Delirium and Dementia

435 medicine teamwork

[**Important** | **Notes** | **Extra** | **Editing file**]

lecture objectives:

- Differentiate delirium from dementia
- Differentiate MCI from Dementia
- Become familiar with common dementia syndromes

Dr taim Said about the slides as source for exam preparation "Yes, as a general guide, though best to read from any text book on anything mentioned in the slides only"

but we still used another resources as mentioned below to make it as perfect as we can

Good luck!

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References: Slides, doctor's note, Davidson, step up, master the boards

Delirium

What is Delirium?

- Delirium usually encompasses: **1.** Acute confusional state **2.** Encephalopathy
- It is not normal to have delirium, however, patients who have symptoms of delirium are dismissed as being sleepy, tired, or just age related changes
- Old age SHOULD NOT excuse confusion or mental impairment
- Delirium is an acute presentation with altered level of consciousness

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, perceptual disturbance) that is not better accounted for by a preexisting, established, or evolving dementia "changes from the patient's baseline"
- 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, and/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.

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
- Poor content of conversation and/or other cognitive deficits (memory loss, disorientation, abnormal language), neuropsychiatric symptoms such as hallucinations (visual, auditory somatosensory…etc) and delusions of harm

NOTE:
Hypervigilance may occur in substance withdrawal (eg: alcohol or sedative)

NOTE:
Hallucinations: Abnormal perceptions, seeing what is not there
Delusions: Strange ideas or thoughts like thinking you're being followed by the FBI

Causes of Delirium

- Metabolic, examples include: dehydration, hyponatremia, hypocalcemia, abnormal thyroid functions, liver and/or renal impairments, hypoglycemia always check glucose levels
- Toxic: ETOH (ethanol) and drugs of abuse
- Infectious (usually in the elderly): 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)

Management of Delirium

(it is a medical emergency)

- The choice of the investigations should be guided by your history and clinical examination findings
- There many causes of delirium, initial investigations 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
- Directly treat the etiology once found

Differential Dx of Delirium

- Non-convulsive seizures
- Sundowning behavior[1]
- Dementia
- Psychiatric disorders
- Aphasias
- Transient Global Amnesia[2] (it usually resolves within 24 hrs.)

Dementia-Major Neurocognitive Disorder

What is Dementia?

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

NOTE:
Guidelines provided by the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM V)

- Learning and memory
- Language
- Executive function[3]
- Complex attention (multitasking)
- Perceptual-motor
- Social cognition (Behaving in a socially accepted manner)
  - Impairment in one or more of these could mean that the patient has dementia

Where:

- The cognitive deficits **interfere with independence in everyday activities** (if it does not interfere with everyday activities it isn't dementia, we may call it Mild Cognitive Impairment[4]).
- The cognitive deficits do not occur exclusively in the context of a delirium
- The cognitive deficits are not better explained by another mental disorder (eg: major depressive disorder, schizophrenia)

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[1] Sundowning, or sundown syndrome, is a neurological phenomenon associated with increased confusion and restlessness in patients with delirium or some form of dementia this is where people tend to be awake during the night and sleepy during daytime, you try to wake them up but they're so sleepy they go back to sleep again

[2] a person comes in with memory impairment within 24hr, يجيك يقول أنا وش جابني هنا؟ with NO history of trauma, it happens to those who are obese?

[3] It's like going on a business trip to Jeddah, you book your own ticket, drop your luggage, get on the plain and receive your luggage from the airport then you order a cab to your hotel, this is all considered executive function.

[4] An example would be in someone is forgetting a lot and keeps adding more and more reminders, طالما هو يمشي حاله it is no dementia, it might be MCI

Delirium Vs. Dementia

Delirium	Dementia
- Acute presentation Time is really important - Altered level of consciousness - Tremors are sometimes present (+ asterixis) - Rapid waxing and waning onset - Visual hallucination are common	- Functional impairment - Normal consciousness - Tremors only in the case Parkinsons - Insidious, progressive course - Hallucinations uncommon

Major Dementias

Neurodegenerative	Other
• Alzheimer's Disease • Lewy Body Dementia • Parkinson's Disease Dementia • Frontotemporal Dementia • Huntington's Disease	• Vascular Dementia (Multi infarct dementia and binswanger disease) • Normal Pressure Hydrocephalus • Creutzfeldt-Jakob Disease • Wernicke-Korsakoff Syndrome • Secondary to infection or systemic illness

NOTE:
Binswanger disease is seen in patients with longstanding HTN and atherosclerosis, it is the insidious onset of diffuse subcortical white matter degeneration.

Another classification of the causes of dementia:

Potentially Reversible	Irreversible

• Hypothyroidism
• Neurosyphilis (Tertiary syphilis)
• Vitamin deficiencies
  ▹ B12 (Cobalamin)*
  ▹ B1 (Thiamin)
  ▹ B9 (Folate)
• Normal pressure hydrocephalus
• Depression (Pseudodementia)
• Subdural hematoma
• Medications (anticholinergics)
	• AlZheimer's
	• Parkinson's
	• Huntington's
	• Lewy Body dementia
	• Multi infarct hematoma
	• Korsakoff syndrome (untreated B1 deficiency)
	• HIV dementia
	• Creutzfeldt Jakob disease

NOTE:
You don't have to have anemia with B12 deficiency to have neurologic disease. How? With B12 deficiency, you cannot convert odd chain FA into succinyl CoA → so they build up and screw up your myelin → you cannot synthesize myelin → dementia, demyelination of posterior columns and lateral corticospinal tracts.

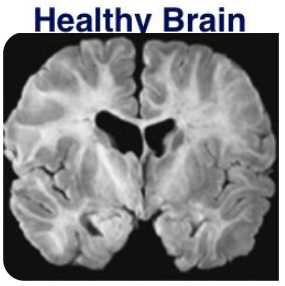
Alzheimer's Disease

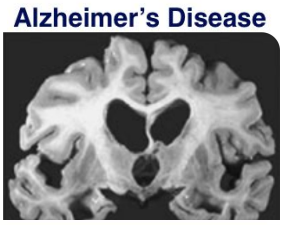
8:53

Clinical Features

- Uncommon under the age of 60
- Represents up to 60-70% of cases of dementia
- Very common and can coexist with any type of dementia
- Decreased memory and new learning is the hallmark of the condition, memory impairment is the first sign of the disease

- Language impairment: Word finding difficulties with circumlocution[5] and anomia[6]
- Executive dysfunction
- Apraxia[7], Unawareness of illness (common)
- Visual-spatial impairments
- Passivity, apathy then agitation
- Delusions
- Depression
- Circadian rhythm disturbances (sundowning)
- Weight loss





NOTE THAT
Atrophy begins in the temporal lobe around the hippocampus, and that's why the memory is affected first. With time, atrophy will involve the entire brain

Major risk factors:

- **Increasing age** (most important)
- (APOE ε 4) The E4 allele for Apolipoprotein E on chromosome 19
- Down Syndrome the majority get it by 40 (gene encoding APP is located on chromosome 21)
- Genetic inheritance (mutations in APP or ɣ-secretase)
- Mid-life vascular risk factors (DM, HTN, Hyperlipidemia, Lack of exercise)
- Brain trauma

Pathophysiology

- Defects in the mechanisms for clearing amyloid beta result in its accumulation forming senile plaques
- Abnormal accumulation of hyperphosphorylated tau protein (a protein involved in intracellular microtubular pathways, altered by the beta results in accumulation and the formation of neurofibrillary tangles
- Defects in the normal clearing of APP (amyloid precursor protein) will lead to the formation of β amyloid that is insoluble, and will aggregate forming plaques that alter nerve to nerve signaling, leading to neuronal cell apoptosis (by tau protein intracellularly), and affect the vasculature predisposing to intracerebral hemorrhage
- Tangles and plaques are pathological hallmarks in Alzheimer's disease (All AlZheimers patients have them but they may also be found in healthy people with normal lifespan on autopsy)
- 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
- In contrast to dementia, Minimal/Mild Cognitive Impairment (MCI) does not interfere with everyday activities
- This is an important curve to show the pathological progress

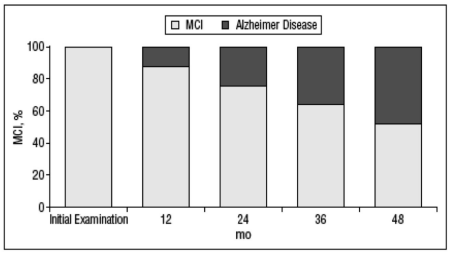
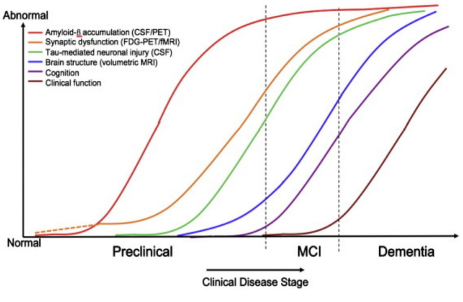


Figure 2. *Annual rates of conversion from mild cognitive impairment (MCI) to dementia over 48 months.*



[5] The unnecessary use of more words
[6] A form of aphasia where a person cannot recall the name of objects like knowing what a pen can do but forgetting its name
[7] **Apraxia** is a motor disorder caused by damage to the brain (specifically the posterior parietal cortex). In which the individual has difficulty with the motor planning to perform tasks or movements when asked, provided that the request or command is understood and he/she is willing to perform the task

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)
- B12 with or without methylmalonic acid levels (more specific)
- Thyroid function tests
- VDRL or RPR (to exclude neurosyphilis)

Lewy Body Dementia

Clinical Features

- Second most common cause of **degenerative** dementia
- Core clinical features includes visual **hallucinations**, **parkinsonian features** (mainly tremors), and **fluctuations** in cognitive ability and level of consciousness (e.g. fluctuating level of orientation)
- Visual spatial impairment[8] (first sign) followed by short term memory, sensitivity to neuroleptics, REM sleep behavior disorder and autonomic dysfunction
- Pathologically there are "Lewy Bodies" present in neurons, which are the result of abnormal synuclein protein accumulation.
- 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
- After years of disease, those with Parkinson's develop Lewy Body dementia

Diagnosis

- Diagnosis is primarily clinical
- PET scan may show decreased occipital lobe metabolism
- Myocardial scintigraphy may be abnormal due to abnormal cardiac sympathetic innervation

Vascular Dementia

Clinical Features

- 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

[8] It is how you interact with the environment, a normal person knows where the chair is in relation to the disk, so he pulls the chair from the disk and orient his body to sit. Getting from one room to another in the house is another example. However, these are impaired here

- Recurrent strokes that accumulate over time, there is a stepwise development of cognitive deficits
- Slowly progressing cognitive deficits due to subclinical progressing of small vessel disease

- Frequently coexists with Alzheimer's disease
- Associated with vascular risk factors
  - Hypertension and hyperlipidemia
  - Diabetes Mellitus
  - Smoking

Frontotemporal Dementia

Clinical Features

- Mean age of onset is 58 (earlier than the other forms of dementia)
- Preferentially involves the frontal and temporal lobes, symptoms depend on the region (lobe) involved, therefore there are variants:
  - Behavioral Variant
  - Primary Progressive Aphasia
  - Semantic Dementia
- Common pathological inclusions include hyperphosphorylated tau protein, TDP-43 protein, or FUS protein

Behavioural Variant

- Associated with personality changes
- Inappropriate social behaviors (disinhibited)
- Lack of insight they do not understand the consequences of their actions
- Binging on certain foods usually carbohydrates
- Emotional blunting
- Rigid and cannot adopt to new situations along with decreased attention modulation
- MRI shows atrophy in the frontal lobes (may be asymmetric)

Progressive non-fluent aphasia

- Patients present first with a non-fluent type of aphasia (similar to a Broca's lesion or stroke)
- Occurs slowly over time, cognition is intact يجيك يشتكي بس مو قادر يتكلم
- MRI may show focal left frontal atrophy

Temporal Variant

- Also known as semantic dementia
- Usually have intact fluency, but comprehension is impaired and decreased naming ability
- MRI may show focal left temporal atrophy.

Normal Pressure Hydrocephalus

Clinical Features

- A rare disorder
- It classically presents with the triad of (this triad is not diagnostic, we rely on the tap)
    - **Gait impairment (ataxia)**: 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 as if their feet are magnetted to the ground
    - **Dementia:** of a subcortical type, where there is executive dysfunction, and psychomotor slowing first. Other features of cognitive impairment develop later on
    - **Urinary incontinence**
- It usually results from impaired CSF absorption at the level of the arachnoid villi
- 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 before 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 (Ventriculoperitoneal shunts are ideal in NPH)
- MRI of the brain may also show dilated ventricles (however CSF pressure is normal)

Creutzfeldt-Jakob Disease

Clinical Features

- Rare, 1 in a million
- It is a prion disorder[9] and can be transmitted (transmissible spongiform encephalopathy)
- Although it is transmissible, we do not say it's infectious
- Prions are abnormally formed proteins that induce pathological transformations in other proteins.
- It has been transmitted after the use of surgical equipment or growth hormones
- 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, hyperreflexia, and + Babinski
- MRI may show abnormal signal intensity in the basal ganglia and cortical ribbon
- EEG shows characteristic periodic sharp wave complexes
- No treatment, patients die within a year
- The bovine variant CJD has been linked to consumption of beef (UK outbreak in the 90s)

TRANSMITIOIN
The defective protein can be transmitted by contaminated harvested human brain products, corneal grafts, dural grafts,or electrode implants and human growth hormone
Can also be:
- Familial
- Sporadic

[9] An interesting read https://www.livescience.com/51191-cannibalism-prions-brain-disease.html

Other Causes of Dementia

- HIV Associated neurocognitive disorder
- Syphilis
- Vitamin B12 deficiency must always be checked as it is reversible
- Autoimmune disorders (eg: SLE)
- Alcohol leading to wernicke-Korsakoff's syndrome, characterized by confabulations to compensate for amnesia

Treatment of Dementia

Cholinesterase Inhibitors:

- 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
- Does not stop disease progression, but may provide transient clinical stability
- NMDA receptor antagonist, memantine, is helpful in moderate to severe alzheimer's disease
- No treatment available for MCI

MCQs

1) A 69-year-old man is taken to his GP by his concerned wife. She complains that he has not been himself for the last year. He has slowly become withdrawn and stopped working on his hobbies. Now she is concerned that he often forgets to brush his teeth. She has noticed he sometimes struggles to find the right word and this has gradually become more noticeable over the last couple of months. She presented today because she was surprised to come home to find him naked and urinating in the living room last week. He has a history of hypertension and is an ex-smoker. The most likely diagnosis is:

A. Depression
B. Frontotemporal dementia
C. Alzheimer's disease
D. Vascular dementia
E. Lewy Body disease

2) A 55-year-old man is noted by his family members to be forgetful and become disoriented. He has difficulty making it to the bathroom in time and complains of feeling as though "he is walking like he was drunk."
which of the following is the most likely diagnosis?

a. Alzheimer's disease.
b. Parkinson disease .
c. Normal Pressure Hydrocephalus
d. Frontotemporal dementia

3) A 55-year-old man is noted by his family members to be forgetful and become disoriented. He has difficulty making it to the bathroom in time and complains of feeling as though "he is walking like he was drunk."
Which of the following therapies is most likely to improve his condition?

A. Intravenous penicillin for 21 days
B. Rivastigmine
C. Treatment with fluoxetine for 9 to 12 months
D. Ventriculoperitoneal shunt
E. Enrollment into alcoholic anonymous

4) A 74-year-old man was noted to have excellent cognitive and motor skill 12 months ago. His wife noted that 6 months ago his function deteriorated noticeably, and 2 months ago another level of deterioration was noted. Which of the following is most likely to reveal the etiology of his functional decline?

A. HIV antibody test
B. Magnetic resonance imaging of the brain
C. Cerebrospinal fluid (CSF) Venereal Disease Research Laboratory (VDRL) test
D. Serum thyroid-stimulating hormone

5)Which of the following are commonly seen in brain imaging of patients with Alzheimer disease?

A. Enlarged cerebral ventricles and atrophic brain tissue
B.Normal cerebral ventricles and atrophic brain tissue
C. Enlarged cerebral ventricles and no atrophy of brain tissue
D. Normal cerebral ventricles and normal brain tissue, acetylcholine
deficiency

6)Compared with dementia, which of the following is a characteristic of delirium?

A. A fluctuating level of consciousness
B. Slow onset
C. Can be due to deficiencies of thiamine or cyanocobalamin
D. Decreased memory ability

Answer key:

1 (B) | 2 (C) | 3 (D) | 4 (B) | 5 (A) | 6 (A)|

Key:

Question 1

The patient has developed a change in their behaviour. They are initially negative symptoms: withdrawal and disinterest in hobbies (as opposed to positive symptoms such as hallucinations). This would be compatible with depression (A) were it not for the development of word finding difficulties and disinhibition. These localize the problem to the temporal and frontal lobes, respectively (B). Although he is hypertensive, the progression has been gradual as opposed to the classically step-wise progression of vascular dementia (D), often these patients have had vascular events. There are no extra-pyramidal (parkinsonian) features to suggest Lewy Body disease (E). Alzheimer's disease (C) tends to affect memory and language before personality. There may be a family history, especially in someone this age, but becomes increasingly common with age. It is important to note that dementias are definitively diagnosed on biopsy/ autopsy, but this is rarely done. Differentiating between the dementias on clinical grounds can be difficult. Brain imaging may help visualizing subcortical infarcts and cortical atrophy.

Question 2

(C) The classic triad for normal pressure hydrocephalus is dementia, incontinence, and gait disturbance; one treatment is shunting the cerebrospinal fluid.

Question 3

(D) The classic triad for normal pressure hydrocephalus is dementia, incontinence, and gait disturbance; one treatment is shunting the cerebrospinal fluid.

Question 4

(B) The stepwise decline in function is typical for multi-infarct dementia, diagnosed by viewing multiple areas of the brain infarct.

Question 5

(A) Alzheimer disease typically has enlarged cerebral ventricles and brain atrophy, whereas normal pressure hydrocephalus has enlarged brain ventricles without brain atrophy.

Question 6

(A) Fluctuating levels of alertness and consciousness are typical of delirium.