"He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all." – William Osler

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MEDICINE
TEAMWORK

# DEMENTIA

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# Dementia

**Dementia:** Loss of memory with impairment of cognitive function that interferes with social and occupational functioning.

It is an acquired syndrome characterized by (the major symptoms):

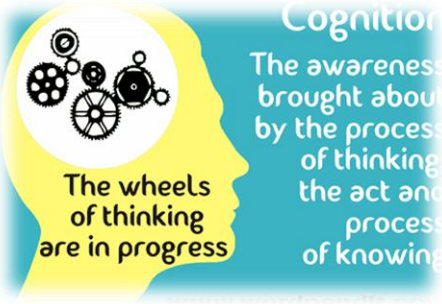
Short-term memory impairment AND at least one of the following:

1-**Aphasia** - language impairments (affecting frontal lobe)

2-**Apraxia** - motor memory impairments (loss of the ability to perform an action ~ function of parietal lobe)

3-**Agnosia** - sensory memory impairments (can't recognize objects by sensation "Astereognosis" damage to somatosensory cortex) or can be visual or auditory.

4-**Abstract thinking / Exec.** function impairments




**Epidemiology:** Prevalence of dementia increases with age.

| Age | Prevalence* | Age | Incidence |
|---|---|---|---|
| >65 | 5-10% | 65-74 | 0.5-1% |
| >75 | 10-20% | 75-84 | 2-4% |
| >85 | 25-50% | 85+ | 6-8% |
| >95 | 40-70% | May level off or declince after age 100 | |

## Etiology & Pathogenesis:

Dementia results from impaired functioning of multiple brain systems in both cortical and sub-cortical areas. Generally this is due to structural brain damage (death of neuronal cells) that is often progressive and relatively irreversible.

## Classification of Dementias:

**1-Primary versus secondary** based on the pathophysiology leading to damaged brain tissue (1ry affecting cortix or sub-cortix & 2ry usually due to other systems e.x: liver failure or hypothyroidism leading to dementia)

**2-Cortical versus sub-cortical** *depending on the cerebral location* of the primary deficits

**3-Reversible versus irreversible** *depending on optimal treatment* expectations

**4-pre senile:** Early (before age 65) versus senile: (late onset) after age 65.

## Types of Dementia : (irreversible)

**1-Alzheimers :** Memory loss (**is the first and major symptom**), Language, Visuospatial, Indifferent to Loss.

**2-Frontotemporal (Picks):** Memory, Marked Personality changes (**the first and the major symptom & later memory loss**), Preserved visuospatial.

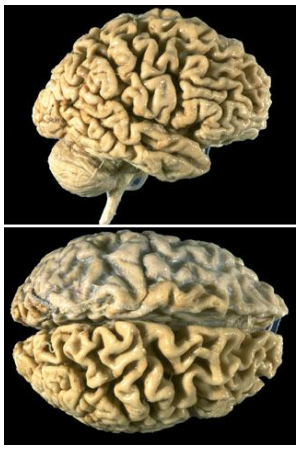
**3-Lewey Body:**Visual hallucinations (**first and the major symptom & later develop memory loss**) , delusions, flucutating mental status.
**4-Parkinson's Disease:**15-30% develop dementia over 5 years ~ it is an extra pyramidal cause of dementia.
**5-Vascular Dementia**: repetitive ischemic stroke attacks lead to dementia.
**6-Progressive Supranuclear Palsy.**
**7-The Rare Birds:**
-Late onset Metobolic Disease
-Creutzfeld-Jacob

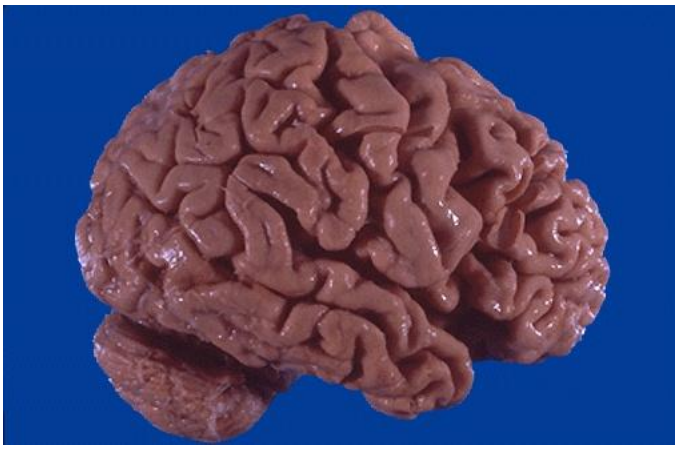
## Most Common Dementias:

**1-Alzheimer's Disease** and Lewy Body Dementias (50-75%)
**2-Vascular Dementias**: stroke (15-20%)
**3-Alcohol-related dementias** (including Korsakoff's (infrequent) and etoh-induced) >> reversible dementia
4-In those under age 65, FTDs may comprise 50% of all dementias
5-HIV dementia - most common dementia in those under age 55>> but it's very rare.

## ALZHEIMER'S Pathophysiology:

**1-Neuritic plaques** -*extracellular* - abnormal insoluble amyloid (beta) protein fragments >> invade and kill the cells.
**2-Neurofibrillary tangles** - *intracellular* - disturbed tau-microtubule complexes (hyperphosphorylated tau)> invade and kill the cells.
3-Cholinergic system degeneration ( in cholinergic system secretion of the brain>> memory and cognitive function impairment) with significant loss of neurons in certain areas (such as Nucleus Basalis of Meynert)
4-Degeneration often begins in **enterorhinal cortex** and progresses to other limbic structures





These brains are notable for sulcal THE SPACES BETWEEN THE GYRI widening….really seen throughout the cortex in the brains on the left, and seen in the frontal regions of the brain on the right.

## Course of AD:

-Insidious onset and progressive course with typical loss of 3 points on **mini–mental state examination** (MMSE) each year and death occurring 8-12 years after diagnosis. >> slowly progressive
-It progress slowly over 8-12 years from mild to moderate and then sever (bed ridden with motor deficit & rigidity due to involvement of basal ganglia) and death occur due to respiratory failure, septicemia or malnutrition.

-Diagnosis by CT&MRI will show atrophy of lobes bilaterally and EEG to assess the function of brain tissue)
-95% of AD are sporadic.

## Dementia Syndrome (Vascular Dementia):

Should be reserved for patients with clear evidence of stroke on imaging or physical examination.
-10-40% of all dementia cases
-10-15% of AD cases are "mixed" Because both VD and AD are common, you can also see "mixed dementias" where one patient may have both disease processes.
-Treatment focused on risk factors that predispose to cerebrovascular illness (Smoking, atrial fibrillation, diabetes, hypertension)

The diagnosis of Vascular Dementia should be reserved for cases where there is some obvious neurological deficit on physical examination or where there is a clear finding on neuroimaging.
Theoretically VD need not be as progressive as Alzheimer's Disease. Families and patients can be informed of this to encourage compliance with treatment. However, if the patient lives long enough, you cannot say that they are guaranteed NOT to get Alzheimer's Disease as well.

## Vascular dementia:

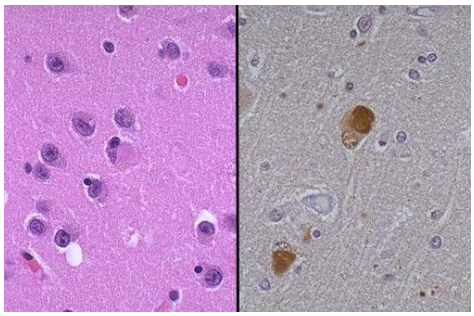
1-is Second most common form of dementia after AD
2- occlusion of arteries should be in both hemispheres (bilateral)
3-One or more strokes, two or more cognitive functions affected.
4-Abrupt onset and stepwise course--different from AD
5-Aka "Binswanger's Disease," "lacunar state," or "multi-infarct dementia."

It includes dementia resulting from cerebral ischemia or hemorrhage (post stroke dementia). Much rarer : dementia from global hypoperfusion (post CABG or post CHF). The second most common form of dementia after Alzheimer's disease is vascular dementia. This form of dementia is caused by one or more strokes. The definition of the dementia is essentially the same as for any other, ie, there should be memory impairment, and one other cognitive deficit associated with a significant decline in functioning. The onset is classically described as abrupt and the decline is classically stepwise, but this may be very difficult to determine.
Other names for this syndrome have included Binswanger's Disease, a "lacunar" state, or multi infarct dementia.

## Lewy Body Pathology:

-Concentric spheres found within vacuoles (eosinophilic cytoplasmic inclusions)
-Seen in *cortex, midbrain and brainstem neurons* in patients with idiopathic parkinsonism, Alzheimer's disease and especially Lewy Body dementias
-The main structural component is alpha-synuclein. Ubiquitin is sometimes seen also.

-cortical lewy bodies found at autopsy in a patient with Lewy Body Dementia. →



## Dementia Syndromes:

Lewy Body vs. Parkinson's:

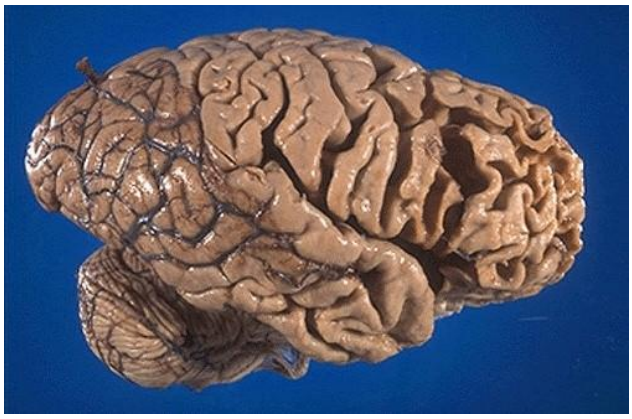
| LD | PD |
|---|---|
| Lewy Bodies are *cortical* | Lewy Bodies in *substantia nigra* |
| motor symptoms more closely linked to the memory problems | motor symptoms precede dementia *for years* |

Lewy bodies are inclusion bodies found in the neuron that kill the cell.
In DLB, Lewy Bodies are *cortical*.

## Dementia Syndromes: Frontotemporal dementia:

Frontotemporal dementias represent another category of neurodegenerative dementias. Pick's Disease is one of the frontotemporal dementias.
The presentation of patients with this type of dementia is characterized by personality changes, disinhibition of behaviors, affect, and executive functioning.
Again, in order for it to warrant the diagnosis of dementia, some memory impairment must be present as well.
It is possible to see localized atrophy on brain imaging in patients with this type of dementia. That is, the atrophy in the frontal or temporal lobes can be more profound than in other areas of brain. The atrophy can even be asymmetric.
Either involving posterior one third of frontal lobe and will affect motor&language. Or affecting anterior two thirds with impairment of thinking, emotion, behavior)

This is a gross brain specimen from an individual with Pick's disease. As you can see the atrophy is most pronounced in the frontal area of the brain although it does exist elsewhere too. The pathologists' jargon for this type of atrophy is "Walnut Brain."



Other things to remember about Frontotemporal Dementias include that they tend to be "presenile" in onset, that is, the typical age of onset is between 50 and 60 years of age.
The ultimate diagnosis is made at autopsy…these dementias also may have characteristic inclusion bodies.

## Additional Risk Factors for Dementia

1-Cerebrovascular disease (and the risk factors for CV disease – including smoking, diabetes, hyperlipidemia, hypertension) is associated with vascular dementia risk
2-Recurrent MDD may be associated with risk of dementia in general. (Kessing and Anderson found risk of dementia to be 6 times higher in patients with 5 or more prior episodes.)[1]
3-Subclinical Hyperthyroidism (especially when antithyroid antibodies are present.[2]

## Genetic risk factors

**Chromosome 19** - autosomal recessive - Apolipoprotein E-4 allele - associated with late-onset disease (not relevant for non-caucasians)

**Chromosome 1, 14, 21** - autosomal dominant mutations - associated with early-onset/familial cases. Amyloid processing genes.
**Chromosome 9** – 'ubiquilin 1' polymorphisms – needs replication

## Other less common dementias (reversible)

1-Primary degenerative dementias
-Diffuse Lewy Body dementias (7-26% of dementias)
-Frontotemporal dementias (Pick's, ALS, Huntington's)
2-Neurological disorders associated with dementia (PSP, Parkinson's dementia, NPH, neoplasms, head trauma, subdurals, demyelinating diseases)
3-Infectious causes
-neurosyphilis, Lyme disease
-post-encephalitic dementias (esp. herpes) patient present with seizure and fever (infection to temporal lobe) if not treated will spread bilaterally causing cell death (treat as soon as possible)
-viral, parasitic, bacterial and fungal meningitidies
-opportunistic infections or brain abscess
-Human prion disease (transmissible spongiform encephalopathies) - sCJD, 'Mad-cow disease'(vCJD), Kuru, fatal familial insomnia.

## General medical causes of dementia

1-Thyroid and adrenal disease.
2-Vitamin deficiency states (thiamin, niacin, B12)
3-Metabolic derangements (hepatic encephalopathy, dialysis dementia, etc.)
4-Medications side effects (sedatives, antihypertensives, narcotics, anticholinergics) also valium.
5-Whipple's Disease, sarcoidosis, Wilson's disease
6-Toxins (heavy metals, organic poisons)

## Rapidly Progressive Dementias (within one week):

1-Hashimoto's Encephalitis (treatable with steroids)
2-Cerebellar degeneration syndromes
3-Transmissible spongifrom encepalopathies (prion diseases)
4-Paraneoplastic syndromes
5-Postviral encephalitis
6-Rare cases of AD, DLB, FTD

## Clinical Presentation:

Always associated with cognitive disturbances and functional impairments
Visuospatial impairments and behavioral disturbances are usually seen as well
*Specific symptoms will vary by type of dementia*

## Memory Impairments

Difficulty learning or retaining new information (*repeated conversations*)
Information retrieval deficits (*can't recall names, list generation deficits*)
Personal episodic memory impairment (*misplacing items*)
Declarative (semantic) memory (WHAT) > procedural (implicit) memory (HOW)

## Language Deficits

List-generation deficits (esp. in AD)
Word-finding difficulties (*naming problems*)
Verbal fluency deficits
Less complex sentence structure
Relatively preserved auditory comprehension (*can understand directions*)

## Visuospatial impairments

Visual recognition impairments (*trouble recognizing familiar faces - **CAPGRAS syndrome** possible*)
Spatial deficits (*getting lost in familiar surroundings, 3-D drawing deficits*)
Executive Function Impairments
Planning, predicting, correlating, abstracting –> Frontal lobe F'n
Taking multiple threads of information and processing it to make a decision (Trails B testing)
Often the first impairment noticed in highly educated/intelligent people
Pronounced deficits often seen in FTDs before overt memory impairment

## Functional Impairments

Deficits appear first in IADLs (*managing finances, driving, shopping, working, taking medications, keeping appointments*)
Eventually problems with ADLs (*feeding, grooming, dressing, eating, toileting*)
Rate and specific pattern of loss will vary by individual and somewhat by diagnosis
**NB**: Functional impairment and performance on cognitive testing may not correlate strongly early in the course of dementia

## Behavioral Symptoms

Nearly universal and often the main focus of treatment. *Inability to manage these symptoms is highly correlated with institutional placement*.

## **PERSONALITY CHANGE**: Occurs early

**passivity** (apathy, social withdrawal)
**disinhibition** (inappropriate sexual behavior or language)
**self-centered behaviors** (childishness, loss of generosity)

**Agitation**
Very common and frequently worsens as the illness progresses
verbal aggression (25%)
physical aggression (30%)
non-aggressive behaviors such as wandering and pacing (25-50%)

**Other Associated Features**
**Depression** (40-50%) - esp. in AD & VD
**Psychosis**
Delusions (30-60%)
Paranoid type (theft, infidelity)
Misidentification type (Capgras, etc.)
Perceptual disturbances (20-40%) - often visual, common in LBD
**Sleep Disturbances** (>50%) - insomnia, sleep-wake cycle problems. *This plus wandering and aggression are highly correlated with care-giver burnout*

## Course & Staging of Dementia

Most have insidious onset with progressive decline over many years
Some are fulminate (JCD e.g.)
Some may remit spontaneously or with treatment (e.g. Thyroid disease, B12 def.)
**AD** - Predictable progression which is the reverse of development. Typically live 4 -10 years after diagnosis and often have symptoms 3-4 years before diagnosis. Women usually outlive men.*
**VD** - ***May*** show step-wise progression. Shorter course than AD. Often see focal findings

## DIFFERENTIAL DIAGNOSIS

**Amnestic syndrome** – short term memory (STM) impairments alone (wakes up without remembering anything (usually resolve within 1-2 days)
Receptive Aphasia - Impaired cognitive functioning due to failure to understand speech
**Mental Retardation** - Impaired intellectual abilities but not necessarily memory (in young patients)
**Pseudodementia** (*Dementia Syndrome of Depression*). 50% of elderly patients with Depressive Pseudodementia go on to develop irreversible dementia within 3-5 years!
Are-related cognitive decline: AKA *Age-associated Memory Impairment (AAMI), Benign Senescent Forgetfulness or Mild Cognitive Impairment (MCI).* Symptoms not currently associated with functional impairment. However, ~25%-35% progress to dementia within 18 months.

**Delirium** - Impairments of consciousness and attention. Commonly seen in dementia
**Acute** brain dysfunction characterized by:
Global symptoms (affecting both cerebral hemispheres) including impairment of consciousness and attention (affect the cortical areas and brainstem). Primary physiological changes with potential for reversibility 'waxing and waning' symptoms – usually worse in evening Life-threatening conditions underlying the syndrome

**Symptoms of Delirium:**
Common symptoms of a delirium include:
Waxing and waning levels of consciousness
Poor attention and disorientation
Disturbed memory (long and short term)
Psychosis
Sleep dysregulation
Fearfulness with agitation and aggression
Seriously impaired insight and judgment

## Delirium vs Dementia (summary)

General rules of thumb:

| Delirium | Dementia |
|---|---|
| Acute | chronic |
| Reversible | irreversible |
| Physiological | Structural |
| Primary attention deficits | primary memory deficits |
| Loss of short and old memory | Loss of short memory only |

Delirium and dementia can coexist; in fact delirium is **very** common in demented patients

## Causes of Delirium: (I WATCH DEATH)

Infectious - encephalitis, meningitis, UTI
- also systemic infections with sepsis, fever
Withdrawal
Acute Metabolic - electrolyte changes, dehydration, blood sugsr changes, acidosis, hepatic or renal failure
Trauma
CNS pathology - seizures, tumors, strokes, etc.
Hypoxia
Deficiencies - b12, thiamine
Endocrine
Acute Vascular
Toxins,Drugs
Heavy Metals

Diagnostic Approach

Early Detection & Screening with Careful history from patient and ***reliable*** informant. PE with focus on neurological exam and cognitive testing
Cognitive testing tools such as MMSE are helpful. Score below 24-27 often concerning depending on premorbid abilities
Functional Assessment tools such as the Functional Activities Questionnaire

## Diagnostic Work-Up

This is done to
(1) rule out disorders besides dementia,
(2) to identify reversible/treatable dementias (13%)
(3) to clarify the specific dementia syndrome
**Routine Assessment**: CBC with diff, serum electrolytes, Ca++, glucose, BUN/CR, LFTs, TFTs, B12 & folate, U/A, RPR
When indicated: Sed. rate, HIV, CXR, heavy metals, neuroimaging, LP, EEG, functional imaging, Lyme titers, endocrine studies, rheumatologic studies

## Guidelines for use of specialized testing

**LP**: Suspicion of metastatic CA, CNS infections, neuropsyphilis, hydrocephalus, vasculitis. Also for dementia <55 and rapidly progressive dementias
[Normal pressure hydrocephalus can present with dementia – ventricals dilated with no clear cause – memory impairment with gait apraxia and sphincter incontinence – treated with shunt and is reversible]
**Neuroimaging** - consider in all new cases. However when no focal symptoms or signs, seizures or gait disturbances in an individual over age 60 - *consider this optional*
**Functional Imaging** (SPECT, PET, MRS): to clarify type of dementia when necessary
**EEG** - can help distinguish delirium from dementia, can help with seizure disorder and CJD (periodic slow wave complexes)

## Neuropsychological Testing

Cognitive testing and functional testing are at odds or there is suspicion of early dementia in a high IQ individual with normal MMSE

Mild impairment in a person with: low IQ or limited education, trouble with English, impairments less than 6 months

*Determining capacity for legal purposes when deficits are mild*

## General Treatment Principles For Dementia

1-Treatment Of Underlying Disease Process (**Primary Treatment**)
2-Management Of Behaviors and Symptoms (**Secondary Treatment**)
Caregiver Support and Education

**Reversible Dementias** May become irreversible if not treated soon enough
.Many dementias may be arrestible if not fully reversible.
Rule out 'depressive pseudodementia' and delirium which can mimic dementia
Some reversible dementias include: hypoT4, B12 def., some infections and tumors, drug-induced syndromes, etc.

## Primary Treatment Strategies:
## (for progressive dementias)

1. **Prevention**

Identify risks and mitigate
Develop neuroprotective strategies for those at risk

2. **Slow or halt progression of illness**

Understanding pathophysiology leads to treatment ideas
**5 year delay in onset ---> 1/3 decrease in prevalence**
Delaying institutionalization by 1 month saves $1.2 billion/yr

3. **Reverse symptoms**

Compensate through augmentation of remaining neurons or other systems
Reversal of destructive processes & regeneration of tissue

## Cholinergic System Strategies:

Reduce Serum anticholinergic load
Precursor strategies (e.g. lecithin and choline)
Receptor/synaptic strategies
Metabolic strategies (anticholinesterases)

## Serum Anticholinergic Load & Cognitive Impairment

-90% of community elderly sample had detectable SA levels
-An SA level >2.8 pmol/Ml was 13X more likely to be associated with an MMSE of 24 or less in the general elderly population than in those with undetectable SA levels
-Univ Of Pittsburgh, AAGP 5th Annual Meeting, 2002

Commonly Prescribed Non-Psyciatric Drugs with Significant Anticholinergic Activity
cimetidine & ranitidine
prednisolone
theophylline
digoxin/Lanoxin
furosemide
nifedipine
diphenhydramine (OTC)
To a lesser extent: codeine, warfarin, dipyradimole, isosorbide dinitrate

## Current AChE Inhibitors:

| | Donepezil (Aricept) | Rivastigmine (Exelon) | Galantamine (Razadyne) |
|---|---|---|---|
| BuChE | Small | Yes | Small |
| Nicotinic modulation | No | No | Yes* |
| Half-life | 50-70 hrs | ½-2 hrs | 5-7 hrs |
| Starting Dose | 5 mg/day | 1.5 mg bid | 4 mg bid |
| Ending Dose | 5-10 mg/day | 3-6 mg bid | 8-12 mg bid |

STRATEGIES TO SLOW OR HALT PROGESSION

**-Calcium channel modulation and excitatotoxic systems attenuation (such as memantine)**
**-Anti-inflammatory/immunosuppressive strategies(e.g. NSAIDs) > not approved**
**-Gene therapy for defective protein regulation**
**-Toxin removal (Desferroxamine, clioquinol) / Ventriculoperitoneal shunting (COGNIShunt)**
**-Amyloid Protein strategies**

## Other Neuroprotective strategies

NGF -- see previous discussion. NGF can't cross blood-brain barrier so must be given intrathecally. Dr Winblad in Stockholm has used it on 2 patients "strongly improved memory", side effects include pain, anorexia and wt. loss.

## Neuroprotective Strategies

Nerve Growth Factor
Acetyl-l(levo) carnitine (ALCAR)
**Estrogen**
**Antioxidants** (Vit E, Gingko, deprenyl)
**'Statins'** (Lipitor, Pravachol) (may lower abnormal amyloid levels)
Rosiglitazone (Avandia) -anti-inflammatory, amyloid processing modulation activities
Physical and mental exercise

## Nutraceutical Strategies:

Vitamin E (antioxidant)
Homocysteine Reduction (folate, B6, B12)
Beta-carotene –
Physician's Health Study II found a cognitive protective effect of 50 mg every other day over two decades of use
Gingko (antioxidant)
Resveratrol (found in red wine)

**Estrogen** :At this point the summary of many studies suggests that ***Hormone replacement therapy (HRT) is questionably effective in slowing the onset of AD in some women***

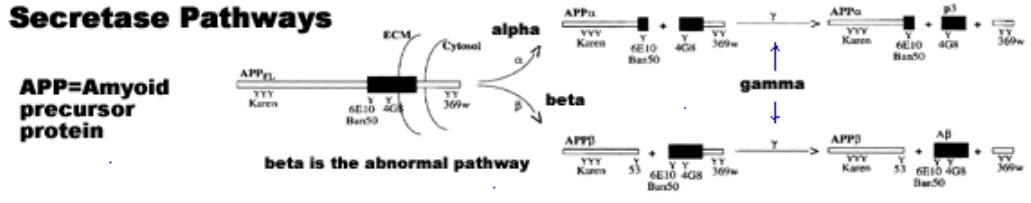
The earlier started, the better. Limited exposure may be best.
Progesterone may be detrimental
Tacrine response can be enhanced by Estrogen
**WHY?** neurotrophic effects, incr. ChAT, high serum E2 suppresses Apo E

Statins: Lovastatin (Mevacor), pravastatin(Pravachol), simvastatin(Zocor), atorvastatin(Lipitor)

May prevent aggregation of B-amyloid in the brain by preventing cholesterol build up. *May activate alpha-secretase*.
Conflicting evidence – recent U of Wash study did not find a benefit, but looked at older individuals on statins only a short while.
Earlier studies were more positive
Not sure if all these drugs are equal…

**Memantine**
-Glutamate is the principal *excitatory neurotransmitter* in brain regions associated with cognition and memory (i.e. it stimulates cholinergic neurons)
-Glutamate hypothesis of dementia suggests that overactivation of these neurons leads to excitatoxic damage to these brain areas (by allowing calcium to continuously 'leak in' to cells). It is post-synaptic receptor sensitivity rather than excess release of glutamate that is the problem.
-Memantine is a weak antagonist of glutamate-gated NMDA receptor channels which prevents overactivation during memory formation but allows normal function

## Abnormal Amyloid Protein Strategies




Most genetic mutations associated with AD affect amyloid processing
Senile plaques contain abnormal amyloid B fragments (that precipitate out of solution easily)

Attack enzymatic pathways that lead to production of abnormal type and amount of amyloid ( beta or gamma-secretase inhibitors)
Enhance alpha-secretase system to promote normal amyloid
Prevent aggregation (NSAIDS may do this!)
Alter the abnormal gene expression
GAG mimetics (glycosaminoglycans) –Alzhemed – interferes with formation of insoluble amyloid protein fragments

## Reversal Strategies:

Destroy the current plaques/amyloid
**Vaccination Strategy:** AN-1792 vaccine is in testing. This is an amyloid B protein fragment which can induce antibodies that bind to plaques and activate microglial destruction processes. Trial halted b/o menigoencephalopathies
**'Plaque busters'**
Alzhemed prevents Amyloid B fragments from forming fibrils
Clioquinol - A metal-protein-attenuating compound (MPAC) that inhibits zinc and copper ions from binding to beta-amyloid, thereby helping to dissolve it and prevent it from accumulating.
Transthyretin shows promise at interfering with toxic effects
Generate new tissue -
neuroregeneration strategies (STEM cells)
neurotransplantation strategies

## General Treatment Strategies For Behavioral Problems

Define symptoms clearly
Rule out other psychiatric illness (e.g. MDD)
Rule out medical causes for the symptoms (e.g. intercurrent illness, medication reactions, etc.)
Identify non-pharmacologic strategies
Pharmacotherapy

## Environmental Strategies

Identify provocations and rectify if possible
Appropriate re-orientation strategies
Optimize sensory input [i.e. correct visual and hearing impairments]
Behavior management strategies that respect the patient's need for control and autonomy (announcing intentions, single-step instructions e.g.)
Optimize physical activity, social stimulation, reminiscing.

## Management Issues

Alleviate patient's distress
Reduce care-giver burden
Delay institutionalization
Assure safety
Patient's often become 'more like themselves'

## Treatment of Depression

Recognize that irritability and/or apathy /withdrawal may be indicative of depression
Allow patient choices and control
Identify pleasurable activities (such as singing old songs, pet therapy, etc.)
Cognitive enhancers (e.g. Aricept) may help
Consider Ritalin for apathy, poor appetite

## Treatment of Agitation/Violence

Identify and reduce provocative stimuli if possible
**Optimize communication** with patient
Environmental modifications
Pharmacotherapy - target underlying cause (neuroleptics, antidepressants, mood stabilizers, beta blockers, buspirone, trazodone)

## Treatment of Psychosis

Recognize common delusions as relating to impaired STM (improving memory may help - e.g. donepezil)
Delusions often fade with time even without tx
Traditional antipsychotics
1-Low potency (chlorpromazine)– orthostasis, sedation, anticholinergic
2-High potency (***haloperidol***)– EPS/TD but otherwise well tolerated
New generations drugs (e.g. olanzapine, quetiapine, risperidone)- less EPS/TD but still see anticholinergic, BP and sedative effects

## Treatment of Wandering

Lock doors (but in a way that is confusing for AD patient but not others)
Wander guards
Decrease agitation (see above)
Environmental changes (such as using visual patterns to redirect wandering, wander gardens)

## Treatment of Insomnia

Sleep hygiene (avoid caffeine, etc.)
Treat causative psychiatric or medical disorders
Phsysiological remedies - melatonin, warm milk, lavendar oil
Medications - Benadryl, benzos, sedating antidepressants or antipsychotics (all these drugs can make memory and confusion worse)
Light Therapy - to reset natural circadian rhythms for sleep

## Sexually Disinhibited Behavior

Includes: sexual talk, sexual acts, implied sex acts, false reporting
Treatment or sexual aggression and/or disinhibition
Psychosocial : reminders, move to private room, clothing modification, staff education
Pharmacological: SSRIs, antiandrogens (medroxyprogesterone acetate, cyproterone acetate), estrogen patches

## Summary

- # Dementia is defined as Loss of memory with impairment of cognitive function that interferes with social and occupational functioning.
- # Major symptoms of dementia include memory loss with at least one of the following (aphasia, apraxia, agnosia)
- # Dementia always occur due to bilateral atrophy or damage of the brain.
- #Alzheimer disease is the most common cause dementia 50-75%.
- # **in AD: Neuritic plaques** -*extracellular* – amyloid (beta) protein fragments and **Neurofibrillary tangles** - *intracellular* - tau-microtubule complexes (hyperphosphorylated tau) > invade and kill the cells.
- # In Alzheimers : Memory loss (is the first and major symptom) , Frontotemporal (Picks) begins with personality and behavioral changes and Lewey Body start with Visual hallucinations.
- # Vascular dementia is Second most common form of dementia after AD.
- #an important goal in treating stroke patients is preventing another attacks of stroke to prevent development of dementia.
- #In Lewy body (eosinophilic cytoplasmic inclusions) found in cortex and midbrain ,alpha-synuclein is the main structural component.
- #in Parkinson's disease Lewy Bodies are found in *substantia nigra.*
- #Delirium is reversible acute impairments of consciousness and attention Commonly seen in dementia.
- # Frontotemporal Dementias tend to be “presenile” in onset, that is, the typical age of onset is between 50 and 60 years of age.
- # Rapidly Progressive Dementias (within one week) usually occur in Hashimoto’s Encephalitis ,Cerebellar degeneration syndromes and Postviral encephalitis.
- # Reversible type is more rapidly progressive than irreversible type and if not treated immediately, it can lead to death of neurons and become irreversible.

**References:**

Doctor's slides and lecture notes