# MEDICINE

## 432 Team

# 50 Dementia


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**COLOR GUIDE:** • Females' Notes • Males' Notes • Important • Additional

# Objectives

Not given

# Dementia

Dementia is a progressive deterioration in intellectual functions typically with preservation of consciousness.

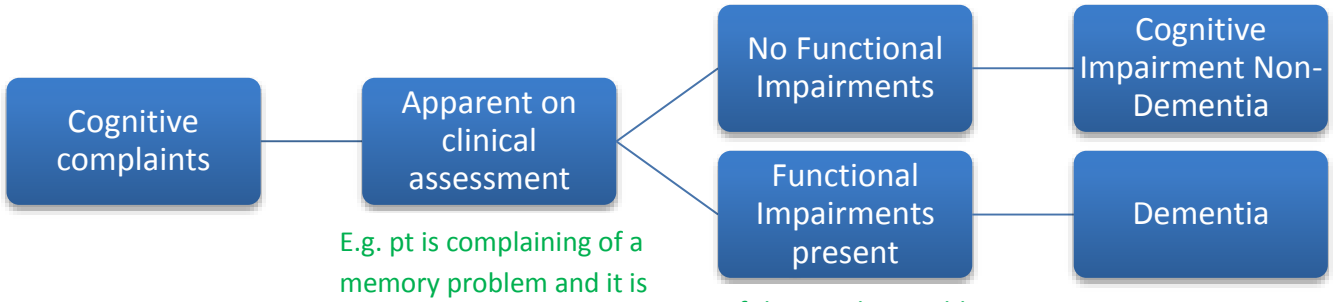
> ***Note:***
>
> *Delirium, usually encompasses: "Acute confusional state" and "encephalopathy"*

## Delirium (acute confusional state)

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) diagnostic criteria for delirium is as follows:

- **Disturbance in attention** (ie, reduced ability to direct, focus, sustain, and shift attention) and awareness.
- **Change in cognition** (eg, memory deficit, disorientation, language disturbance, and perceptual disturbance) that is not better accounted for by a preexisting, established, or evolving dementia.
- **The disturbance develops over a short period** (usually hours to days) and tends to fluctuate during the course of the day.
- **There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by a direct physiologic consequence of a general medical condition, an intoxicating substance, medication use, or more than one cause.**

## Dementia or Cognitive Impairment?



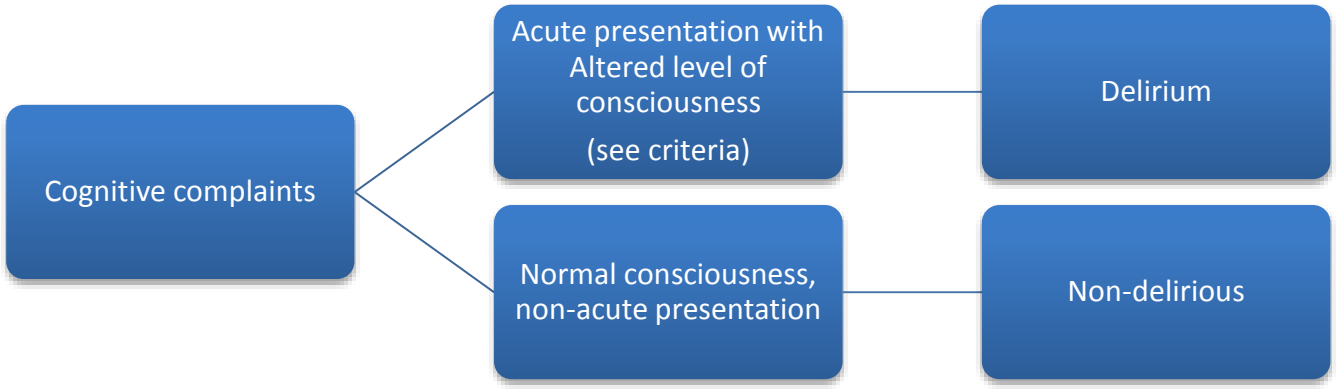

E.g. pt is complaining of a memory problem and it is documented on clinical assessment.

E.g. if the pt is being able to get along with their memory problem by using notes and reminders, this is not functional impairment.

Functional impairment is when they can't get through their daily activities even with reminders.

The key difference between dementia and cognitive impairment is the ability to function.

# Dementia or Delirium?




It is not normal to have delirium, while this statement is obvious, patients' who have symptoms of delirium are dismissed as being sleepy, tired, or just age related changes. BEING OLD ≠ being confused or mentally impaired.

***Note(s):***

*Delirium can be reversed, find the underlying cause and treat it, unlike dementia that has permanent degeneration.*

## Important clues to recognize delirium:

- Patient will not be able to give you a history.
- Rapid development of symptoms (hours or days).
- Change in level of consciousness.
- When the patient appears awake, assess level of attention (not being able to hear you because his attention is altered).
- Poor content of conversation and/or other cognitive deficits (memory loss, disorientation, and abnormal language), neuropsychiatric symptoms such as hallucinations (visual, auditory somatosensory…etc.) and delusions of harm (ex: thinking that CIA is trying to catch them or do them harm).

The opposite, hypervigilance, may occur in substance withdrawal (e.g.: alcohol or sedative). (In agitated delirium they appear more awake and alert but in fact they are not attentive or focused).

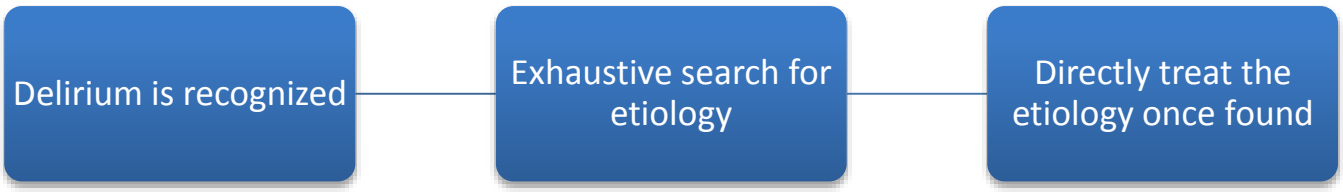
## Causes of Delirium:

- Metabolic, examples include dehydration, hyponatremia, hypocalcemia, abnormal thyroid functions, liver and/or renal impairments, hypoglycemia.
- Toxic: ETOH and drugs of abuse.
- Infectious: UTI, pneumonia, or infections that result in systemic manifestations.
- Side effects of drugs or the abrupt discontinuation of certain drugs like benzodiazepines.
- Post surgery (anesthetics, pain)
- Disorders of the central nervous system (large strokes, Post-seizures, infections)

## What can look like delirium? (DDx:)

- Non-convulsive seizures (in older patients usually but can occur at any age, they look confused but actually they are seizing from inside, if an EEG is done it will show the presence of seizures).
- Sundowning behavior (a multitude of behavioral problems occur in the evening or when the sun is setting, can be part of dementia or other behavioral problems).
- Dementia
- Psychiatric disorders (ex: schizophrenia)
- Aphasias
- Transient Global Amnesia (short term memory loss and recovery within 24 hrs but their level of consciousness is normal).

## Delirium management



Delirium is a symptom that you have to look for the underlying cause.

The choice of the investigations should be guided by your history and clinical examination findings.

There are many causes of delirium, so an initial investigation may include (but not limited to) the following:

- CBC, electrolytes, urea, creatinine, LFT, ESR, TSH +/- Auto-immune evaluation
- Arterial blood gases
- Urinalysis and toxicology screen
- Chest X-ray, EKG
- CT head, EEG, Lumbar Puncture

# Dementia-Major Neurocognitive Disorder (DSM V)

Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains*:


- Learning and memory
- Language (a gradual development of aphasia not an acute onset like in stroke)
- Executive function (problems in planning and initiation)
- Complex attention (ex: attending a lecture needs complex attention)
- Perceptual-motor (a condition called apraxia it is the inability to perform a certain task or skill that you used to do well despite having normal motor function ex: lose the ability to brush your teeth which you are used to do despite there is no paralysis or weakness)
- Social cognition (not knowing what is appropriate to say or do socially)

The cognitive deficits interfere with independence in everyday activities.

The cognitive deficits do not occur exclusively in the context of a delirium (if there is recovery in a day or two by treating the underlying cause this is delirium not dementia).

The cognitive deficits are not better explained by another mental disorder (e.g. major depressive disorder, schizophrenia)

## Major Dementias

- Neurodegenerative:
  - Alzheimer's Disease
  - Lewy Body Dementia
  - Parkinson's Disease Dementia
  - Fronto-temporal Dementia
  - Huntington's Disease
- Other:
  - Vascular Dementia
  - Normal Pressure Hydrocephalus
  - Creutzfeldt-Jakob Disease
  - Wernicke-Korsakoff Syndrome
  - Secondary to infection or systemic illness

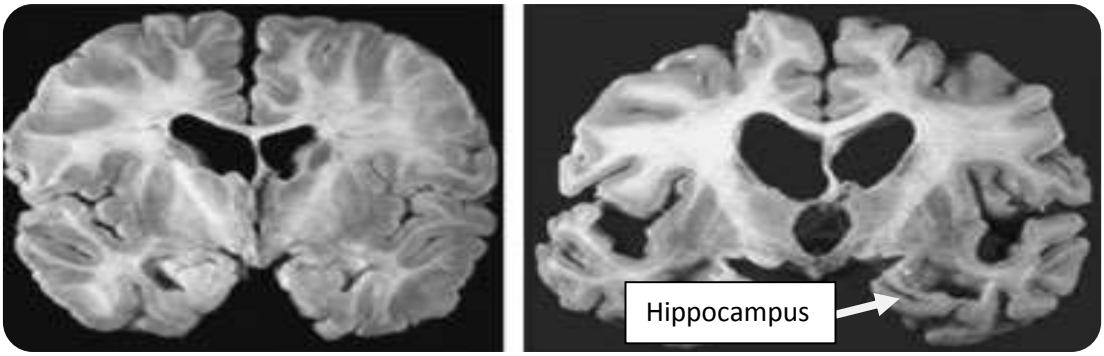
# Alzheimer's disease

- Uncommon under the age of 60.
- Decreased memory and new learning is the hallmark of the condition.
- Language impairment: Word finding difficulties with circumlocution (the use of many words were fewer would do) and anomia (the inability to name objects or to recognize the written or spoken name of objects).
- Executive dysfunction.
- Apraxia, Unawareness of illness.
- Visual-spatial impairments.
- Passivity, apathy (don't care or not interested) > agitation.
- Delusions.
- Depression (tend to start early in the course).
- Circadian rhythm disturbances (sundowning).
- Weight loss.

## Risk Factors for AD:

Major risk factors:

- Increasing age
- (APOE ε4) The E4 allele for Apolipoprotein E on chromosome 19 (found in 40% of Alzheimer's patients but not used for diagnosis cause many people have the gene but do not develop Alzheimer).
- Down Syndrome (with age they develop brain degeneration)
- Specific inherited types
- Mid-life vascular risk factors (DM, HTN, Hyperlipidemia, Lack of exercise)
- Brain trauma




Normal

The hippocampus is atrophied and is the site of memory as well as the whole brain is atrophied

## Mild Cognitive Impairment


Patients with MCI may remain with MCI, may go back to normal, or may progress to dementia. The risk of conversion to dementia is 15% per year

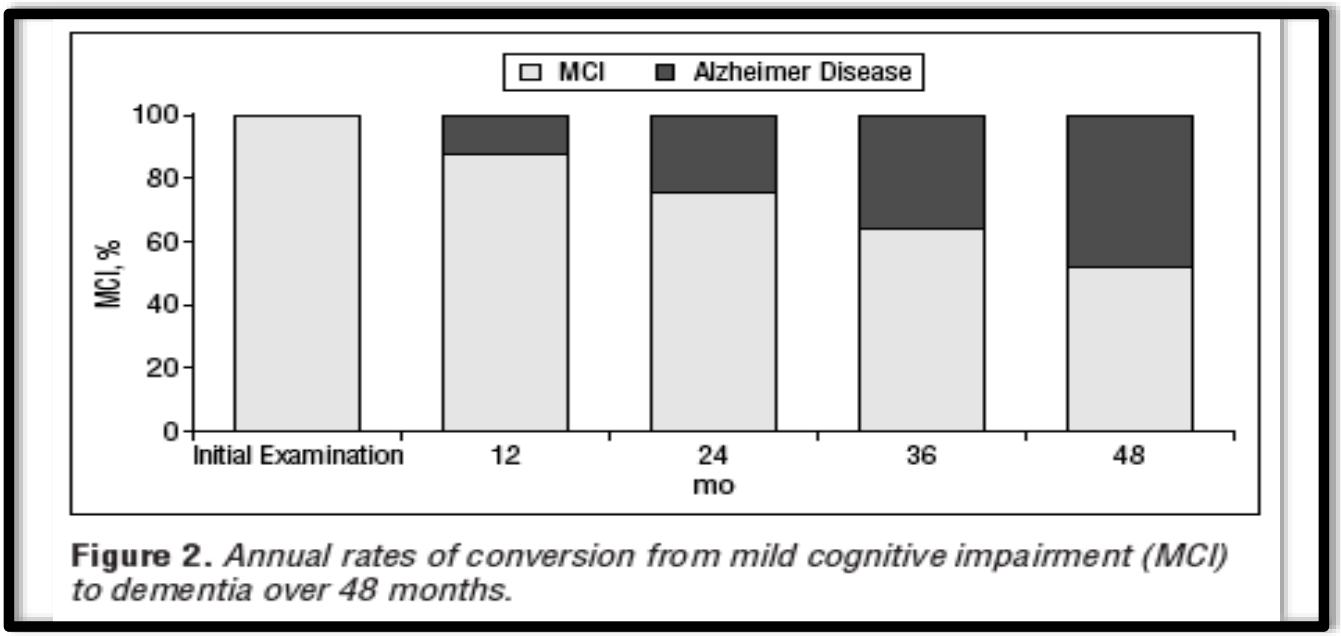
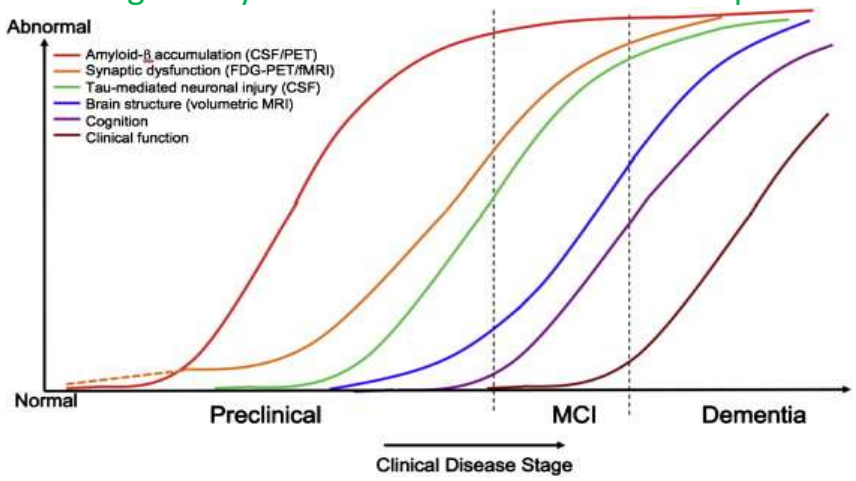



**Figure 2.** *Annual rates of conversion from mild cognitive impairment (MCI) to dementia over 48 months.*

50% of pt with MCI will develop Alzheimer disease over 48 months. In the normal population it is 1-2%.

## Pathophysiology:

- Defects in the mechanisms for clearing amyloid beta results in its accumulation and form senile plaques.
- Abnormal accumulation of hyper-phosphorylated **tau** protein results in accumulation and the formation of neurofibrillary tangles.
- **Tangles and plaques are pathological hallmarks in Alzheimer's disease.**
- The resultant loss of neurons and synapses is responsible for the clinical profile
- The neuronal loss in the basal forebrain region is responsible for a cholinergic deficit (not enough acetylcholine in the brain which is important for memory).




## Diagnosis

- **Diagnosis is clinical**

- Rely on history and cognitive/neuropsychological assessments that demonstrates a slowly progressing cognitive disorder which causes impairments in daily life.

- Brain structure on MRI may demonstrate medial temporal atrophy bilaterally.

- PET scans can demonstrate decreased metabolism in temporal and parietal regions.

- Cerebrospinal fluid might show low Amyloid beta, and elevated Tau (not specific).

# Lewy Body Dementia

- Second most common cause of "degenerative" dementia.
- Core clinical features include **visual hallucinations, Parkinsonism, and fluctuations in cognitive ability and level of consciousness.**
- Other symptoms include visual spatial impairment > short term memory, sensitivity to neuroleptics (they develop rigidity and makes it worse), REM sleep behavior disorder (normally in REM sleep we are paralyzed and do not act out our dreams but with REM sleep behavior disorder they lose this paralysis and start kicking and punching during their sleep) and autonomic dysfunction (postural hypotension, erectile dysfunction or urinary incontinence).
- Pathologically there are "Lewy Bodies" present in neurons, which are the result of abnormal synuclein protein accumulation.
- Diagnosis is primarily clinical.
- PET scan may show decreased ***occipital lobe*** metabolism.
- Myocardial scintigraphy may be abnormal due to abnormal cardiac sympathetic innervation

**Parkinson's disease Dementia is similar to LBD. The difference is that a clear history of PD with NO cognitive impairment precedes the development of dementia by at least a year.**

# Vascular Dementia

- Occurs secondary to:
  - A single stroke in a region important to cognition such as hippocampus or thalamus, or a large stroke that affects multiple lobes.
  - Recurrent strokes that accumulate over time, there is a step-wise development of cognitive deficits.
  - Slowly progressing cognitive deficits due to subclinical progressing of small vessel disease.
- Associated with vascular risk factors (HTN, DM, Hyperlipidemia, & smoking)
- Frequently coexists with Alzheimer's disease.

# Frontotemporal Dementia

Mean age of onset is 58

Preferentially involves the **frontal** and **temporal** lobes, symptoms depend on the region (lobe) involved, therefore there are variants:

- Behavioral Variant is associated with personality changes, inappropriate social behaviors (disinhibited), lack of insight, Binging on certain foods, emotional blunting, rigid and cannot adopt to new situations, along with decreased attention modulation. MRI shows atrophy in the frontal lobes (may be asymmetric).
- Primary Progressive Aphasia: patients present first with a non-fluent type of aphasia (similar to a Broca's lesion). MRI may show focal left frontal atrophy. (start talking slowly, trouble pronouncing words, it is like a Broca's aphasia developing slowly over time)
- Semantic Dementia (temporal variant of FTD): Usually have intact fluency, but comprehension is impaired and decreased naming ability. MRI may show focal left temporal atrophy. (more lateral while in Alzheimer it's in the hippocampus more in the medial temporal lobe) (similar to Wernick's aphasia developing slowly over time, lose the ability to comprehend the words)
- Executive dysfunction with the involvement of frontal lobe.

Common pathological inclusions include hyperphosphrylated tau protein (there will be no tangles and plaques formation), TDP-43 protein, or FUS protein

# Normal Pressure Hydrocephalus:

- A rare disorder
- It classically presents with gait impairment, urinary incontinence along with the dementia. However these features are not unique to NPH. (like in Lewy body dementia may develop urinary incontinence cause of autonomic dysfunction or gait problems cause of parkinsonism)

- Dementia is of a subcortical type, where there is executive dysfunction, and psychomotor slowing first. Other features of cognitive impairment develop later on.
- The typical gait has been described as "magnetic", the patient may shuffle their feet on the ground with a normal or wide base, some may have some features of Parkinsonism.
- It usually results from impaired CSF absorption at the level of the arachnoid villi. (their basal rate is normal but if you stress it for any reason may cause raised ICP)
- In Secondary NPH, there is usually a history of a previous meningitis, inflammatory disorder, or subarachnoid hemorrhage. Idiopathic NPH is when there is no preceding explanation for the condition.
- Patients who present with gait impairment > cognitive impairments have better prognosis if identified early.
- Some patients will improve after a lumbar puncture that removes 30-50 cc of CSF. If this test is positive, than a CSF shunting procedure is performed.
- The MRI brain may also show dilated ventricles (however CSF pressure is normal).

# Creutzfeldt-Jakob Disease

- Rare, 1 in a million
- It is a prion disorder and can be transmitted (transmissible spongiform encephalopathy)
- Can be sporadic CJD, genetic CJD, bovine CJD or iatrogenic
- Prions are abnormally formed proteins (distinct abnormal folding, not an organism) that induce pathological transformations in other proteins. (one prion comes in contact with other protein will transform it to a prion)
- It has been transmitted after the use of surgical equipment or growth hormones (iatrogenic)

- CJD presents as a rapidly progressing dementia, disease duration usually 6 months. Myoclonic jerks may occur.
- Any picture of cognitive impairment may occur, as may other neurological symptoms like Parkinsonism, ataxia, field defects, spasticity, hyper-reflexia, and + Babinski.
- MRI may show abnormal signal intensity in the basal ganglia and cortical ribbon
- EEG shows characteristic periodic sharp wave complexes (in about 40% of patients)
- No treatment, patients die within a year.
- The bovine variant CJD has been linked to consumption of beef (UK outbreak in the 90s)

# Other causes of dementia

- HIV Associated neurocognitive disorder
- Syphilis
- Vitamin B12 deficiency
- Thyroid dysfunction (myxedema madness)
- Autoimmune disorders (eg: SLE)
- Alcohol leading to Wernicke-Korsakoff's syndrome, characterized by confabulations (fill in the memory gaps with fantastic stories) to compensate for amnesia
- These are possibly reversible if treated.

# Management of dementia

Cholinesterase Inhibitors (increasing ACh):

- Drugs such as Donepezil, rivastigmine and galantamine which increase the presence of central nervous system acetylcholine help with cognitive and behavioral symptoms in Alzheimer's dementia but it is not beneficial in patients with MCI (the cholinesterase inhibitors such as prostigmine used in myasthenia gravis is peripherally acting)ACh is important in forming memories.
- Does not stop disease progression (the amyloid deposition and the pathological process is still going on), but may provide transient clinical stability.
- NMDA receptor antagonist, memantine, is helpful in advanced Alzheimer's disease (NMDA is a transmitter that mediates cell death so we try to block it).
- No treatment available for MCI

## SUMMARY

1. Delirium usually encompasses: "Acute confusional state" and "encephalopathy".
2. Important clues to recognize delirium (read page 3).
3. **Causes of Delirium:** metabolic, toxic, infectious, side effects of drugs or the abrupt discontinuation of certain drugs like benzodiazepines, post-surgery (anesthetics, pain), and disorders of the central nervous system.
4. Delirium is a symptom that you have to look for the underlying cause.
5. **Alzheimer's disease:** Uncommon under the age of 60, decreased memory and new learning is the hallmark of the condition, language impairment, executive dysfunction, and apraxia.
   Major risk factors: Increasing age, (APOE ε4) The E4 allele for Apolipoprotein E on chromosome 19, Down syndrome, specific inherited types.
   Pathophysiology: Defects in the mechanisms for clearing amyloid beta results in its accumulation and form senile plaques
6. **Lewy Body Dementia is** second most common cause of "degenerative" dementia. Core clinical features include visual hallucinations, parkinsonism, and fluctuations in cognitive ability and level of consciousness. Pathologically there are "Lewy Bodies" present in neurons, which are the result of abnormal synuclein protein accumulation.
7. **Management of dementia:** Drugs such as Donepezil, Rivastigmine and Galantamine which increase the presence of central nervous system acetylcholine help with cognitive and behavioral symptoms in Alzheimer's dementia

# Approach to Dementia

## Dementia and Cognitive Impairment

## DIFFERENTIAL DIAGNOSIS OF PTOSIS

**PRIMARY PROGRESSIVE DEMENTIA**

- **ALZHEIMER'S** slow insidious cognitive decline but otherwise no physical findings, mini mental status examination globally low, CT may show white matter change, mostly a diagnosis of exclusion, but accounting for 60% of dementias
- **VASCULAR** acute stepwise or slow progressive decline, focal neurological deficits, mini mental status examination patchy, CT may show white matter change, pure vascular dementia uncommon, more frequently occurs with Alzheimer's like dementia (mixed vascular)
- **PARKINSON'S** Parkinsonian symptoms for a long time, slow decline, Parkinson's patients have 6X increased risk for dementia
- **LEWY BODY** Parkinsonism, persistent visual hallucinations, progressive decline, fluctuating cognition especially attention/alertness, marked adverse hypersensitivity to typical antipsychotic medications, supportive features include syncope, delusions, and sleep disturbance
- **FRONTOTEMPORAL** prominent impairment in executive function, disinhibited or passive presentation, impaired judgment, significant social indifference, declining hygiene, prominent language deficits but amnesia less noticeable early on, early primitive reflexes/incontinence, late akinesia/rigidity/tremor, MMSE may be normal, abnormal clock drawing, CT frontal temporal atrophy
- **PRION DISEASE** Creutzfeldt Jakob disease

**POTENTIALLY REVERSIBLE DEMENTIA (<1%)**

- **METABOLIC** alcoholism, vitamin B12, hypothyroidism
- **STRUCTURAL** NPH, subdural hemorrhage, neoplastic, vascular
- **INFECTIONS** chronic meningitis, HIV, neurosyphilis, Whipple's
- **INFLAMMATORY** vasculitis, Hashimoto encephalitis, multiple sclerosis
- **DEMENTIA MIMICS** depression, delirium, developmental disorder, age associated memory impairment

## CLINICAL FEATURES

**RATIONAL CLINICAL EXAMINATION SERIES:**

**DOES THIS PATIENT HAVE DEMENTIA?**

**MINI MENTAL STATE EXAMINATION (MMSE)**

Orientation to place (5), time (5), immediate and delayed recall (6), spell 'WORLD'' backward (5), 3 step commend (3), name 2 objects (2), close your eyes (1), repeat sentence 'No, if's, and's, or but's'' (1), write a sentence (1), intersecting pentagons (1).

Maximum score is 30, generally <24 is impaired but varies with education and age

**MEMORY IMPAIRMENT SCREEN** recall four objects (an animal, a city, a vegetable, and a musical instrument). Two points for free recall of each object and one point if prompting needed (''Tell me the name of the city.''). Maximum score is 8. Takes

4 min

**APPROACH** ''to detect cognitive impairment of at least moderate severity, consider the mini mental

state examination. The Hopkins Verbal Learning Test or the Word List Acquisition Test may be used to screen for mild impairment in highly educated patient. If very little time is available, consider the Memory Impairment Screen or the Clock Drawing Test. If plenty of time is available, consider the Cambridge Cognitive Examination, Modified Mini Mental State Examination, Community Screening Interview for Dementia, or the Montreal Cognitive Assessment''

# Questions

1) If a patient with rapid progressive dementia associated with myoclonus, the most likely diagnosis is:
   a. Creutzfeldt-Jakob Disease
   b. Frontotemporal Dementia
   c. Lewy body Dementia
   d. Normal Pressure Hydrocephalus

2) If a patient with dementia associated with urinary incontinence, the most likely diagnosis is?
   a. Creutzfeldt-Jakob Disease
   b. Frontotemporal Dementia
   c. Lewy body Dementia
   d. Normal Pressure Hydrocephalus

3) All of the following can cause **reversible** dementia expect:
   a. Neurosyphilis.
   b. Vitamin B12 deficiency.
   c. Hyperkalemia.
   d. Hypothyroidism.

***432 Medicine Team Leaders***

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**Answers**:

1st Questions: A

2nd Questions: D

3rd Questions: C