DEMENTIA 2017

"Unforgettable, that's what you are . . ."
Recorded by Nat King Cole, 1951, lyrics by Irving Gordon

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"A mind is a terrible thing to waste."
-Official motto of the United Negro College Fund

"A wrong-doer is often a man that has left something undone, not always he that has done something."
Marcus Aurelius Antoninus A.D. 121-180

Disclosures

- 1997 – 2002 Lecturer on Pfizer Speaker's Bureau
- Stockholder, Pfizer
  - Generic names will be used
  - No recommendation of company products

Dementia Is Personal

The challenge we face

- We are seeing an aging population among our patients
- Elderly individuals are living longer than before
- The prevalence of dementia increases with age
- Larger numbers of our patients will present to our offices with dementia
- Many of our current patients are being underserved, undermanaged, undertreated and ignored
- Money and resources are being squandered
- Patients and their families are looking to us for help
- We need to be providing care for these patients as well

History of Dementia

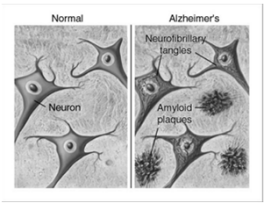
- Senility

- Auguste Deter

- Dr. Alois Alzheimer

Auguste Deter's Autopsy

- Brain was significant for numerous abnormal findings:
  - Amyloid plaques
  - Neurofibrillary tangles
- Findings presented at a conference November 3 1906
- Pathologic features of Alzheimer's disease



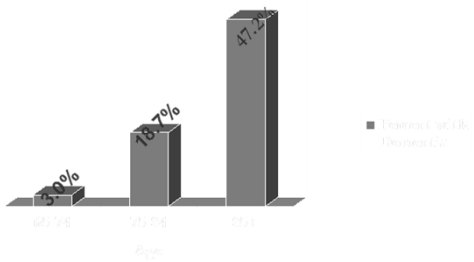
"Presenile Dementia"

- Alzheimer's disease considered to be a disorder of younger patients
- Mimic natural progression of senility
- Retrospective analysis of "senile" elderly revealed the same pathognomonic features
- "Senility" is and always has been dementia

Dementia

- Diminished mental function is not a natural consequence of the aging process
- Dementia is always pathologic
- Individuals with dementia need to undergo a complete and thorough medical evaluation

Prevalence of Dementia



Demographics

- Women are at greater risk for developing dementia than men
  - May be due to longer lifespan
- African Americans twice as likely as whites to develop dementia
- Hispanic Americans are 1.5 times more likely than non-Hispanic whites

from **Nowrangi MA, Rao V & Lyketsos CG. Epidemiology, Assessment, and Treatment of Dementia. *Psychiatric Clinics of North America*.2011;(34, Issue 2): 275–294**

Differential Diagnosis of Dementia

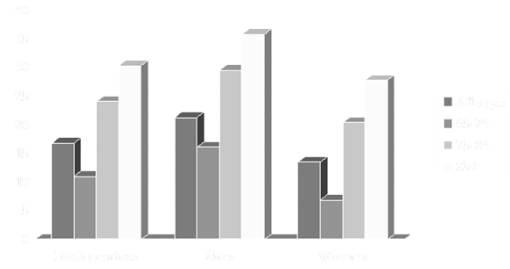
Diagnosis	%	Diagnosis	%
Alzheimer's disease	56.8	Huntington's disease	0.9
Vascular	13.3	Mixed	0.8
Depression	4.5	Infection	0.6
Alcohol	4.2	Subdural hematoma	0.4
Normal Pressure Hydrocephalus	1.6	Traumatic Brain Injury	0.4
Metabolic	1.5	Anoxic	0.2
Drugs	1.5	Miscellaneous	3.7
Parkinson's disease	1.2		

13.2% of diagnoses are potentially reversible

Mild Cognitive Impairment (MCI)

- Patient is cognitively impaired, but is not demented
- Clinical criteria:
  - Cognitive complaint
  - Cognitive impairment (usually memory)
  - Essentially normal cognition
  - Preserved activities of daily living
  - Not demented

Prevalence of MCI



From Graham JE, et al. Prevalence and severity of cognitive impairment with and without dementia in an elderly population. *Lancet* 1997; 349:1793-96

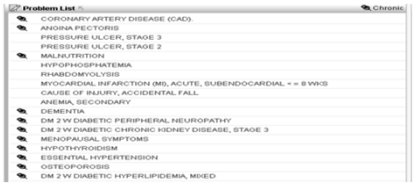
MCI & Dementia

- Patients with MCI will progress to Alzheimer's disease at a rate of 10% to 15% per year
- Healthy control subjects convert at a rate of 1% to 2% per year

From Petersen RC, et al. Current Concepts in Mild Cognitive Impairment. *Arch Neurol* 2001;58:1985-1992

Dementia & Co-morbidity

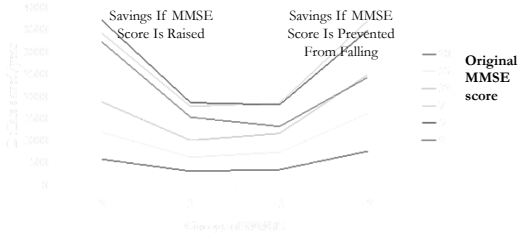
- Other medical disorders can contribute to the demented state
- Other conditions can be identified during the dementia evaluation



Costs of Dementia

- Higher hospitalization rates
- Higher emergency room utilization
- Decreased adherence with therapy for other medical conditions
- Increased utilization of extended care facilities

Medical Cost Savings With Improvement of Cognitive Status



From Ernst RL, Hay JW, Fenn C, Tinklenberg J & Yesavage JA. Cognitive function and the costs of Alzheimer disease. *Arch Neurol* 1997;54:687-693

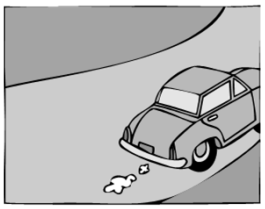
Advance Planning

- Involve patients in earlier stages of disease
- Legal & economic decisions
- Identify responsible parties
- Estate planning
- POLST

Living Arrangements

- Who does patient live with?
- Who is available?
- Consider referral to Care Guidance (on eReferral)

Driving



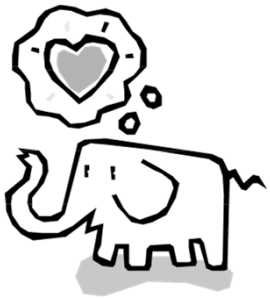
- Patients with mild dementia at no greater risk of causing accidents
- Anyone with moderate-to-severe dementia at greater risk of causing accidents
  - MMSE < 20
  - Mid-range and lower scores on other assessment scales

Who Has Dementia?

- Missed appointments
- Prescriptions unfilled
- Concern of family
- Worsening of other medical conditions
  - Rising $HgbA_1c$
  - Elevated blood pressure
  - Deteriorating lipid control
  - Unexplained weight loss
  - Development of pressure ulcers
  - Increased rates of ER/UC visits & hospital admissions

Assessment of memory

- Occasional lapses of memory are normal
- Context is important
- Consider functional status
- Utilize objective measure



Memory tests

- There are many published quick memory tests for primary care practice
- Few have established reliability or predictive value
- Folstein Mini-Mental State Examination (MMSE) is the most famous
  - Helpful in designating stages
  - Capacity determination
  - Driving

Problems With MMSE

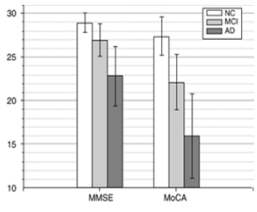
- Lack of sensitivity
- Language availability
  - Spanish version available
  - Limited other languages
- Proprietary
  - Copyrighted
  - Legal experts doubt that copyright holders can claim exclusivity

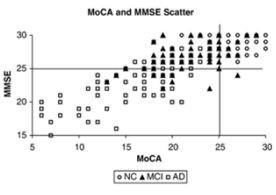
Alternatives to MMSE

- SLUMS (St. Louis University Mental Status)
  - Used by VAMC
  - www.stlouis.va.gov/GRECC/SLUMS_Details.pdf

- MOCA (Montreal Cognitive Assessment)
  - Consortium of specialists in dementia, including UCLA
  - Multiple languages
  - www.mocatest.org

Sensitivity of MOCA





From Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, Cummings JL & Chertkow H. The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment. *J Am Geriatr Soc* 2005;53:695-699

Assessment of mood

- Depression is a cause of decreased mental function in the elderly
- Depression can also be incipient symptom of Alzheimer's disease

Geriatric Depression Scale

	NO
YES	
YES	
YES	
	NO
YES	
	NO
YES	
YES	
	NO
YES	
YES	
	NO
YES	
YES	

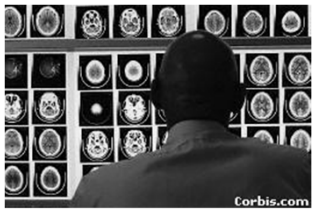
Scoring: Normal 0-5, above 5 may suggest depression

Workup

- Laboratory:
  - Strongly recommended: CBC, Electrolytes, Calcium, Glucose, Creatinine, Albumin, TSH, B_{12} level, Serologic test for syphilis
  - Consider for special circumstances: HIV, ESR, ANA, Heavy metal screen, Drug screens
- Neuroimaging
  - Looking for tumors, subdural hematomas, normal pressure hydrocephalus
  - 3.5% of patients with dementia
  - CAT scan perfectly adequate

Neuroimaging

- Generalized cerebral atrophy is nonspecific and is normal with age
- Look for periventricular atrophy



Diagnosis of Alzheimer's Disease

- Progressive cognitive decline
- Normal mood
- Lack of other causative medical condition
- Lack of structural abnormality in the brain

Pillars of Treatment

- Treating the disease
- Treating the symptoms
- Supporting the patient
- Supporting the caregiver

Treatment Options

- Cholinesterase inhibitors
  - Monotherapy only for mild dementia
- N-methyl-D-aspartate (NMDA) receptor–antagonists
  - Can be used in monotherapy
  - Best when combined with cholinesterase inhibitors for moderate-to-severe dementia
- In patients with severe dementia, treatment with NMDA receptor antagonists & cholinesterase inhibitors may help to decrease psychotic episodes

Histochemical actions of cholinesterase inhibitors

- Affected neurons noted to have cholinergic synapses on dendrites
- Cholinergic-depleted brains demonstrate memory deficit
- Cholinesterase inhibitors may enhance trophic effects on non-affected neurons

Comparisons

	Rivastigmine (Exelon)	Galantamine (Razadyne)	Donepezil (Aricept)
Dosing	BID (SR available)	BID (SR available)	QD
Tolerability	++	+++	++++
Possible dosage adjustment	-	Renal/liver disease	-
Dosage forms	Pill, liquid & patch	Pill & liquid	Pill
Generic availability	Yes	Yes	Yes

No required testing for any of these agents

Considerations

- All cholinesterase inhibitors are effective
- No good comparison trials have been published
  - None will probably ever be conducted
- Start with lowest dose, and increase dosage step-wise, over 4-6 weeks
- Improvement in mental function will occur over one year

Considerations *(continued)*

- Stopping medication will result in loss of acquired function
- If medication is restarted shortly after cessation, lost function may be re-attained
- Increasing dosage above recommended dose may be counterproductive
- Some anecdotal evidence for improvement of function when patients are switched from one agent to another

Actions of glutamate

- Damage to neurons is associated with enhancement of excitatory neurotransmitters, especially glutamate.
- Activation of glutaminergic receptors, especially the N-methyl-D-aspartate (NMDA) receptor–channel complex, leads to a pronounced increase in toxic intracellular calcium ion.

Actions of glutamate *(continued)*

- The hippocampus and the middle layers of cerebral cortex are regions high in glutamate receptors.

Memantine

- Moderate-affinity, uncompetitive, NMDA receptor antagonist
- Combination of memantine and donepezil given to patients with moderate-to-severe Alzheimer's disease for 24 weeks
- Patients treated with combination showed significant improvement in all measures of cognitive function when compared to donepezil/placebo treated patients
- Can be used with any cholinesterase inhibitor

Future Prospects

- Immunotherapy
- Inhibitors of β-amyloid production
- Nerve growth factor (NGF)

Complications of Dementia

- Depression
- Psychosis/Delusions
- Wandering
- Sleep disturbances

Antidepressant Use in Dementia

Medication	Effect compared to placebo
Clomipramine	Superior
Moclobemide (MAOI, not available in U.S.)	Superior
Sertraline	Superior
Citalopram	Superior
Imipramine	No difference
Fluoxetine	No difference
Paroxetine	No difference

Theoretically, venlafaxine, mirtazapine, secondary amine TCAs, or a MAOI may be effective, but little to no research has been done

From Lyketsos CG, Olin JT. Depression in Alzheimer's disease: overview and treatment. *Biol Psychiatry*. 2002;52243- 252

Delusions/Psychosis

- Most conventional antipsychotic medications will worsen cognitive function in patients with Alzheimer's disease
- Treat behaviors that place the patient at risk for harm to himself or to others
- Intervene only if the behavior impairs functional capacity or interferes with the delivery of needed medical care

Atypical antipsychotics

Long-term treatment with antipsychotics

- Recent reports of increased health risks with long-term use of antipsychotics
- May be selection bias
- Until prospective, double-blind placebo-controlled studies are completed, we should limit treatment to as little a time as possible

Valproic acid

- Several studies have shown that valproic acid is useful for treatment of psychosis associated with dementia
- Few ill effects reported
- Routine monitoring of CBC's, liver functions and therapeutic drug levels are recommended
  - Monitoring drug levels to help prevent overtreatment

Wandering

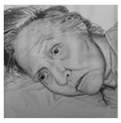
- Use ID bracelets, necklaces
- Install exit alarms

Sleep disturbances

- Decline of both REM and non-REM sleep with progression of Alzheimer's disease
- Non-pharmacologic treatment is preferable:
  - Reduce daytime naps
  - Restrict time in bed
  - Increase daytime activity
  - Exposure to bright light, especially sunlight, during waking hours
- If medication used, one should use short-acting agents
- Trazodone is particularly helpful

Hospice & Palliative Care

- Hospice
  - Criteria very restrictive
    - Ability to speak six or less words
    - Cannot walk without personal assistance
    - Cannot sit up without assistance
    - Loss of ability to smile
    - Loss of ability to hold up head independently
    - MMSE 0/30



Hospice & Palliative Care *(continued)*

- Hospice *(continued)*
  - Patients should have had one of the following within the past 12 months:

Aspiration pneumonia

Multiple stage 3 and 4 pressure ulcers

Pyelonephritis

Septicemia

Recurrent fever after antibiotics

Inability to maintain sufficient fluid and calorie intake
- 10% weight loss during the previous six months
- Serum albumin <2.5 gm/dl

Hospice & Palliative Care (continued)

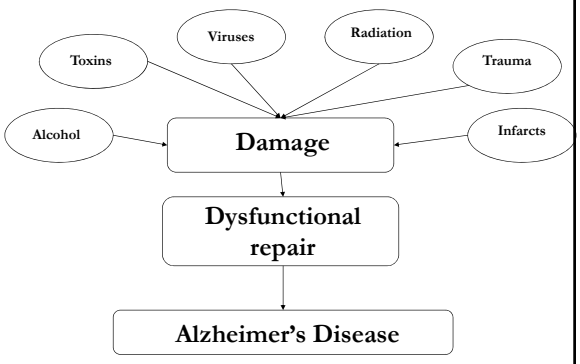
- Palliative care
  - Homebound or taxing effort to leave home
  - Skilled need:
    - Wound(s)
    - Catheter
    - Feeding tube
  - Managed symptom(s):
    - Pain
    - Behavioral issues
    - Constipation

Hospice & Palliative Care (continued)

- Many patients with dementia will qualify for Hospice or Palliative Care due to concurrent conditions

Prevention

- Currently no effective preventive treatment
- To develop Alzheimer's disease requires damage and dysfunctional repair
- Dysfunctional repair is inherited, damage is acquired



Caring For the Caregivers

- Depression
  - 30-55% of caregivers
  - Independent of the severity of family members' dementia
- Elevated blood pressure & lipids
- Lack of exercise & sleep
- Increased use of psychoactive substances

Health effects of caregiving persist for over 4 years after the death of the demented family member or placement in a long-term nursing facility

HealthConnect tools

- SmartSets for Dementia are available
- Dementia SmartPhrases, MMSE, Geriatric Depression Scale and a treatment instruction message are available in the Geriatric Folder at http://dms.kp.org/docushare/dsweb/View/Collection-53545

Conclusion

- Evaluate
- Treat
- Advocate