Alzheimer's Disease

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Introduction

Goals of the discussion

- Have a better understanding of dementing diseases.
- Feel more comfortable understanding this illness and the diagnosis.
- Have basic understanding of the medications available for this illness.
Alzheimer’s Disease

- What is Alzheimer’s?
- Who is at risk?
- What are the stages?
- How is a patient diagnosed?
- What can we do for treatment?
Alzheimer’s Facts

- Degenerative brain disorder.
- The MOST Common type of demyelinating illness of the elderly.
- Prevalence increases with age, uncommon before age 65.
- Majority of patients are female.
- Characterized by insidious, irreversible cognitive decline.
Dementia

- Latin – ‘out of mind’
- Syndrome that is progressive and affects at least 1 cognitive function with decline in memory
- Assoc. w/ an Alert person
- Insidious onset
- Relentless progression
Dementia con’t

- **Cortical symptoms (AD)** — difficulty forming new memories, aphasia, apraxia, agnosia, visual-spatial impairment

- **Subcortical (vascular dementia)** — cognitive slowing, impaired memory retrieval and attention, apathy, depression, mood liability and disinhibition, EPS
Dementia types

- 60% all demented patients have AD type.
- 20% have Parkinson’s or Vascular type.
- 15% have Mixed dementia.
- 5% have ‘other’
  - Picks
  - Lewy body
  - Multiple Sclerosis
  - Cancer
  - Alcoholic
Alzheimer’s Prevalence

- 8% > age 65
- 20% > age 75
- 50% > age 85

- 2/3 of Demented patients on Autopsy have Alzheimer’s.
### Alzheimer’s Costs

<table>
<thead>
<tr>
<th>Setting of care</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>$1543</td>
<td>$2508</td>
<td>$3011</td>
<td>$2306</td>
</tr>
<tr>
<td>Community</td>
<td>$1158</td>
<td>$1874</td>
<td>$2266</td>
<td>$1549</td>
</tr>
<tr>
<td>Institutional</td>
<td>$2840</td>
<td>$3069</td>
<td>$3288</td>
<td>$3130</td>
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Based on 1996 costs and nursing home admissions that a 1 month delay in nursing home placement could yield a savings of $1.12 billion annually. (Estimated cost per patient of nursing home care is estimated at $42,000/yr)
Co-morbidity

- Other diseases of the elderly:
  - 50% with arthritis
  - 35% with hypertension
  - 30% with heart disease
  - 10% with diabetes
Gross Anatomical changes

- Atrophy of frontal, temporal, and parietal cortex.
- Widening of sulci between gyri.
- Enlargement of ventricular system.
Microscopic changes

- **Senile plaques** – Amyloid (extracellular) structure in neocortex and hippocampus. Dense and insoluble.

- **Neurofibillary tangles** – intracellular inclusion bodies made of paired helical filaments, composed of tau protein.

- Neurons surround a central core of an abnormal protein (Amyloid), preventing normal function.
AD Characteristics

- Marked by personality changes and impaired judgment.
- Progressive decline in intellectual function that interferes with:
  - ADL
  - Behavior (social skills)
  - Cognitive ability
Who is at risk for AD?

- Risk increases with age.
- Down’s syndrome
- Illiteracy or low education
- Parkinson’s disease
- Family history of:
  - AD
    - first degree relative = 3x (35%)
    - APOE4 = 3x (35%)
    - Autosomal Dominant = 100%
  - Parkinson’s disease
More AD risk

- ? Increased with:
  - Advanced parental age
  - Hx depression
  - Hx heavy alcohol use
  - Hx head trauma

- ? Decrease with:
  - Arthritis or heavy NSAID use
  - Oral estrogen use
  - Ginko Biloba
  - Anti-oxidant use
AD stages

- Early
- Mid-stage
- Severe
- Terminal
AD progression

- Typically progression occurs over 8 – 10 years (extremes of 2 – 20 years).
- Patients noted to have more rapid cognitive decline if:
  - Psychotic symptoms
  - Early age of onset
  - Seizures occur
  - Extra pyramidal features
What to look for:

Aphasia, Apraxia, Agnosia, Dysnomia, and disturbance in executive function.

ADL impairment

Cognition changes and decreased ability to perform common tasks with ease and completeness.
**Definitions:**

<table>
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<tr>
<th>Aphasia – language disturbance</th>
<th>Apraxia – reduced ability to carry out motor function despite intact mental function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agnosia – failure to recognize common objects</td>
<td>Executive function – Plan, organize, sequence, and abstract thinking</td>
</tr>
</tbody>
</table>
Activities of Daily Living

- Toileting
- Feeding
- Dressing
- Grooming
- Ambulation
- Bathing
Personality changes

- Depressive - passivity, disinterest, withdrawal
- Agitation – Anger, suspicion
- Social relationship confusion
Early AD stage

- ADL decline
- Misplacement of items w/o self retrieval
- Impaired acquisition of new information
- Inability to recall recent conversation or event
- Personality changes
More Early symptoms

- Dressing inappropriately
- Poor: judgment, attention, problem solving
- Day/date/time disorientation and confusion
- Speech hesitancy and decreased verbal output
- Dysnomia – word finding difficulty
Delirium

- Confusion with over activity of autonomic nervous system – treat and evaluate for cause
  - ? intoxication (amphetamine)
  - ? withdrawal (alcohol, benzodiazepines, barbiturates)
  - ? systemic toxic state (fever, sepsis)
Acute Confusion

- Inability to maintain a coherent thought stream.
- Need to treat, but need to determine cause.
  - Toxic
  - Infection or infarct
  - Epilepsy
  - Mass
Mid-stage

- Progressive decline
- Suspicious
- Written and verbal language impairment
- Agitation, restlessness, wandering
- Day/night disorientation
- Aggression
- Delusions
- Hallucinations
Agitation a symptom, not a diagnosis

- Verbal – yelling, moaning, preservation, crying, belligerent
- Motor – pacing, fidgeting, restless, sleep disturb., aggression
- Psychotic – delusions, suspicious, hallucinations
Anxiety symptoms

- Facial expressions
- Guarding
- Tension
- Shaking
- Hyper vigilance
- Attention inability
- Physical complaints
- Resists care
Depressive symptoms

- Irritable
- Dysphoric
- Tearful
- Sleep disturbance
- Anorexia
- Apathy
- Numerous somatic complaints
Risky Behaviors

- Wandering
- Elopement
- Sexually inappropriate behavior
- Rummaging
- Hoarding
- Stealing
Severe or End Stage

- Total dependence for ADL
- Hallucinations
- Minimal remnant of memory
- Restricted verbal output
- Urinary and fecal incontinence
- Tonic-clonic seizures
Terminal

- Bedridden
- Uncomprehending
- Vegetative state
- Weight loss
- Dysphasia
“Extra Care Required”

- Pressure sores
  - Poor nutrition
  - Decreased activity
- Dehydration
  - Non-verbal
  - Trying not to be incontinent
  - Swallowing problems
- Infection
Prognosis

- Death, if not due to some other cause, is usually due to:
  - Aspiration
  - Inanition
  - Pulmonary embolism
  - Infection
Diagnosis

- History
  - Past medical
  - Past surgical
  - Past social
  - Family
- Exam
- Testing
Alzheimer’s Differential

- Depression – may have both, especially if >65
- Drug effect
- Thyroid abnormality
- B12 deficiency
- Normal Pressure Hydrocephalus
- Subdural hemotoma
- Tumor
Barriers to diagnosis

- Futility – thought either by the physician, care giver, or the patient.
- Denial
- Fear that diagnosis will result in negative effects
Objective Evaluation

- Lab: CBC, CMP, Thyroid, RPR, B12, ?HIV
- Cognitive Tests – MMSE, Clock drawing, Short Blessed Test, Information/Memory/Concentration – and need longitudinal testing
- Imaging – CT, MRI, PET, ?CXR
Quick Evaluations

- Clock Draw

- 3 Word Recall
Mini-Mental Status Exam

- **Evaluates:** (retest 2 times annually)
  - Orientation
  - Registration
  - Language
  - Attention and Calculation
  - Recall

- **Scoring** (24 is the cutoff)
  - 30 – 20 Mild
  - 19 – 10 Moderate
  - < 9 Severe
Alzheimer’s Treatment Goals

- **Instrumental ADL**
  - Phone, appliance use, shopping, hobbies, money management, food preparation, mail, comprehension

- **Basic ADL**
  - Dressing, Eating, Toileting, Bathing, Ambulating
Treatment needs

- Prevent further progression at earliest point.
- Toileting problems
- Sleep disturbances
- Weight loss
- Depression and Anxiety
- Inappropriate behavior
Dementia Medications

- Atypical antipsychotics
- Antidepressants
- Cholinesterase inhibitors
- Dopamine Agonists
- Stimulants
Prevent or slow further memory loss

- Goal is to keep these individuals as independent as long as possible.
- Different meds available for this:
  - Tacrine
  - Donepezil
  - Galantamine
  - Rivastigmine
Anticholinesterase Inhibitors

- Precise mechanism of action is unknown.
  - The 2 newer agents also affect the Nicotinic receptors. The clinical significance of this is unknown.
  - All 3 of the newer agents affect, improve or slow deterioration of:
    - General function
    - Cognition (memory and thinking)
    - ADL
    - Behavior
Chemically in the AD pt.

- Decrease acetylcholinesterase
- Decreased choline acetyltransferase
- Loss of cholinergic neurons
- Loss of acetylcholine availability
- Loss of muscarinic receptors
Cholinergic Hypothesis

- Meds developed to enhance central cholinergic function.

- Proposed link between: cognitive decline and loss of cholinergic neurotransmission (hippocampus and cortex).

- Improve cognitive and global function by increasing cholinergic function.
Tacrine

- First drug developed for treatment.
- Not used any longer due to side effects, and better meds available.
Donepezil

- Side effect profile of this medication is very similar to newer generation meds.
- Shown positive results.
- Simple dosing schedule
- Simple titration schedule
Galantamine

- A competitive and reversible agent that enhances cholinergic function.
- Start with 4 mg bid with food for 4 weeks.
- Maintenance is 8 mg bid with food.
- Treatment goals are to sustain cognition and preserve global function/performance.
Rivastigmine

- 3 to 12mg daily (divided bid)
- Requires monthly titration
- Side effects similar to others in class
Treatment success

- Maximize function
- Maintain independence
- Continue in own home environment

ALL depends on early medication initiation and continuation.
Anticholinesterase Inhibitors

- **Needs:**
  - To show positive results
  - Tolerability
    - Side effect
    - Financial
    - Dosing schedule
    - Drug interaction
Caution with anticholinergics

- Antispasmodics
- TCA
- Conventional antipsychotics
Making things worse

- Levodopa/carbidopa
- Cimetidine
- NSAID
- Antihistamine
- TSA
- Antiarrhythmics
- Anticonvulsants

But some of these may be needed in certain circumstances.
Other disturbances

- Motor restlessness
- Verbal or physical aggression
- Irritability
- Dysphoria
- Delusions
- Hallucinations
- Sleep disturbances
- Wandering
Behavior not likely to respond to meds.

- Wandering
- Inappropriate verbalizing
- Inappropriate sexual behavior
- Willfuness
- Hoarding/appropriating
- Inappropriate voiding
Toileting problems

- Meds
- Behavior
  - Timing of use
  - More Velcro and less buttons/zippers
  - Watch for non-verbal clues
Sleep disturbance

- Meds
  - Try to line up side effects with patient needs
- Environmental
  - Alter ‘naps’, feeding, and activity times
Inappropriate behavior

- Not completely understood.
- Can be multifactorial.
- The toughest problem to treat.
- Can be delayed if Anticholinesterase meds are used early in disease course.
Real Life

- About 4 million Americans have this disease.
- This number will more than double in the next 50 years.
Higher MMSE scores correlate with increased ability to perform activities of daily living (ADLs)

Galasko D, 1996.
Treatment expectations

In Alzheimer’s disease, clinical success is defined as:

- Improvement
- No change
- Less-than-expected decline