Living with younger-onset Alzheimer's: A personal perspective

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alzheimer's association®
Session Overview

Guided Discussion

• Life before the diagnosis
• Diagnostic process
• Life after diagnosis
  • Changes and challenges
• Living well with the disease
Early-Stage experience

- Get Educated
- Sharing the Diagnosis with Others
- Stay Connected/Get Support
- Early Diagnosis
- Planning for the Future

Living Well with Dementia
Before the diagnosis
Before the diagnosis
Receiving the diagnosis

Dealing with the diagnosis

- Frightened
- Sad
- Confused
- Embarrassed
- Overwhelmed
- Denial
- Anger
- What else??
Lessons From My Mom

- Focus on the positive
- Stay busy
- Help Others
- Learn Something New
- Be Thankful!
- Be Cheerful
- Be Forgiving
- Enjoy Family and Friends.
Living well with dementia

- Early Diagnosis
- Get Educated
- Sharing the Diagnosis with Others
- Stay Connected/Get Support
- Planning for the Future
- Acceptance
- You are More than the Diagnosis
- Live Healthy
- Maximize Independence

You are More than the Diagnosis

Maximize Independence
**Impact on identity**

- **Profession**
- **Personality Traits**
- **Hobbies**
- **Relationship**
- **Values & Beliefs**
Live Healthy

Intellectual
- Attend lectures or classes
- Read, write, and journal
- Have discussions
- Play games and puzzles

Emotional
- Express your feelings
- Laugh and joke
- Do things that bring you joy

Social
- Spend time with family
- Talk and interact with friends
- Meet new people

Vocational
- Participate in hobbies
- Volunteer your time/expertise
- Mentor others

Physical
- Get adequate sleep
- Eat a well-balanced diet
- Don’t use tobacco and avoid excessive alcohol

Spiritual
- Engage in prayer, worship or rituals
- Participate in services
- Meditate or reflect
- Spend time in nature
Cynthia’s New Life
Live Healthy: Intellectual/Vocational
National Early-Stage Advisory Group
Clinical trial participation
Live Healthy: Spiritual

- Prayer
- Meditation
- Centering

- Music
- Scripture
- Practice gratitude
Live Healthy: Social/Emotional

• Hobbies
• Time with friends
Live Healthy: Physical

• Physical challenges
• New activities
Handout

How do YOU live well with Alzheimer’s or other dementia?

**Intellectual**
- Attend lectures or classes
- Read, write, and journal
- Play games and puzzles

What do you currently do?

What would you like to try?

What do you need to be successful?

**Social**
- Spend time with family
- Talk and interact with friends
- Meet new people

What do you currently do?

What would you like to try?

What do you need to be successful?

**Physical**
- Stay Active/Exercise
- Get adequate sleep
- Eat a well-balanced diet

What do you currently do?

What would you like to try?

What do you need to be successful?
Maximizing Independence

• Current challenges and how others provide support
  – Living alone with Alzheimer’s
  – Planning for the future
  – Knowing when to walk in front/beside/behind the person with Alzheimer’s
Questions?
Demystifying Dementia: Clinical Presentations & Creative Therapies

Alyssa Vigliotti, B.A.
Medical Student Class of 2019
Penn State College of Medicine
Financial Disclosures

• I have no financial disclosures.
Objectives

• To understand the classification of different types of dementia and how they present clinically
• To identify a range of creative, psychosocial therapies for the treatment of the dementias
• To review evidence for the efficacy of using TimeSlips in dementia care
What is Dementia?

• A disorder characterized by a decline in cognition involving one or more cognitive domains
  • Learning, memory, language, executive function, complex attention, perceptual-motor, social cognition

Photo: http://www.weallhaveuniquebrains.com/intro-to-dementia/
Symptoms & Signs Of Dementia

- You find yourself struggling to remember recent events or dates
- You find it hard to follow conversations or TV shows
- You find yourself forgetting the names of friends or everyday objects
- You find yourself repeating words, and forgetting what you were saying
- You find difficulties thinking and responding
- You feel anxious, depressed or angry and notice behavioral changes
- You feel a decline in the ability to talk, read or write
- You feel confused, even when in a familiar environment

Photo: AdvancedHearing.com
Conclusion: The majority of community-dwelling older persons have brain pathology. Those with dementia most often have multiple brain pathologies, which greatly increases the odds of dementia. *Neurology*® 2007;69:2197-2204
Alzheimer’s Disease

• Most common form of dementia in elderly
• Characteristically a disease of older age
• Memory impairment is the most common initial symptom
Distinctive Memory Impairment

• Loss of episodic memory – memory of events occurring at a particular time and place
  • Memory of Recent Events – lost first
  • Immediate Recall
  • Memory of Distant Events
The Alzheimer Elephant Problem

- It’s amyloid!
- No, it’s tau!
- Yep, amyloid it is!
- Clearly it’s oxidative stress!
- It simply must be amyloid!
- Surely, it’s inflammation!
Diagnosis

- History
- Cognitive testing
- Clock drawing
- Neuropsychologic testing
- Physical Exam
- Rule out Reversible Causes
Dementia with Lewy Bodies

- 2nd most common type of degenerative dementia
- Distinctive features: visual hallucinations, parkinsonism, cognitive fluctuations, sleep disorders
- Memory affected later in the course

[Image of Lewy Body]
Frontotemporal Dementia

- Can present anytime from 2\textsuperscript{nd} to 9\textsuperscript{th} decade
- Associated with progressive change in personality and behavior
- Associated with progressive language and motor difficulties
Vascular Dementia

- Caused by inadequate blood supply to brain
- Clinical manifestations vary
  - Prominent deficits in executive function early in course
- No uniform diagnostic criteria
Parkinson Disease with Dementia

• Executive dysfunction, impaired visuospatial function
  • Less prominent memory dysfunction
  • Preserved language function
• Visual hallucinations
Less Common Disorders

- Creutzfeldt-Jakob disease
- Huntington Disease
- HIV Associated Dementia
Risk Factors for Cognitive Decline

- High blood pressure, diabetes, poor nutrition, social isolation
- Heart disease
- Family history of dementia
- Psychological factors: stress, depression, sense of having little control

Photo: Alzheimer's Society
Pharmacologic Treatments

- Cholinesterase Inhibitors
- Memantine – glutamate receptor antagonist
Unsuccessful Investigational Drugs for Alzheimer’s Disease
1998-2014

Total Unsuccessful Drugs | Total Approved Medicines
123 | 4

Non-Pharmacological Treatments

- Behavioral therapy
- Reality orientation
- Validation therapy
- Reminiscence therapy
- Art therapy
- Music therapy
- Aromatherapy
- Multisensory approaches

Non-pharmacological interventions in dementia
Simon Douglas, Ian James & Clive Ballard
Creative Aging Programs

An offering of programs for adults to engage in creative lifelong learning. Programs explore the rich potential of aging and offer opportunities to impact the community’s health and wellbeing.

ALZHEIMER’S CAFÉ AT FRYE CAFÉ

Enjoy companionship, good food, music, and relaxing fun at the Frye Café, preceded by a Gallery Discussion.

BRIDGES

Home-based creative arts experiences for adults living with dementia.
Therapy Cats for Dementia Patients, Batteries Included

By ANDY NEWMAN | DEC. 15, 2016

Cuddly Robots

They blink, they meow, they snuggle. These cats are therapy robots that provide comfort to elderly dementia patients. By ANDY NEWMAN on December 15, 2016. Photo by Christian Hansen for The New York Times.
Music Therapy
TimeSlips

- Inexpensive, group storytelling program
- Fosters engagement, alertness, and creativity for persons with dementia
- Shown to improve caregiver-resident relationships
Clinical Trials: Dementia

- 50+ clinical trials currently in Pennsylvania
  - Pharmacologic treatments
  - Caregiver support and education
  - Neuroimaging
  - Health Care Use and Costs
- ~300 clinical trials in the United States
10 Ways to Love Your Brain

1. Break a sweat
2. Hit the books
3. Butt out
4. Follow your heart
5. Heads up!
6. Fuel up right
7. Catch some zzz’s
8. Take care of your mental health
9. Buddy up
10. Stump yourself
Objectives

- History of Time Slips
- Creating Time Slips
- Executing/Implementing Time Slips
Time Slips

- The aim of “Time Slips Story Telling” is to inspire seniors and others with dementia to share their imaginations; allow for others to see beyond memory loss; to recognize the strengths of people with dementia; and to improve the quality of life for those with dementia and their caregivers.
Time Slips Facts

- Originally developed in 1998 by Anne Basting, Ph.D.
- This method was designed to find new avenues for imagination and creative expressions for individuals with degenerative mental disorders
- Have participants imagine a story, not remember what happened in the past
Key Time Slip Elements

- Make it a weekly activity
- Follow a format
- Have storytellers sit in a circle
- Make introductions
- Explain the activity
- Reread a previous time slip
Create the Scene

- Eliminate background noise
- Set up a dedicated space
- Have the following items:
  - Sketchpad
  - Bright makers
  - Copies of the picture for each storyteller
Go with the Flow

You do not have to write the story down if you feel it will distract from enjoying the moment.

Options for record keeping:
- Voice recorder
- Note taker
Redefine Story Telling

- Creative story telling does not need a beginning, middle or end
- Characters can have 5 names
- There can be more than one answer
- Words might not make sense

- “It can be scary for people to let go of literal language. But if you can follow to where the person is, you can find a new way to connect to your loved one.” - Anne Basting
What Picture Should I Use?

The more unrealistic the picture the better!

- Try not to use family related photos
  - They raise the possibility of right and wrong answers
- Use large, colorful pictures that are out of the ordinary
- Example:
  - Animals in costumes
Ask the Right Questions!

- The wording of the questions is the most critical.
- Ask open ended questions, such as:
  - “What should we call this person?”
  - “Where are they going?”
  - “What could this be?”
  - “What is going on here?”
Questions to Avoid

- Avoid questions that could be answered with yes or no
- Outlawed questions:
  - “Who is this?”
  - “What is this?”
- Remember: there are no wrong answers
Try, Try, Again

- If the method doesn’t work one day, don’t be afraid to try again
- Engage family members, staff, and volunteers
- Don’t get discouraged
Keep Focused

- The whole idea is creative story telling
- Responses might be negative, crass, incorrect, or bring up family baggage
- Don’t frown upon their answers
- Validate all comments, and move on
Repeat

- Repeat the story they are creating often
- After hearing multiple ideas, create it into a sentence
- Once the story is completed, the facilitator reads the story out loud to the group to make sure they have captured all creativity
- When story is complete, don’t forget to celebrate
Sharing Stories

- Type up the stories and print on a copy of the image
- Have a copy made for each storyteller
- Keep a Time Slip book
- Have family members, volunteers, and staff read the stories
Let’s Get Started!
Other pictures you could use...

- Sometimes the hardest thing to find is the pictures...
- See handouts to get ideas
Let your imagination soar..

“Time slips opens story telling to everyone by replacing the pressure to remember with the freedom to imagine…”

TimeSlip website
Questions?

- Liz Plozner Chalfa
- Liz.PloznerChalfa@junipercommunities.com
- 814-234-3141 ext.5300
Music: A tool for finding joy in living with Alzheimer’s Disease and Dementia

Dr. Rachel A. Cornacchio
Director, Graduate Program in Conducting
Messiah College
Music as Therapy

- Support from the literature
- Stories
- Activities for group and/or private music therapy

- Agitation
- Stress
- Social
- Cognition
- Memory
- Emotion
A Review of Literature
Cognition and Emotion

- regular music activities
- 89 PWD-caregiver dyads
- 10 wk intervention
  - singing, music listening or standard care
- Singing beneficial in improving working memory in mild dementia
- Music listening beneficial in supporting working memory and improving memory in PWD (non AD) with moderate dementia
- Both conditions alleviated depression in PWD with mild dementia
All musically informed intervention strategies in this review have been described as producing positive effects on agitation including improving relaxation, increasing attention span, decreasing pain, and improving social skills of PWD not living in institutions.
an eightweek intervention that had older adults listening to preferred music for 30 min, two times per week, for two weeks, followed by no music for two weeks
demonstrated that agitation levels are significantly reduced after listening to 30 minutes of music.
Building new memory

an 80-year-old violinist with Alzheimer’s type dementia was able to learn and have partial memory of a musical composition he had not known pre-diagnosis.

Access to old memories

the researchers quote a participant who used music as therapy at home with her husband who had dementia: ‘Through the war years we danced a lot and he remembered the old tunes, and of course we shared them a lot in our later years’
music interventions provide an opportunity for the person with dementia to continue to engage with their caregiver in similar ways to what they had prior to a diagnosis

‘... just being able to be together and enjoy and listen to something we both love is a benefit. To share something is a good thing and this is still something we want to do and are able to do...’

the making of music, through singing or the playing of an instrument, was an effective method of expressing one’s emotions without the use of words
Music serves to reduce nonaggressive behaviors of agitation significantly.
Structured movement and rhythm techniques are more effective than singing.
Music can serve as a distraction for agitation: distraction through interaction.
Caregiver Stress

- Individualized music was shown to reduce the stress in caregivers, more than it was for the patient
- Group music therapy enabled caregivers opportunities to share feelings and emotions
Stories
She seldom opens her eyes and is quite unaware of her surroundings. On Sunday when she hears the hymns being sung in church service, tears roll down her cheeks and she is mouthing some of the words.
A quiet little lady who often can be found in the day room, on the piano, picking out some of the melodies she enjoyed back in the 40’s.
When her son visits and plays some of the old hymns and sings the melody, Elsie chimes in with a harmony part, remembering every word of every verse.
He mingles easily with staff and fellow residents, but especially enjoys entertaining the nurses. He stands at the nurses’ station singing “I’m Forever Blowing Bubbles,” “Daisy, Daisy,” “Come Josephine, in My Flying Machine,” with a big grin on his face.
When he knows that there is a musical program in the day room, he quickly summons a nurse to escort him. He listens intently and at the end of every song, loudly calls out, “Very Good!”
Ideas for incorporating music into interactions with patients with ADRD
Singing

Establish routine with hello and goodbye songs
  - Oh what a beautiful morning
  - Goodbye song

Match the mood of the patient with ADRD to the music being listened to or created
  - **high** agitation=fast tempo
  - **relaxed**=slow tempo

Hearing songs sung while using lyric sheets creates better memory of those lyrics
Movement

- Walking while listening to music or singing unaccompanied
- Mimicking dance movements while listening to music
- Incorporate motions into singing
**Instruments**

- Use a variety of percussion instruments to keep time while listening or singing music
  - Elvis
- Provide familiar instruments to those with music backgrounds
- “Play” their name on an instrument
- Tap different moods on drums
  - Etta James
  - Bennett
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<td>1.</td>
<td>Use the same hello and goodbye song to define your time spent</td>
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<td>2.</td>
<td>Often commence with songs that are most familiar</td>
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<td>3.</td>
<td>Key songs should be used to “draw out” specific individuals</td>
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<td>4.</td>
<td>Choose active methods in the middle of each session – movement, instruments</td>
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<td>5.</td>
<td>End with songs that are slower to allow patient with ADRD to feel calm</td>
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Nugent, 2000


History of AD: The Past, Present, and Future

James Siberski MS, CMC
Misericordia University
jsibe@msn.com
NINTH CENTURY B.C. EGYPT

• Earliest known record of chronic forgetfulness

• Third century possible 1st description of Alzheimer’s

• Fourteenth century England 1st verbal exam to screen for memory issues (coming soon)

• Nineteenth century Emil Kraepelin Dementia Praecox
Emma de Beston

- A record of an Examination of Emma de Beston in Cambridge 1383.exists. Emma was asked
- 1. whence she came, said she didn’t know.
- 2. She knew there were seven days in the week but could not name them.
- 3. She said she had had 3 husbands but couldn’t name one.
- 4. She was asked how many shillings there were in 40 pence. she did not know.
- 5. Asked if she would take 40 silver groats or 40 pence she said they were the same value.

They found she was not of sound mind having neither sense nor memory nor sufficient intelligence to manage herself her lands and her goods. By inspection she had the face and countenance of an idiot.
History of AD and other Dementia’s (Neurocognitive Disorder)

Roger Bacon (c. 1220-1292)
- Franciscan friar
- English philosopher
- Oxford professor

- Old age could be thwarted off by:
  - eating a controlled diet
  - proper rest
  - exercise
  - moderation in lifestyle
  - good hygiene
  - inhaling the breath of a young virgin
History of AD and other Dementia’s (Neurocognitive Disorder)

• It’s also widely recognized by historians, including Berchtold and Cotman, that many of the victims of the 17th century witch trials in Europe and the United States who were burned at the stake may have been simply afflicted with dementia.

• Public understanding of dementia didn’t enter the modern age until the German psychiatrist, Alois Alzheimers, described the first case of what we now know as Alzheimer’s Disease in 1910, classifying it as a subtype of “senile dementia.”
Two Biblical Miracle Herbs Now Shown to Help Alzheimer's

- **Rosemary** is known as the “herb of remembrance” and is the plant that once sheltered the Virgin Mary in her flight to Egypt.

- As a Biblical healing plant, it has long been used to enhance memory as well as lessen heart palpitations, increase energy, cure cataracts, and aid many other health problems.

- Ancient healers used **sage** not only to improve memory and brain function, but also for such diverse conditions as heart blockages, infertility, and extending longevity, among others.
ALZHEIMER’S DISEASE
A CENTURY OF SCIENTIFIC AND CLINICAL RESEARCH
The global impact of dementia

Around the world, there will be 9.3 million new cases of dementia in 2015, one every 3 seconds.

- 46.8 million people worldwide are living with dementia in 2015.
- 74.7 million in 2030.
- 131.5 million in 2050.

This number will almost double every 20 years.

Much of the increase will take place in low and middle income countries (LMICs):
- In 2015, 58% of all people with dementia live in LMICs, rising to 64% in 2030 and 68% in 2050.

BUT!

The total estimated worldwide cost of dementia in 2015 is US$ 818 billion. By 2018, dementia will become a trillion dollar disease, rising to US$ 2 trillion by 2030.

If global dementia care were a country, it would be the 18th largest economy in the world exceeding the market values of companies such as Apple and Google.

Much of the increase will take place in low and middle income countries (LMICs):
- In 2015, 58% of all people with dementia live in LMICs, rising to 64% in 2030 and 68% in 2050.

We must now involve more countries and regions in the global action on dementia.

The World Alzheimer Report 2015 was independently researched by King’s College London and supported by Sage.
Declining Dementia Rates

• Senior citizens today are better educated than even half a generation ago

• People with more education tend to earn more money and have better access to health care. They’re less likely to smoke, more likely to exercise and less likely to be overweight. People with more education also may live in safer neighborhoods and have less stress

• People who are better educated may have more intellectually stimulating jobs and hobbies that help exercise their brains
Grim Picture of Alzheimer's in Aging Baby Boomers

• More than 28 million baby boomers will have Alzheimer's disease (AD) by 2050, and they will account for nearly 25% of Medicare spending by 2040, according to a new analysis.

• The risk of Alzheimer's increases with age, and as baby boomers get older — because of the size of the generation — the number of people developing the disease will rise to levels far beyond anything we've seen. The size of this generation is the major factor here.
If it is not AD then what is it?

<table>
<thead>
<tr>
<th></th>
<th>Normal Aging</th>
<th>AD (Alzheimer’s disease)</th>
<th>VaD (Vascular dementia)</th>
<th>DLB (Dementia w/Lewy bodies)</th>
<th>FTLD (Frontotemporal lobe dementia)</th>
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<td></td>
<td>• Reduced speed of mental processing and choice reaction times</td>
<td>• Short-term memory loss, impaired executive function, difficulty with activities of daily living, time and spatial disorientation, language impairment, personality changes</td>
<td>• Impaired abstraction, mental flexibility, processing speed, and working memory</td>
<td>• Visual hallucinations</td>
<td>• Progressive behavioral and personality changes that impair social conduct (apathy, disinhibition, etc.)</td>
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<td>• Benign forgetfulness that is mild, inconsistent, and not associated with functional impairment</td>
<td>• Verbal memory is better preserved</td>
<td>• Slower cognitive decline</td>
<td>• Spontaneous parkinsonism</td>
<td>• Language impairment</td>
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<td>• Dementia occurs within several months of a stroke</td>
<td>• Memory impairment is not as severe</td>
<td>• Cognitive fluctuations</td>
<td>• Possibly preserved episodic memory</td>
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<td>• Earlier presentation of psychosis and personality changes</td>
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<td>• REM sleep disturbances</td>
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1. □ memory complaints
   □ Objective memory loss (MMSE: MOCA: )
   □ Preservation of function
   □ General condition normal
   □ no other explanation for memory loss

2. □ Cognitive decline within 3 months of CVA / TIA
   □ Focal neurological symptoms
   □ Focal neurological signs
   □ Abrupt onset / stepwise decline
   □ Previous CVA or TIA

3. □ Visual hallucinations – (detailed / recurrent)
   □ Pronounced fluctuation in cognition over hours / days
   □ Parkinsonism (especially rigidity) /
     bradykinesia
   □ Executive function worse than memory
   □ Neureleptic sensitivity
   □ Unexplained falls / loss of consciousness

4. □ Behavioral changes: disinhibition / apathy
   □ Impulsivity / poor judgment
   □ Self neglect / socially inappropriate
   □ Executive function worse than memory
   □ Language problems
   □ Abnormal gait

5. □ Incontinence early in course of dementia
   □ Rapidly progressing dementia
   □ Gait abnormality

Mild cognitive impairment (MCI)
Vascular Dementia (VAD)
Mixed AD/VAD
Lewy Body
Dementia
Frontotemporal Dementia
Normal Pressure Hydrocephalus

• An extended family in Colombia with a genetic mutation causing Alzheimer’s may help scientists prevent the disease someday
Alzheimer’s Disease Theories

• No new drug has been marketed for nearly 20 years
• A number of theories have been proposed to explain the cause of AD but to date, no one theory can adequately explain all aspects of the disease
• Precise mechanisms for AD progression are also unclear
• There are 3 major theories (Cholinergic, Amyloid, Tau) that are currently regarded as the most likely explanation for AD
• They are being used as the basis for therapeutic development
Amyloid Cascade Hypothesis

• This has been the main focus of research to date
• Beta-amyloid (Aβ) is the main component of amyloid plaques (one of the pathological hallmarks of AD)
• Scientists now have a detailed understanding of how this protein fragment is clipped from it’s parent compound amyloid precursor protein (APP) by two enzymes – beta-secretase and gamma-secretase
• Researchers are developing medications aimed at every point in the amyloid processing pathway
Neurofibrillary Tangles (NFT’s)

- It has been postulated that after the deposition of amyloid plaques that a cascade ensues
- This leads to inflammation and ultimately formation of neurofibrillary tangles (NFT’s) – the other major hallmark of AD
- This causes problems with neurotransmitters and neuronal function in the brain and ultimately neurone death
Anti-Amyloid strategies - Immunotherapy

• Initial studies showed that injecting animals with beta-amyloid lead to a good antibody response and clearing of the amyloid plaques from their brains

• Subsequent human studies were prematurely ceased (2002) due to development of brain inflammation (meningoencephalitis) in 6%

• However, there was evidence that the treatment had removed amyloid plaque

• The concept of active immunization hasn’t been abandoned yet – several pharmaceutical companies are in the early phases of developing new active vaccines  MORE LATER
Far fewer drug trials have focussed on tau
Interest has grown recently because of difficulties with anti-Aβ treatments
Mouse and primate models of AD show amyloid plaques that respond to anti-amyloid therapy but these animal models don’t replicate the tau pathology seen in human AD
Aged dogs develop an AD-like disorder with amyloid and NFT’s
Treatment of these animals with anti-amyloid therapies reduces plaque load but doesn’t alter cognition or change tau pathology
There is a very robust correlation between tau pathology and clinical measures of dementia
Methylthioninium Chloride (Methylene Blue)

- First drug targeting tau
- Drug is derived from the dye used to stain NFT’s in neuropathological studies
- Primarily inhibits tau aggregation
- Phase 2 study showed cognitive benefits
- SPECT and FDG-PET results also encouraging
- Phase 3 trial for mild-moderate AD (both TQEH and RAH finished recruiting) will be finished February 2016
Other tau therapies

• Several other drugs that inhibit the development of tau have been studied.
• Observational studies in geriatric patients taking chronic lithium for BPAD were found to have reduced risk of developing AD.
• Lithium inhibits chemical changes in tau that leads to formation of NFT’s.
• Studies on Lithium have been mixed – some have shown benefit with very low doses in mild cognitive impairment, others have shown worsening confusion – further studies are needed.
Neurotransmitters and Receptors

• Serotonergic receptor in the brain is a promising drug target for Alzheimer’s Disease
• There is good evidence that this receptor is involved in memory and learning
• Some research suggests that these inflammatory processes are the underlying cause of AD and that it leads to Aβ and tau accumulation
• Large number of therapeutic trials of NSAID’s in AD (1993-2004) incl: Ibuprofen, indomethacin, naproxen, celecoxib, rofecoxib and other anti – inflammatory meds such as prednisolone
• All were negative
Vitamins and Anti-oxidants

• In 2014 a group of Oxford University researchers assembled all the best clinical trial data involving 22,000 people and concluded that taking B vitamins and folate doesn’t slow mental decline as we age, nor is it likely to prevent AD

• Vitamin D – primarily has functions in bone health and metabolism but may also have anti-oxidant and anti-inflammatory properties

• not clear whether Vitamin D deficiency is causally related to cognition or is a marker for another process

• not confirmed that Vitamin D supplementation will have positive effect on cognition
Vitamins and Anti-oxidants

- Vitamins E, C and beta-carotene (pre-cursor for Vitamin A) – all powerful anti-oxidants
- Multiple clinical trials provide evidence that supplements with these compounds did not alter cognitive outcomes in MCI, AD or healthy elderly but results still debated
- Ginkgo-biloba has been studied in trials
  - Reasonably firm evidence that it does not alter the risk of dementia or improve cognitive
- Omega-3 fatty acids found in fish oil and nuts – thought to be neuroprotective
  - Studies have failed to show any improvement in cognition in AD patients
  - In elderly without AD – inconclusive evidence that they may slow cognitive decline
Mediterranean diet

• This diet is rich in fruits, vegetables, olive oil, legumes, whole grains and fish

• Studies have shown that people that closely follow a Mediterranean diet are less likely to have AD than those who don’t

• Research suggests that a Mediterranean diet may –
  -slow cognitive decline in older adults
  -reduce the risk of MCI progressing to AD
  -slow the progression of AD and prevent disease-related deaths
Diet in Alzheimer’s Disease

• A recent study looked at 3 different diets:
  1. Mediterranean diet
  2. DASH diet (designed to treat hypertension – low salt and sugar)
  3. MIND diet (Combination of the above 2 diets)- emphasizes natural plant-based foods, limited saturated fats, encourages consumption of berries and green leafy vegetables (known to specifically benefit brain health)
Diet in Alzheimer’s Disease

• People that strictly followed any of these 3 diets had a lower risk of AD
• Even a modest adoption of the MIND diet approach such as eating 2 vegetable servings per week, 2 berry servings per week and one fish meal per week appeared to lower the risk of AD
• Researchers speculate that making healthy food choices may improve cholesterol and blood sugar levels and overall vessel health which may in turn reduce risk of MCI and AD
• Another theory is that a Mediterranean diet may help prevent brain tissue loss
• More studies are needed to know to what degree this diet prevents AD or slows cognitive decline
“Brain Training”

• This is quite broad and can include a range of structured mentally stimulating activities such as:
  ➢ crosswords
  ➢ learning a new language
  ➢ reading a book
  ➢ undertaking further education
  ➢ dedicated computerised brain training activities that focus on memory, attention or other cognitive functions
• Recent studies have found that “computerised brain training” is only modestly effective at improving cognitive performance in healthy older adults
• Further studies are about to start to see whether intensive computerised training can stop the progress of cognitive decline and the onset of dementia
Integrated Cognitive Stimulation and Training Program

- Integrated Cognitive Stimulation and Training Program (ICSTP) utilizing computer based programs, blended with paper and pencil exercises generally had positive effects on cognitive and memory functioning scores compared to a matched control group in individuals aged 65 years and above.

- These effects were sustained with no additional treatment after eight weeks.

- Statistically significant improvements of scores on the Dementia Rating Scale occurred for mildly and moderately impaired treatment participants.
Brain Training Protects Against Cognitive Decline, Dementia

• A cognitive training program targeting speed of processing in healthy elderly adults cut the risk for dementia nearly in half over a 10-year period in the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study

• The speed training used in the ACTIVE study is available as an exercise called Double Decision. It is one of the exercises in BrainHQ www.brainhq.com, an online cognitive training program from Posit Science.
The stimulation electrodes are implanted chronically. DBS is an established therapeutic option in Parkinson’s disease, dystonia, and tremor. DBS has evolved to be one of the most effective treatments in Parkinson disease.

Deep transcranial magnetic stimulation (dTMS), already approved for treatment-resistant depression, is proving beneficial for obsessive compulsive disorder (OCD), adult attention-deficit/hyperactivity disorder (ADHD), and other psychiatric conditions, according to new research.
Deep transcranial magnetic stimulation (dTMS), already approved for treatment-resistant depression, is proving beneficial for obsessive compulsive disorder (OCD), adult attention-deficit/hyperactivity disorder (ADHD), and other psychiatric conditions, according to new research.

Patients with Alzheimer's disease (AD) who received repetitive transcranial magnetic stimulation (rTMS) to the prefrontal cortex experienced improved auditory sentence comprehension, results of a new study suggest. The improvement was apparent after 2 weeks and persisted for 8 weeks.

It is likely that brain stimulation might interact with the intrinsic ability of the brain to restore damaged functions, by increasing the recruitment of compensatory functional networks and the plasticity of the system.
Co morbid conditions

VNS was originally developed as a treatment for epilepsy. However, scientists noticed that it also had favorable effects on mood, especially depressive symptoms.

DBS has been studied as a treatment for depression or obsessive compulsive disorder (OCD).
TMS AND ECT

Neuronix’s neuroAD is already commercially available in Europe, Asia and Israel for slowing disease progression in mild to moderate Alzheimer cases.

The novel technology combines transcranial magnetic stimulation (TMS) and cognitive training of specific brain regions to slow the rate of mental deterioration in patients with mild to moderate Alzheimer’s and other neurodegenerative disorders. Study participants received the intervention daily for six weeks.

Prolonging Remission in Depressed Elderly (PRIDE) study continue to support the use of right unilateral electrode placement and ultrabrief pulse stimuli as an optimal means of achieving a rapid response, and even remittance, within a week of delivering three courses of electroconvulsive therapy (ECT) in geriatric patients with major unipolar depression.
A Combo Therapy for Agitation in Alzheimer Disease

• Researchers from the Cleveland Clinic have published a preliminary 10-week randomized trial assessing the efficacy of dextromethorphan hydrobromide (Syrup is a combination of an antihistamine and a cough suppressant)/quinidine sulfate (Quinidine is an oral drug that’s used to treat and prevent irregular heart rate. Quinidine sulfate can also be used to treat malaria) in reducing agitation in patients with probable Alzheimer disease

• 88% of the patients completed the study.

• The results showed significantly reduced measures of agitation, including occurrence and severity of symptoms.

• Patients treated with only dextromethorphan/quinidine had an average of 51% reduction in the measure of agitation from baseline to week 10 compared with a 26% reduction in those treated only with placebo.

• The rate of adverse events was relatively low but included falls, diarrhea, and urinary tract infections.
"Your green pills are all gone. Do you wanna take a blue and a yellow?"
• Targeting multiple disease-related proteins is an important new approach. If you think about what we are doing today, we are really targeting Alzheimer's disease with one target, one drug, and we see a potential for incremental benefit, but we are going to need a combination approach.

• All major diseases that have been successfully treated or cured have had a combination therapy approach. Alzheimer's is not going to be any different,"
The Program!

• The 36-point program is personalized to each patient, based on test results that indicate what might be affecting the plasticity signaling network of that patient’s brain. Interventions are comprehensive and, for one patient, included:
  • Eliminating simple carbohydrates, gluten, and processed food from her diet
  • Adding yoga, meditation, and exercise
  • Increasing intake of fruits, vegetables, and fish
  • Sleeping 7 to 8 hours a night
  • Taking methylcobalamin, vitamin D3, fish oil, and CoQ10 each day and, at night, melatonin
  • Switching to an electric flosser and toothbrush
  • Reinstating hormone replacement therapy
  • Fasting 12 hours between dinner and breakfast and 3 hours between dinner and bedtime
  • Within 3 to 6 months after the program’s start, a participant and 8 other participants showed marked improvement that was sustained throughout the study, the longest patient follow-up lasting 2.5 years
F, female; M, male; 3/3, ApoE 3/3; 4/3, ApoE 4/3; C677T, the C677T mutation in methylene tetrahydrofolate reductase (MTHFR); FH, family history; aMCI, amnestic mild cognitive impairment; SCI, subjective cognitive impairment; FDG-PET+, fluorodeoxyglucose positron emission tomography interpreted as typical of Alzheimer's disease; amyloid PET+, amyloid PET scan read as abnormal, indicative of amyloid accumulation; NPsych+, quantitative neuropsychology tests showing abnormalities typical of AD; MoCA, Montreal Cognitive Assessment; MemTrax, an iPhone

<table>
<thead>
<tr>
<th>Patient</th>
<th>History, evaluation</th>
<th>Diagnosis</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>67F 3/3</td>
<td>2yr memory ?; FH+</td>
<td>aMCI</td>
<td>Normal x 2.5 yrs; working</td>
</tr>
<tr>
<td>69M 4/3</td>
<td>12yr memory ↓; FDG-PET+, NPsych+</td>
<td>Early AD</td>
<td>&quot;Clearly improved;&quot; working</td>
</tr>
<tr>
<td>70M 4/3</td>
<td>4yr memory ↓; NPsych+, failed MemTrax</td>
<td>AD</td>
<td>Improved; MemTrax passed</td>
</tr>
<tr>
<td>75M 3/3</td>
<td>1yr memory ↓</td>
<td>SCI</td>
<td>Improved; working</td>
</tr>
<tr>
<td>75F C677T</td>
<td>1yr memory ↓</td>
<td>aMCI/early AD</td>
<td>Improved</td>
</tr>
<tr>
<td>55F 3/3</td>
<td>4yr memory ↓</td>
<td>aMCI/early AD</td>
<td>Normal; working</td>
</tr>
<tr>
<td>72M 3/3</td>
<td>7yr memory ↓</td>
<td>aMCI</td>
<td>Improved; working</td>
</tr>
<tr>
<td>55M 4/3</td>
<td>2yr memory ↓</td>
<td>SCI</td>
<td>Normal; working</td>
</tr>
<tr>
<td>63F 4/3</td>
<td>FH dementia, mild memory ↓</td>
<td>SCI</td>
<td>Normal, negative amyloid PET; working</td>
</tr>
<tr>
<td>60F 4/3</td>
<td>4yr rapid decline; MoCA 6, amyloid PET+</td>
<td>Late AD</td>
<td>Decline</td>
</tr>
</tbody>
</table>
Assessment

Sensory Memory
- Sight
- Smell
- Sound
- Taste
- Touch

Short-Term Memory
- Attention
- Rehearsal
- Elaboration and Organization

Long-Term Memory
- Retrieval

Lost

Lost
Assessment

Cognitive tests
Behavior tests
Neuro exam
Objective tests

History
Dementia Work-Up

• H&P
• **Objective** cognitive measurement (Computer Testing)
• Diagnostics
  • Labs
  • Imaging ?
  • More specific testing (e.g., neuropsychometric)?
• Diagnosis
• **Family** meeting
New Checklist Tests Behavior Change as First Sign of Dementia (MBI-C)

- Mild behavioral impairment (MBI), not memory woes, may be the first sign of mild cognitive impairment (MCI) or dementia

- MBI is defined as a syndrome of neuropsychiatric symptoms (NPS) that start later in life and are sustained for at least 6 months.

- Not a blip in behavior or reacting to a loss, but a real, meaningful change in behavior

- Evidence shows that older adults with normal cognition and neuropsychiatric symptoms are more likely to become cognitively impaired and develop MCI than are people without neuropsychiatric symptoms
**Mild Behavioral Impairment Checklist (MBI-C)**

Date: 

Rated by: 
- Clinician
- Informant
- Subject

Location: 
- Clinic
- Research

Circle “Yes” **only** if the behavior has been present for at least 6 months (continuously, or on and off) and is a **change** from her/his longstanding pattern of behavior. Otherwise, circle “No”.

Please rate severity: 1 = **Mild** (noticeable, but not a significant change); 2 = **Moderate** (significant, but not a dramatic change); 3 = **Severe** (very marked or prominent, a dramatic change). If more than 1 item in a question, rate the most severe.

<table>
<thead>
<tr>
<th>This domain describes interest, motivation, and drive</th>
<th>YES</th>
<th>NO</th>
<th>SEVERITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has the person lost interest in friends, family, or home activities?</td>
<td>Yes</td>
<td>No</td>
<td>1 2 3</td>
</tr>
<tr>
<td>Does the person lack curiosity in topics that would usually have attracted her/his interest?</td>
<td>Yes</td>
<td>No</td>
<td>1 2 3</td>
</tr>
<tr>
<td>Has the person become less spontaneous and active — for example, is she/he less likely to initiate or maintain conversation?</td>
<td>Yes</td>
<td>No</td>
<td>1 2 3</td>
</tr>
<tr>
<td>Has the person lost motivation to act on her/his obligations or interests?</td>
<td>Yes</td>
<td>No</td>
<td>1 2 3</td>
</tr>
<tr>
<td>Is the person less affectionate and/or lacking in emotions when compared to her/his usual self?</td>
<td>Yes</td>
<td>No</td>
<td>1 2 3</td>
</tr>
<tr>
<td>Does she/he no longer care about anything?</td>
<td>Yes</td>
<td>No</td>
<td>1 2 3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>This domain describes mood or anxiety symptoms</th>
<th>YES</th>
<th>NO</th>
<th>SEVERITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has the person developed sadness or appear to be in low spirits? Does she/she have episodes of tearfulness?</td>
<td>Yes</td>
<td>No</td>
<td>1 2 3</td>
</tr>
<tr>
<td>Has the person become less able to experience pleasure?</td>
<td>Yes</td>
<td>No</td>
<td>1 2 3</td>
</tr>
<tr>
<td>Has the person become discouraged about their future or feel that she/he is a failure?</td>
<td>Yes</td>
<td>No</td>
<td>1 2 3</td>
</tr>
<tr>
<td>Does the person view herself/himself as a burden to family?</td>
<td>Yes</td>
<td>No</td>
<td>1 2 3</td>
</tr>
<tr>
<td>Question</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>-----</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>Has the person become more easily frustrated or impatient? Does she/he have troubles coping with delays, or waiting for events or for their turn?</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Does the person display a new recklessness or lack of judgement when driving (e.g. speeding, erratic swerving, abrupt lane changes, etc.)?</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Has the person become more stubborn or rigid, i.e., uncharacteristically insistent on having their way, or unwilling/unable to see/hear other views?</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Is there a change in eating behaviors (e.g., overeating, cramming the mouth, insistent on eating only specific foods, or eating the food in exactly the same order)?</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Does the person no longer find food tasteful or enjoyable? Are they eating less?</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Does the person hoard objects when she/he did not do so before?</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Has the person developed simple repetitive behaviors or compulsions?</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Has the person recently developed trouble regulating smoking, alcohol, drug intake or gambling, or started shoplifting?</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
</tr>
</tbody>
</table>

**This domain describes following societal norms and having social graces, tact, and empathy**

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has the person become less concerned about how her/his words or actions affect others? Has she/he become insensitive to others’ feelings?</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Has the person started talking openly about very personal or private matters not usually discussed in public?</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Does the person say rude or crude things or make lewd sexual remarks that she/he would not have said before?</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
University of Pennsylvania Smell Identification Test (UPSIT)

• Clearly, odor identification impairment is an early sign of Alzheimer's disease and can be used to supplement a diagnostic workup

• The UPSIT involves scratching a surface, sniffing the odor that's released, and identifying it from a multiple-choice list. The test is scored from 0 (no correct answer) to 40 (all answers correct).

• A low score indicates a decreased ability to correctly identify odors.

• The loss of odor identification, which is based on memory, is not the same as an impaired sense of smell

• The sense of smell does get impaired in AD, but not until much later in the disease

• The full UPSIT, which takes about 20 minutes to complete

• There are many false-positives in, for example, heavy smokers, those with a respiratory infection, and those with certain other conditions
MMSE vs. MoCA

• Both stage AD as mild, moderate, or severe

  ▪ MoCA emerging as the preferred brief assessment tool
    ▪ Superior sensitivity in detecting mild cognitive impairment
    ▪ Increased sensitivity to executive & language dysfunction

  ▪ Sensitivity and Specificity (%) MoCA and MMSE:

<table>
<thead>
<tr>
<th>Group (n)</th>
<th>≥ 26</th>
<th>&lt; 26</th>
<th>&lt; 26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal controls (90)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild Cognitive Impairment (94)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alzheimer’s Disease (93)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MoCA</td>
<td>87</td>
<td>90</td>
<td>100</td>
</tr>
<tr>
<td>MMSE</td>
<td>100</td>
<td>18</td>
<td>78</td>
</tr>
</tbody>
</table>
Screening Tool Selection

Montreal Cognitive Assessment (MoCA)
• Sensitivity: 90% for MCI, 100% for dementia
• Specificity: 87%

St. Louis University Mental Status (SLUMS)
• Sensitivity: 92% for MCI, 100% for dementia
• Specificity: 81%

Mini-Mental Status Exam (MMSE)
• Sensitivity: 18% for MCI, 78% for dementia
• Specificity: 100%

Larner 2012; Nasreddine et al., 2005; Tariq et al., 2006; Ismail et al., 2010
MoCA Scoring: Sam

Montreal Cognitive Assessment (MoCA)
Version 7.1 Original Version

Visual-Spatial/Executive

- Copy cube
- Draw clock (ten past eleven)

Score: 4/5

Naming

- Rhinoceros
- Lion
- Camel

Score: 3/3
MoCA Scoring: Sam

<table>
<thead>
<tr>
<th>MEMORY</th>
<th>Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FACE</td>
</tr>
<tr>
<td>1st trial</td>
<td>✔</td>
</tr>
<tr>
<td>2nd trial</td>
<td>✔</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ATTENTION</th>
<th>Read list of digits (1 digit/sec.). Subject has to repeat them in the forward order</th>
<th>Subject has to repeat them in the backward order</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[ ✔ ] 2 1 8 5 4</td>
<td>[ ✔ ] 7 4 2</td>
</tr>
<tr>
<td></td>
<td>2/5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LANGUAGE</th>
<th>Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[ ] FBACMNAAJKLBAKDEAAAAJAMQFAAB</td>
</tr>
<tr>
<td></td>
<td>0/71</td>
</tr>
</tbody>
</table>

| SERIAL 7 SUBTRACTION STARTING AT 100 |
| [ ✔ ] 93                                |
| [ ] 86                                  |
| [ ] 64                                  |
| [ ] 179                                 |
| [ ] 72                                  |
| [ ] 64                                  |
| [ ] 56                                  |
| 4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt |
| 2/3                                      |

<table>
<thead>
<tr>
<th>ABSTRACTION</th>
<th>Similarity between e.g. banana - orange = fruit [ ] train - bicycle [ ✔ ] watch - ruler</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1/2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DELAYED RECALL</th>
<th>Has to recall words WITH NO CUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>FACE</td>
<td>VELVET</td>
</tr>
<tr>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ORIENTATION</th>
<th>[ ✔ ] Date</th>
<th>[ ✔ ] Month</th>
<th>[ ✔ ] Year</th>
<th>[ ✔ ] Day</th>
<th>[ ✔ ] Place</th>
<th>[ ✔ ] City</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6/6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

© Z. Nasreddine MD
www.mocatest.org
Normal ≥ 26 / 30
TOTAL 2/30
Add 1 point if ≤ 12 yr. ed.
Diagnosis – Based on data

• Rule out reversible causes B12, thyroid, Vitamin D, NPH etc.
• Alzheimer's patients taking both cholinesterase inhibitors and anticholinergic medications, may have no benefits as these two drugs antagonize each other, and neither will work
• Medications with strong anticholinergic side effects are well known for causing cognitive impairment in AD patients
• Rule out delirium
  • Minor Neurocognitive Disorder - 1-2 SD < mean, 0.5 SD decline from patient’s baseline
  • Major Neurocognitive Disorder - > 2 SD below mean
  • Due to what?????????????????
National Institute on Aging (NIA) have issued the first new criteria and guidelines to diagnose Alzheimer's disease in 27 years

- New stages
- **Stage 1** — asymptomatic cerebral amyloidosis;
- **Stage 2** — amyloidosis plus evidence of "downstream" neurodegeneration; and
- **Stage 3** — amyloidosis, neuronal injury, plus subtle cognitive/behavioral decline.
National Institute on Aging (NIA) have issued the criteria and guidelines to diagnose Alzheimer's disease.

- **Stage 1**: Asymptomatic amyloidosis
  - High PET amyloid tracer retention
  - Low CSF Aβ1-42

- **Stage 2**: Amyloidosis + Neurodegeneration
  - Neuronal dysfunction on FDG-PET/fMRI
  - High CSF tau/p-tau
  - Cortical thinning/Hippocampal atrophy on sMRI

- **Stage 3**: Amyloidosis + Neurodegeneration + Subtle Cognitive Decline
  - Evidence of subtle change from baseline level of cognition
  - Poor performance on more challenging cognitive tests
  - Does not yet meet criteria for MCI

**MCI ➔ AD dementia**
Treatment

• Look for co-morbid, apnea, depression, infections, sleep problems etc.
• Treat co-morbid
• Avoid unnecessary drugs.. Do not medicate staff anxiety
• End stage think hospice
• Use it or lose it - Use it and improve it (function)
• Avoid excess disability
Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo.
Drugs that prevent the breakdown of acetylcholine, a brain chemical involved in memory & other functions related to thinking

- ↑ acetylcholine = ↑ cognitive abilities

FDA-approved medications*

- Donepezil (Aricept)
- Galantamine (Razadyne)
- Rivastigmine (Exelon)

*Tacrine, the first cholinesterase inhibitor approved in 1993, is rarely used now due to its potential to cause liver damage
Normal Brain Cells

Neurotransmitters (AChE) - being sent - message being communicated to the next cell
Normal Brain Cells

Once the message is sent, then enzymes lock onto the messenger chemicals and take them out of circulation so a new message can be sent.
Brain Cells with Alzheimer’s

- Plaques
- Tangles
- Less neurotransmitter
- Further to go to get to the next cell

Enzymes (AChE inhibitors) – get to them BEFORE they deliver their message
What do Alzheimer’s drugs DO?

Alzheimer’s drugs provide FAKE messenger chemicals that distract the enzymes. They attach to the Fake AChE & the message can get thru.

*Aricept, Exelon, Razadyne*
For Patients With Dementia: To E or Not to

• Vitamin E (alpha-tocopherol) stands out as having the greatest evidence for possible benefit in slowing down the progression of AD and other forms of dementia.

• Vitamin E is an antioxidant and may mitigate the oxidative stress that is thought to contribute to the neuropathology of AD.

• Vitamin E has been shown by large randomized controlled studies to decrease the rate of progression of AD in people with mild to moderate disease.

• However, the magnitude of this effect is very modest and may not be clinically noticeable.

• In addition, high-dose vitamin E should be recommended with caution in patients with increased risk for bleeding and those with known coronary heart disease or congestive heart failure. Vitamin E supplementation has no role in the prevention of dementia.
• Plasticity – the ability to be moulded / shaped (from Greek "plastos")

• Preventing ‘excess’ or unnecessary disability
  ► Making the most of remaining ability
  ► Managing impact of cognitive impairment
  ► Improving social context and emotional coping
Activity Therapy

• The more meaningful your activity program is to the resident, the less negative behavior you will and the residents will function better
Sensory training
• Inability to interact with the environment.
• Not oriented to themselves
• Repetitive exercises

Reality Orientation
Used with the moderately confused or those at risk to be confused.
Consistent, accurate information

Remotivation
Start to reuse communication skills in-group
Structured five step procedure

Reminiscing
Client remembers forgotten incidences and strives to communicate and recapture emotions
Trained listener

Other approaches and therapies
Advanced Remotivation
Resocialization,
, Integrated Cognitive Stimulation, DBT, CBT, Stress management

Validation Therapy
The impaired

Very much for the WELL
Non-pharmacological intervention to Alzheimer patients

1. ADL, activities of daily living; BPSD, behavioral and psychological symptoms of dementia.

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Cognitive</th>
<th>ADL</th>
<th>BPSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive training</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cognitive rehabilitation</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cognitive stimulation therapy</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Snoezelen/multisensory stimulation</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Reality orientation</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Reminiscence therapy</td>
<td>+</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>Validation therapy</td>
<td>+</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>Physical activity</td>
<td>+</td>
<td>+</td>
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<td>Light therapy</td>
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<td>Music therapy</td>
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<td>Aromatherapy</td>
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<td>Animal-assisted therapy</td>
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Drugs in pipeline 2/2/2017
Solanezumab (amyloid-targeting monoclonal antibody) although not statistically significant ..., 

- It is very safe and well tolerated;

- That the drug has a small beneficial effect on disease progression at the stage of mild dementia;

- That earlier intervention seems advantageous, because treatment of mild dementia was more effective than treatment of moderate dementia.

- Other ongoing solanezumab trials continue into 2017
Aducanumab (Biogen), another amyloid-targeting monoclonal antibody

• Received fast-track designation from the US Food and Drug Administration (FDA)

• Early findings showed encouraging improvement in memory loss as well as amyloid reduction among patients with mild or preclinical AD.

• Statistically significant reductions in amyloid plaque compared to placebo
Yet, another antiamyloid monoclonal antibody therapy, Crenezumab (Genentech

• A concern with amyloid-targeting antibodies is the possibility that even if plaque is reduced, cognitive function may not improve
Another, solution currently being explored is to prevent amyloid from forming in the first place with drugs designed to inhibit BACE. Verubecestat (Merck)

- BACE, an important enzyme in the production of beta-amyloid development in the brain.
- "BACE inhibitors represent an upstream inhibitor of amyloid formation

- As opposed to the antibodies previously discussed that are a downstream treatment designed to attack amyloid plaque that is already formed

- Another investigational BACE inhibitor, AZD3293, made by Lilly in partnership with AstraZeneca, is also currently in phase 3 trials
The majority of late-phase clinical trials continue to address amyloid despite increasing pressure to look for other therapeutic targets.

• Why it did not work? the subjects were simply not early enough in the disease process.

• **Nonamyloid Candidates**
  • An experimental agent LMTX (TauRx) targets tau tangles, A first-in-class tau-targeting vaccine, AADvac1 (AXON Neuroscience), is currently being studied in a phase 2 clinical trial
  • Mioglitazone (multiple brands), a type 2 diabetes drug, is being evaluated for the prevention of AD on the theory that it decreases inflammation associated with the disease
  • CSP-1103 (CERESPIR), a first-in-class microglial modulator, is also designed to target inflammation. In is currently in phase 2 trials
Long Inland Ice Tea Cocktail

• In the future Alzheimer's disease may be treated similarly to HIV, where a person would actually take a cocktail,
• Maybe one part is an amyloid inhibitor
• Maybe another deals with tau
• Maybe another to keep synaptic connections between brain cells healthy
• A holistic approach, possibly incorporating pharmacologic interventions along with the evidence-based lifestyle changes that have been associated with a reduction in the risk for dementia