



Down Syndrome and Alzheimer's Disease

Heather S. Anderson, M.D.
Director, KU Down Syndrome Dementia Clinic
Director, Education Core, KU Alzheimer's Disease Center




Overview

- What is Alzheimer's disease?
- Risk factors for Alzheimer's disease, including Down syndrome
- Symptoms of Alzheimer's disease in Down syndrome
- Behavior in Down syndrome
- Diagnosing Alzheimer's disease
- Other causes of confusion
- Treatments



Alzheimer's Disease vs. Dementia

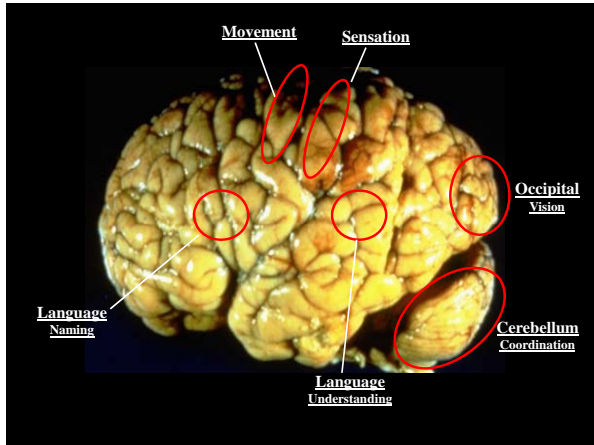
- Dementia
 - A syndrome of progressive decline in cognitive function, significant enough to interfere with daily life

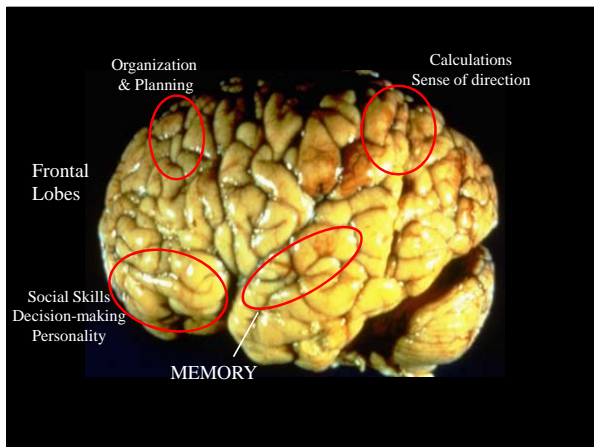


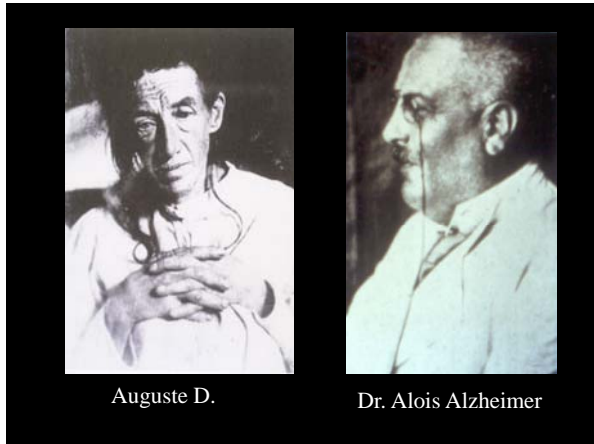
Alzheimer's Disease vs. Dementia

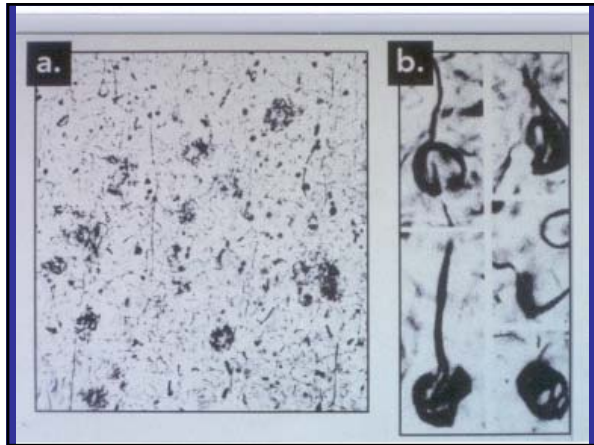
- Causes of dementia
 - Alzheimer's disease (most common)
 - Stroke(s)
 - Frontotemporal dementia
 - Parkinson's disease
 - Dementia with Lewy bodies
 - Hydrocephalus
 - Head trauma
 - Others











What is Alzheimer's Disease?

- Most common cause of dementia
- Marked by early memory impairment, executive dysfunction

KU ALZHEIMER'S DISEASE CENTER
The University of Kansas

Alzheimer's Facts

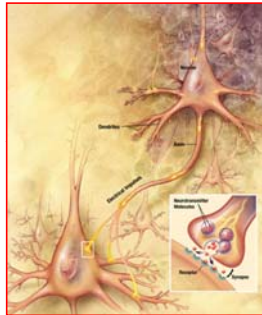
- 5.4 million Americans have AD in 2011
- One in eight (13 percent) over 65 have AD
- Every 69 seconds someone develops AD
- \$183 billion in direct and indirect costs to Medicare, Medicaid, and businesses

Alzheimer's Association, 2011

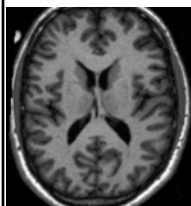


What happens in Alzheimer's?

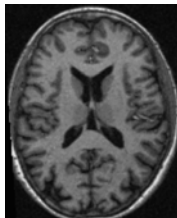
- The brain is composed of billions of neurons
- AD disrupts the health of neurons and communication between neurons



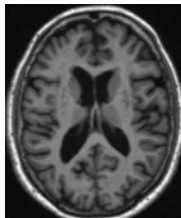
Brain size declines with age and Alzheimer's Disease



39 year old man

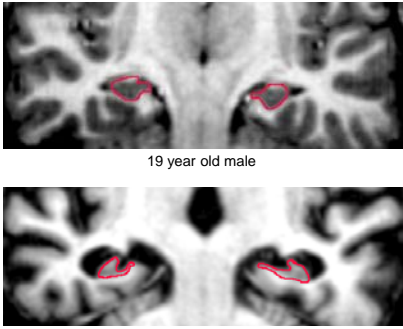


72 year old non-demented woman



75 year old woman with mild AD

Hippocampal volume declines early in Alzheimer's disease




19 year old male

86 year old female with AD

Risk of Alzheimer's Disease

- Factors increasing the risk
 - Physical inactivity
 - High physical activity is associated with ~40% reduced risk of developing cognitive decline and dementia


Karp, et al. Dement. Geriatr. Cogn. Disord. 2006
Abbott, et al. JAMA 2004
Wilson, et al. JAMA 2002
Laurin, et al. Arch. Neurol. 2001



Risk of Alzheimer's Disease

- Factors increasing the risk
 - Mid-life (40-44 years) cardiovascular risk factors associated with increased risk of dementia later in life
 - 24% increased risk with midlife hypertension
 - 46% with midlife diabetes
 - 42% with midlife high cholesterol
 - 26% with midlife smoking
 - Additive risk when combining 2 or more risk factors


Whitmer, et al. Neurology 2005



Risk of Alzheimer's Disease


- Factors increasing the risk
 - Family history – 4-10 times greater risk
 - Maternal family history?
 - Cognitively normal adults with a maternal family history of late-onset Alzheimer's disease have greater amounts of atrophy in the precuneus and parahippocampus/hippocampus regions over 2 years compared to paternal- or no family history of Alzheimer's disease
 - Perhaps a higher risk for developing Alzheimer's disease

Honea, et al. Neurology 2011



Risk of Alzheimer's Disease

- Down syndrome
 - Trisomy 21
 - Amyloid Precursor Protein (APP)
- Plaques and tangles in the brain tissue
 - Present in the brains of nearly all adults with Down syndrome by the age of 40 (Malamud, 1972; Wisniewski et al. 1985)




Risk of Alzheimer's Disease in Down Syndrome

- Obesity
 - Individuals with Down syndrome are more likely to be overweight or obese than other individuals with intellectual disability (Stancliffe 2011)
 - Intellectual disability & DS – mean BMI 30.40
 - Intellectual disability only – mean BMI 28.55
 - Intellectual disability & autism/PDD – mean BMI 27.42
 - Intellectual disability & CP – mean 24.53

	Obese (BMI ≥ 30)	Overweight or Obese (BMI ≥ 25)
Down syndrome	44.3%	72.7%
U.S. population	33.8%	68.0%

(Flegal, et al 2010)



Risk of Alzheimer's Disease in Down Syndrome

- Sedentary Lifestyle
 - Levels of physical activity in non-athletic adults without intellectual disability were twice as high compared to adults with an intellectual disability (Vis, et al. 2011)
 - No significant difference between Down syndrome and other causes of intellectual disability



Epidemiology

- In the general population
 - Roughly 10% of people 65 and older
 - Nearly 50% of people 85 and older
- Clinical symptoms of dementia in Down syndrome
 - <10% between 30-39 years of age
 - 10-25% between 40-49 years
 - 20%-50% between 50-59 years of age
 - 50-70% by 60-70 years of age
 - Variable, however seems to progress more quickly than in general population



Symptoms – General Public

- Forgetfulness (conversations; appointments; medicines; names)
- Repetition of questions, statements
- Misplacing items
- Difficulty planning activities
- Getting lost



Symptoms – Down Syndrome

- 1st symptom is usually behavioral changes
 - Disorientation to time/place
 - Personality or productivity changes
 - Increased apathy or inactivity
 - Inability to perform activities of daily living
- Memory loss may not be first symptom noticed



Behavioral Changes

- Disorientation to time/place
 - Missing family birthdays
 - Difficulty with time changes
 - Difficulty with transportation to/from work, etc.
 - Difficulty remembering work schedule
 - Getting lost in familiar areas
 - Later on – difficulty with weekend vs. week day



Behavioral Changes

- Personality changes
 - Aggression/spitting/hitting/kicking
 - Irritability
 - Anxiety
 - Depression
 - Forgetting to take something with them to work, etc.



Behavioral Changes

- Productivity changes
 - Difficulty staying focused/easily distracted
 - Needing reminders to perform tasks
 - Anticipating breaks at work
- Increased apathy or inactivity
 - Need to rule-out depression or sleep disorder
 - Not interested in previously enjoyed activities
 - Less interested in going places and doing things



Behavioral Changes

- Inability to perform activities of daily living
 - Difficulty dressing
 - Difficulty bathing
 - Difficulty toileting
- Later on – Difficulty eating



Diagnosing Alzheimer's Disease

- No brain scan or blood test can make the diagnosis
- Detailed History
 - Characteristics and pattern of changes
 - Importance of informant / caregiver



Cognitive Assessment

- Can't use the MMSE
- Down Syndrome Dementia Questionnaire
 - Scores out of 100
 - Lower score indicates stronger independence and cognitive function
- Brief Praxis Test
 - Scores out of 80
 - Higher score indicates stronger ability to comprehend and follow simple commands



Examination

- Physical Examination
 - Heart
 - Lung
 - Examine any painful areas
- Neurological Examination




Laboratory Tests

- Thyroid hormone
 - High proportion of Down Syndrome patients have abnormally low thyroid hormone
- Vitamin B12
- Lab tests to consider
 - Vitamin D
 - RPR




Imaging

- MRI or CT of the brain
 - Rule-out stroke, abscess, tumor, other structural problems
 - Length of study
 - CT takes just a couple of minutes
 - MRI takes 30+ minutes
 - May need sedation for the imaging




Summary: Diagnosis of Alzheimer's disease

- Key: History and physical
- Rule out other potential causes
 - Physical examination
 - MRI or CT scan
 - Labs: Vitamin B12, Thyroid
 - Depression
- PET scans, psychometric tests
 - Not essential to diagnosis
 - Limited sensitivity compared to history from informant




Other Causes of Confusion

- Psychiatric symptoms/conditions
 - Depression
 - Death or loss of a loved one
 - Anxiety
 - Obsessive compulsive disorder
- Stress




Other Causes of Confusion

- Changes in home or work environment
 - Roommates
 - Staff
 - Personal/quiet space
 - Disruptions in daily schedule
 - Bullying/disruptive behavior
 - Influence




Other Causes of Confusion

- Medications
 - Pain medications
 - Lortab, Percocet, morphine, codeine, etc.
 - Anxiety medications
 - Ativan (lorazepam), Xanax (alprazolam), etc.
 - Sleep aides
 - Ambien (zolpidem), Sonata (zaleplon), Lunesta (eszopiclone)
 - Anticholinergic medications
 - Elavil (amitriptyline), Pamelor (nortriptyline)
 - Benadryl (diphenhydramine)
 - Bladder medications, particularly Ditropan




Other Causes of Confusion

- Medications, cont.
 - New or discontinued medications
 - Changes in dosage or timing
- Pain
 - Headaches
 - Neck pain
 - Back pain




Other Causes of Confusion

- Sleep apnea
 - Up to 100% of adults with DS have abnormal sleep studies
 - 83% of these showed sleep apnea
- Other factors affecting sleep
 - Depression
 - Anxiety
 - Pain
 - Environmental factors



Treatment

- Address treatable conditions
 - Limit sedating medications
 - Treat metabolic issues
 - Treat sleep disorder




Treatment

- Treat psychiatric symptoms/conditions
 - Celexa (citalopram)
 - Lexapro (escitalopram)
 - Desyrel (trazodone)
- If psychiatric symptoms are not easily treated, consider a referral to psychiatry




Treatment of Alzheimer's Disease

- Two classes of approved medications
 - **Acetylcholinesterase inhibitors** → increase acetylcholine levels
 - Aricept (donepezil)
 - Razadyne (galantamine)
 - Exelon (rivastigimine)
 - **NMDA antagonist**
 - Namenda (memantine)
 - Found to not be effective in Down syndrome




Treatment of Alzheimer's Disease

- Aricept (donepezil)
 - FDA approved for mild, moderate, severe AD
- Exelon capsules and patch (rivastigimine)
 - FDA approved for mild, moderate AD
- Razadyne (galantamine)
 - FDA approved for mild, moderate AD



Treatment

- Physically active
- Mentally active
- Socially active



Psychiatric Symptoms and/or Behavior

- Prevalence in adults with DS, no dementia
 - Approximately 26%
 - Most frequent = conduct disorder, aggression, stereotyped behavior, and attention deficit disorder
 - Perhaps an underestimate
 - Signs and symptoms of bad behavior are often attributed to mental retardation


Collacott, Cooper, & McGrother, 1992
Meyers & Pueschel, 1991



Depression in Adults with Down Syndrome

- Percentage of patients with depression
 - 18.4% of non-demented adults with DS
 - 44% of adults with DS and possible dementia
 - 60% of adults with DS and definite dementia


Urv, TK 2008



Behaviors in Adults with Down Syndrome and Dementia

- Compared to younger non-demented individuals with Down syndrome
 - More irritation
 - Fearful
 - Restlessness at night
 - Sadness
 - Suspiciousness
 - Loss of appetite

Haveman, et al. 1994



Adaptive Behavior in Middle-Age Adults with Down Syndrome

- No significant age-related decline in skills is seen
 - Excluded individuals with significant medical disorders (dementia, depression, hypothyroidism)
- If age-related changes are identified, it is important to assess physical and psychological factors

Prasher 1998



Adaptive Behavior in Middle-Age Adults with Down Syndrome

- Particular areas of decline in skills in early stages of dementia
 - Independent functioning
 - Eating
 - Toilet use
 - Cleanliness
 - Appearance
 - Care of clothing
 - Dressing and undressing
 - Travel
 - Numbers and time
 - Responsibility
 - Socialization




Evaluation of Behavior Changes in Adults with Down Syndrome

- Consider the individual's underlying personality/behavior
- Change in behavior could represent
 - Depression/anxiety/stress
 - Pain
 - Physical or neurological condition such as cervical stenosis
 - Dementia




Where To Go For An Evaluation

- KU Down Syndrome Dementia Clinic
 - Call (913) 588-6820
- New patient evaluations
 - Heather Anderson, M.D.
 - First Thursday afternoon of the month
- Follow-up evaluations
 - Anne Arthur, ARNP




Where To Go For An Evaluation

- KU Sleep Medicine Clinic
 - Call (913) 588-6820
- Suzanne Stevens, M.D.
 - Overnight sleep studies
 - Overnight oxygen levels
 - Sleep Medicine Clinic appointments



Where To Go For An Evaluation

- Down Syndrome Guild of Greater Kansas City
 - (913) 384-4848
- Alzheimer's Association – Northwest Missouri Regional Office, St. Joseph, MO
 - Brenda Gregg
 - Phone: 816.364.4467
 - email: brenda.gregg@alz.org



Where To Go For An Evaluation

- Research Opportunities
 - University of California-Los Angeles (UCLA)
Department of Psychiatry
 - Brain imaging project focused on detecting early signs of Alzheimer's disease in adults with Down syndrome age 40 and over with and without signs of dementia
 - For more info contact UCLA at 310-206-7392



Where To Go For An Evaluation

- Research Opportunities
 - University of California-Irvine
 - Dr. Ira Lott (714) 456-5333
 - Kennedy Krieger Institute and Johns Hopkins University
 - Wayne Silverman, PhD (443) 923-2738