD is second only to cancer as the greatest health fear (see also MetLife Foundation, 2006 MetLife Foundation. (2006). MetLife foundation Alzheimer's survey: What America thinks. Retrieved from <https://www.metlife.com/assets/cao/foundation/alzheimers-2011.pdf>
- Consequently, there is growing media coverage and thus increased public awareness of cognitive aging and related diseases such as dementia and AD. The image conveyed is mostly negative (Peel, 2014 Peel, E. (2014). Individuals suffering from AD are stereotypically seen as incompetent, as are older people in general.
- This phenomenon is now generally referred to as 'dementia worry' (or 'perceived threat of AD') and defined as 'an emotional response to the perceived threat of developing dementia, independent of chronological age and cognitive status' (Kessler et al., 2012 Kessler, E.-M., Bowen, C. E., Baer, M., Froelich, L., & Wahl, H.-W. (2012).

Stereotype Threats

- Members of a stigmatized group, such as older people, will underperform in a particular domain like memory, when they are reminded that “older persons have poor memory”
- Studies have shown that older persons who have a normal score on the MMSE have shown that stereotype threats (ST) can cause older people to perform at pathological levels on executive tasks.
- It becomes very important for clinicians to be cautious when conducting neuropsychological assessments to conclude that the person has Dementia when in fact they are underperforming due to Dementia worry.

Drugs in the Pipeline

- "The drug, known as BAN2401, targets amyloid, a protein that accumulates in the brain and forms plaques that can compromise nerve cells. It was shown to be successful in slowing the progression of mild cognitive impairment in 856 patients with early Alzheimer's.
- "This is the first late-stage, anti-amyloid antibody study to successfully achieve statistically significant results at 18 months, further validating the amyloid hypothesis," Lynn Kramer, chief clinical officer and chief medical officer with the Neurology Business Group at Eisai, which developed the drug along with Biogen, said according to the Washington Post."
- <https://globalnews.ca/news/4357425/alzheimers-dementia-drug-breakthrough/>

Drugs in the Pipeline, continued

- "Building on an earlier breakthrough, Professor Giovanna Mallucci and her team at the University of Cambridge have identified two drugs that can block the death of brain cells in mice with a neurodegenerative disease.
- The researchers also tested the drugs on mice with [frontotemporal dementia](#). They were particularly looking at how drugs affected the protein tau, which forms harmful clumps in several forms of dementia, including [Alzheimer's disease](#). They found that the drugs were also able to prevent the death of brain cells and improve memory abilities in these mice.
- The next steps are for these drugs to be tested in animals that have Alzheimer's disease and to begin testing the antidepressant - already a licensed drug - in people in the earlier stages of Alzheimer's."
- <https://www.alzheimers.org.uk/research/care-and-cure-magazine/new-job-old-drugs>

Drugs in the Pipeline, continued

- A paper was published in *Molecular Psychiatry* (2018) as a collaborative work between two laboratories led by Professor Xin-Fu Zhou, University of South Australia and Professor Yanjiang Wang, the Third Military Medical University.
- "We discovered an increase in the neurotrophin signalling pathway that is related to life and death of nerve cells, known as proNGF/p75, and then found blocking its functions was shown to reduce cell damage.
- "Thus, in this paper we not only discovered a signaling pathway but also invented a potential drug for treatment of such diseases."
- Given this strong evidence now available, the next stage is a clinical trial and South Australian biotech company Tiantai Medical Technology Pty Ltd has recently acquired a licence to further develop and commercialise this medical technology.
- Professor Zhou says this industry involvement means there is an opportunity to translate the discovery into a treatment of Alzheimer's disease and other tauopathies.

The Peanut Butter Test

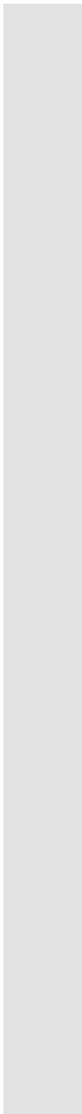
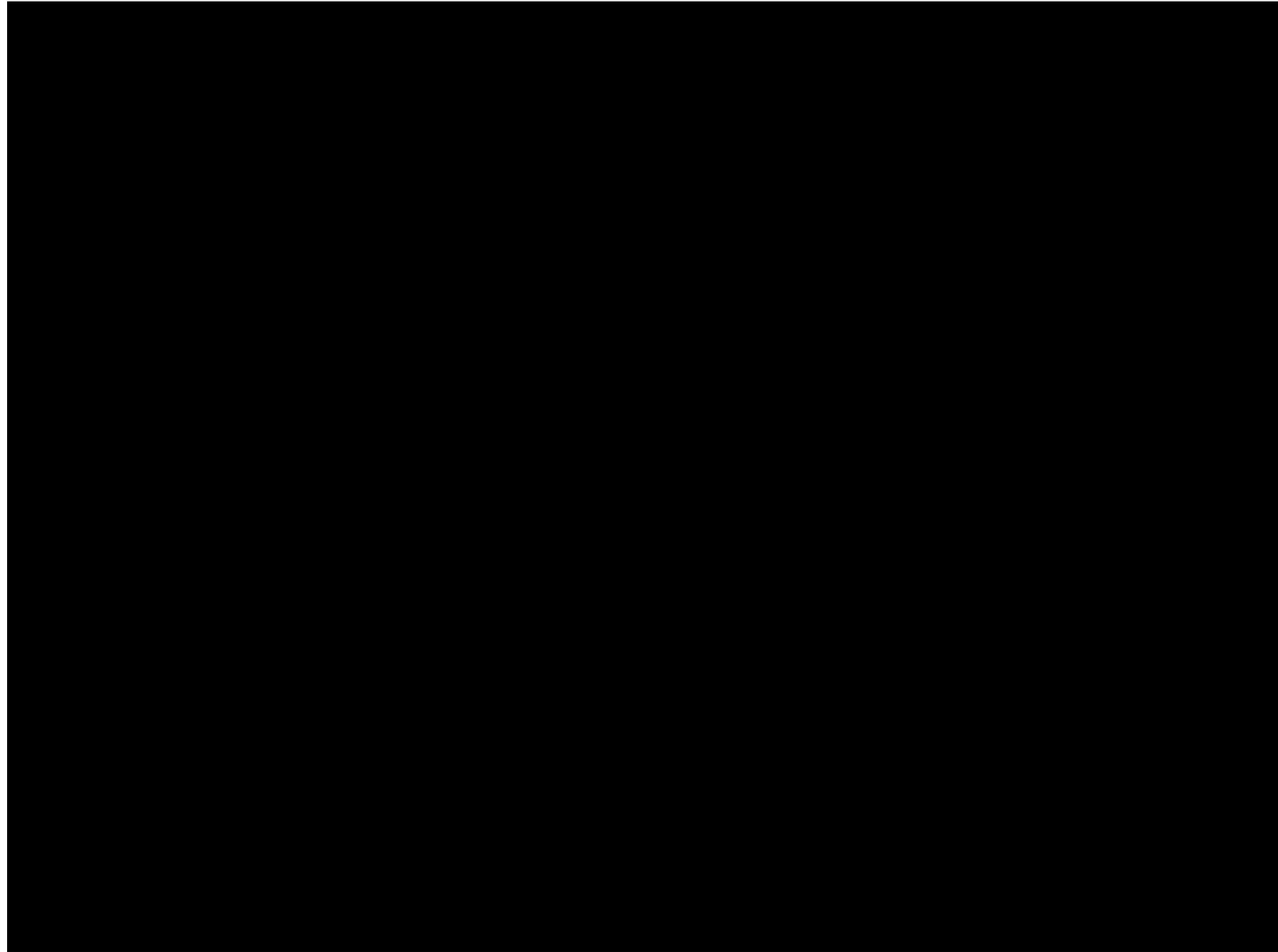
- The ability to smell is associated with the first cranial nerve and is often one of the first things to be affected in cognitive decline.
- The scientists found that patients in the early stages of Alzheimer's disease had a dramatic difference in detecting odor between the left and right nostril -- the left nostril was impaired and did not detect the smell until it was an average of 10 centimeters closer to the nose than the right nostril had made the detection in patients with Alzheimer's disease
- <https://www.sciencedaily.com/releases/2013/10/131010092427.htm>

New Leads for Dementia Research

- Scientists Propose a New Lead for Alzheimer's Research
- Aug. 14, 2018 — Scientists have suggested a potential link between iron in our cells and the rare gene mutations that cause Alzheimer's disease, which could provide new avenues for future research
- Aug. 13, 2018 — The use of benzodiazepines and related drugs (Z drugs) is associated with a modestly increased risk of Alzheimer's disease, according to a recent study from the University of Eastern Finland
- Aug. 9, 2018 — New research has uncovered a higher rate of dementia in older adults after the initiation of hemodialysis. The study, which appears in an upcoming issue of the *Clinical Journal of the American Society of Nephrology (CJASN)*, also found that dementia in dialysis patients is linked with a higher risk of early death.
- Aug. 9, 2018 — A class of cancer drugs called PARP inhibitors could be useful for treating and preventing brain disorders, including amyotrophic lateral sclerosis (ALS), also called Lou Gehrig's disease, and some forms of frontotemporal degeneration (FTD), by halting the misplacement of specific proteins that affect nerve cells, according to a study published in *Molecular Cell* by researchers in the the School of Arts and Sciences and the Perelman School of Medicine at the University of Pennsylvania.
- https://www.sciencedaily.com/news/health_medicine/alzheimer's/

Dementia Jeopardy

- jeopardylabs.com/play/dementia-78



Useful Links

- [US](#)
- <https://www.webmd.com/alzheimers/types-dementia#1>
- https://www.uptodate.com/contents/treatment-of-dementia?source=search_result&search=dementia&selectedTitle=2~150#H1
- [UK](#)
- <http://dementia.ie/information/links>
- [Other sites & Citations](#)
- https://compendiumapp.com/post_4xQlen-Ly
- <https://www.mdcalc.com/phq-9-patient-health-questionnaire-9>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC128397/>
- Megan Fresson, Benoit Dardenne, Marie Geurten & Thierry Meulemans (2017) The effect of stereotype threat on older people's clinical cognitive outcomes: investigating the moderating role of dementia worry, *The Clinical Neuropsychologist*, 31:8, 1306-1328, DOI: [10.1080/13854046.2017.1307456](https://doi.org/10.1080/13854046.2017.1307456)

