



Psychiatry team 441



# Neurocognitive Disorders

*By Dr. A. Alwehaibi*

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## Objectives:

- ◀ To know the types and diagnostic criteria of neurocognitive disorders.
- ◀ To understand their etiology, presentation, severity, and complications.
- ◀ To know the lines of management of neurocognitive disorders.

## Color index:

- ◆ Important
- ◆ Golden
- ◆ Textbook

- ◆ Old notes (439/438)
- ◆ New notes (441)
- ◆ Extra

# Introduction to Neurocognitive Disorders

## ◀ Case Vignette

- Abdullah is a 72-year-old male. He was brought to the Emergency Department by his son for vomiting, new onset urinary incontinence, confusion, and incoherent speech for the past 2 days.
- The patient was disoriented and could see people climbing trees outside the window. He had difficulty sustaining attention, and his level of consciousness waxed and waned. He had been talking about his deceased wife. Patient was also trying to pull out his intravenous access line.
- Past history included diabetes mellitus, hyperlipidemia, osteoarthritis, and stroke.
- On examination, the patient was drowsy and falling asleep while practitioners were talking to him. Patient was not cooperative with the physical examination and with a formal mental status examination.
- Limited examination of the abdomen indicated that it was flat and soft with normal bowel sounds. The patient moves all 4 limbs.
- Laboratory test results revealed elevated BUN and creatinine levels, and the urinalysis was positive for urinary tract infection. CT scan of the head showed cortical atrophy plus an old infarct.
- The patient's family physician had recently prescribed Tylenol with codeine for the patient's severe knee pain 5 days earlier.

## ◀ Analysis

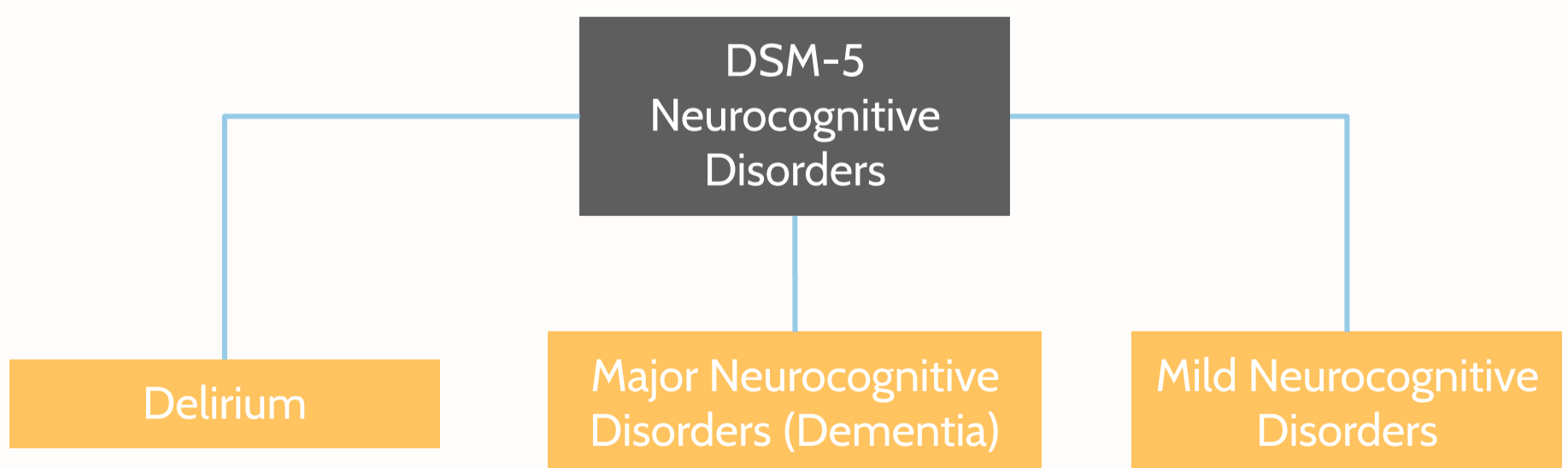
- Analysis of symptoms, MSE and psychopathology especially perception; differential diagnosis discussion (including drug intoxication and withdrawal):
  - Analyze the symptoms (presented and expected) in this case and signs, including mood, thoughts, cognition, perception and physical aspects.
  - Discuss other elements related to the case includes possible etiological reasons.
  - Discuss the initial possible diagnosis of this case and different types of such clinical presentation
  - What goes against psychosis? Age, visual hallucinations
  - Cortical atrophy may be due to dementia or aging
  - Old infarct: might suggest vascular dementia, or a previously unrecognized lacunar infarct
  - MSE abnormalities: perception (hallucinations), consciousness (waxing and waning), cognition (difficulty sustaining attention)
  - Possible etiologies: sepsis, renal failure (uremic encephalopathy), medication-induced, pneumonia (most common cause in males), UTI (most common cause in females)

# Neurocognitive Disorders

- Disruption in one or more of the cognitive domains, and are also frequently complicated by behavioral symptoms.
- Neurocognitive disorders exemplify the complex interface between neurology, medicine, and psychiatry.
- Neurocognitive disorders are unique in psychiatry because the etiology and the subsequent pathophysiology are often known.
- The criteria for major and mild neurocognitive disorder are based on six key cognitive domains:
  1. **Complex attention:** sustained attention, divided attention, selective attention, processing speed
  2. **Executive function:** planning, decision making, working memory, responding to feedback/error correction, overriding habits, mental flexibility
  3. **Learning and memory:** immediate memory, recent memory (including free recall, cued recall, and recognition memory)
  4. **Language:** expressive language (including naming, fluency, grammar and syntax) and receptive language
  5. **Perceptual motor ability:** construction and visual perception
  6. **Social cognition:** recognition of emotions, theory of mind (i.e., ability to understand another person's mental state), behavioral regulation

## Key Definitions

1. **Attention:** ability to focus on a specific stimulus with the exclusion of others
2. **Awareness:** ability to perceive and be conscious of experiences
3. **Arousal:** a prerequisite for attention, indicates responsiveness to external stimuli. States of arousal: coma, stupor, wakefulness and alertness
4. **Consciousness:** a product of arousal, includes orientation, awareness of self and environment
5. **Confusion:** the inability to formulate clear coherent thoughts and speech



## ◀ Introduction

- Acute onset of fluctuating cognitive impairment (**global**) and a disturbance of consciousness.
- Delirium is a syndrome, not a disease, and it has many causes, all of which result in a similar pattern of signs and symptoms.
- **Delirium is acute brain failure.**
- A common disorder:
  - Hospitalized medically ill (10-30%).
  - Hospitalized elderly (10-40%).
  - Postoperative patients (up to 50%). “especially orthopedic and open heart surgeries”
  - Near-death terminal patients (up to 80%).
- Classically, delirium has a sudden onset (hours or days) and a brief and fluctuating course.
- Rapid improvement when the causative factor is identified and eliminated.
- Abnormalities of mood, perception, and behavior are common psychiatric symptoms.
- Reversal of sleep-wake pattern.
- Tremor, asterixis, nystagmus, incoordination, and urinary incontinence are common.

## ◀ Prognosis (**BAD PROGNOSIS**)

- May progress to coma, seizures or death, particularly if untreated.
- Increased risk for postoperative complications, longer post-operative recuperation, longer hospital stays, long-term disability.
- Elderly patients 22-76% chance of dying during that hospitalization.
- Several studies suggest that up to **25% of all patients with delirium die within 6 months.**

## ◀ Risk factors

- Extremes of age.
- Number of medications taken. (polypharmacy)
- Preexisting brain damage (e.g., dementia, cerebrovascular disease, tumor).
- History of delirium.
- Alcohol dependence. (Delirium Tremens) Will be discussed later...
  - A common scenario is of an alcoholic patient abstaining from food and drink prior to a surgical procedure and subsequently developing delirium a few days after the surgery due to alcohol withdrawal
- Diabetes.
- Cancer.
- Sensory impairment.
- Malnutrition.
- Delirium is the final common pathway of any medical condition that impair cerebral oxidative metabolism

## ◀ Causes “I WATCH DEATH”:

- Infections: encephalitis, meningitis, sepsis.
- Withdrawal: ETOH, sedative-hypnotics, barbiturates.
- Acute metabolic: acid-base, electrolytes, liver or renal failure.
- Trauma: brain injury, burns\*.
- CNS pathology: hemorrhage, seizures, stroke, tumor (don't forget metastases).
- Hypoxia: CO poisoning, hypoxia, pulmonary or cardiac failure, anemia.
- Deficiencies: **thiamine**, niacin (**pellagra, often occurs from tryptophan deficiency, resulting in both reduced serotonin and niacin levels**), B12.
- Endocrinopathies: hyper or hypo-adrenocortisolism, hyper- or **hypoglycemia**.
- Acute vascular: hypertensive encephalopathy and shock.
- Toxins or drugs: pesticides, **solvents**, medications, drugs of abuse:
  - **Anticholinergics (e.g., TCAs)\*\***, narcotic analgesics, sedatives (BDZ), **Digoxin**, and steroids.
- Hheavy metals: lead, manganese, mercury.

## ◀ Life Threatening Causes of Delirium (WHHHIMP):

- Wernicke's encephalopathy.
- Hypoxia.
- Hypoglycemia.
- Hypertensive encephalopathy.
- Intracerebral hemorrhage.
- Meningitis/encephalitis.
- Poisoning.

\*Cause delirium due to the following: Fluid loss, pain and the medication for pain

\*\* Anticholinergics cause confusion so be careful when prescribing them to the elderly



## DSM-5 Criteria for Diagnosis of Delirium

- A. A disturbance in attention (reduced ability to focus, sustain and shift attention) and awareness (reduced orientation to the environment).
- B. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate in severity during the course of the day.**
- C. An additional disturbance in cognition (e.g. memory deficit, disorientation (cornerstone of delirium), language, visuospatial ability) or perception.
- D. The changes in criteria A & C are not better explained for by a preexisting, established or evolving neurocognitive disorder or not in the context of coma.
- E. There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of another medical condition or substance.

Specify whether: (1) Substance intoxication delirium, (2) Substance withdrawal delirium, (3) Medication-induced delirium, (4) Delirium due to another medical condition, (5) Delirium due to multiple etiologies

Specify if

1. Acute: Lasting a few hours or days.
2. Persistent: Lasting weeks or months.

Specify if

- **Hyperactive:** The individual has a hyperactive level of psychomotor activity that may be accompanied by mood lability, agitation, and/or refusal to cooperate with medical care. (may be accompanied by psychosis)
- **Hypoactive:** The individual has a hypoactive level of psychomotor activity that may be accompanied by sluggishness and lethargy that approaches stupor. **(More likely to go undetected)**
- **Mixed level of activity:** The individual has a normal level of psychomotor activity even though attention and awareness are disturbed. Also includes individuals whose activity level rapidly fluctuates. (most common)

\*The Criteria was removed from the Dr slides this year (441).

# Clinical Features

- Prodrome (Restlessness, Anxiety, Sleep disturbance).
- Fluctuating course.
- Attentional deficits.
- Arousal /psychomotor disturbance.
- Impaired cognition.
- Sleep-wake disturbance.
- Altered perceptions.
- Affective disturbances.

# Work-Up

- History.
- **Confusion Assessment Method (CAM)**
  - To Identify delirium in the healthcare setting (takes 5 minutes)
  - Highly specific and sensitive
  - Requires acute and fluctuating onset, inattention and either disorganized thinking or altered level of consciousness
- Interview- also with family, if available.
- Physical, cognitive, and neurological exam.
- Neurocognitive Tests.
- Vital signs, fluid status.
- Review of medical record (Anesthesia and medication record review).

# Mini-Mental State Exam

- Tests orientation, short-term memory, attention, concentration, constructional ability.
  - MoCA is better for dementia and mild impairments but it takes longer to perform (Keep in mind possible confounders (e.g., education, general knowledge, ability to write))
- 30 points is perfect score.
- **< 20 points suggestive of problem.**
- Not helpful without knowing baseline.

Feature 1: Acute onset or fluctuating course	Score	Check here if Present
Is the patient different than his/her baseline mental status? OR Has the patient had any fluctuation in mental status in the past 24 hours as evidenced by fluctuation on a sedation/level of consciousness scale (i.e., RASS/SAS), GCS, or previous delirium assessment?	Either question Yes →	<input type="checkbox"/>
<b>Feature 2: Inattention</b>		
<b>Letters Attention Test</b> (See training manual for alternative pictures) <b>Directions:</b> Say to the patient, "I am going to read you a series of 10 letters. Whenever you hear the letter 'A,' indicate by squeezing my hand." Read letters from the following letter list in a normal tone 3 seconds apart. <b>SAVEAHAART or CASABLANCA or ABADBADAAY</b> Errors are counted when patient fails to squeeze on the letter "A" and when the patient squeezes on any letter other than "A."	Number of errors >2 →	<input type="checkbox"/>
<b>Feature 3: Altered level of consciousness</b>		
Present if the Actual RASS score is anything other than alert and calm (zero)	RASS anything other than zero →	<input type="checkbox"/>
<b>Feature 4: Disorganized thinking</b>		
<b>Yes/No questions</b> (See training manual for alternate set of questions) 1. Will a stone float on water? 2. Are there fish in the sea? 3. Does one pound weigh more than two pounds? 4. Can you use a hammer to pound a nail? Errors are counted when the patient incorrectly answers a question. <b>Command</b> Say to patient: "Hold up this many fingers" (Hold 2 fingers in front of patient) "Now do the same thing with the other hand" (Do not repeat number of fingers) *If the patient is unable to move both arms, for 2" part of command ask patient to "Add one more finger" An error is counted if patient is unable to complete the entire command.		
<b>Overall CAM-ICU</b>		<input type="checkbox"/> CAM-ICU positive (delirium present)
Feature 1 plus 2 and either 3 or 4 present = CAM-ICU positive		<input type="checkbox"/> CAM-ICU negative (no delirium)

BOX 4.4 Diagnosis of Delirium by the Confusion Assessment Method
The diagnosis of delirium by the confusion assessment method (CAM) requires the presence of features 1, 2 and either 3 or 4 (Inouye et al., 1990).
<b>Feature 1: Acute onset and fluctuating course</b> Was there an acute change from the patient's baseline? Did the (abnormal) behavior fluctuate in severity?
<b>Feature 2: Inattention</b> Did the patient have difficulty keeping track of what was being said?
<b>Feature 3: Disorganized thinking</b> Was the patient's thinking disorganized or incoherent (rambling conversation, unclear or illogical flow of ideas)?
<b>Feature 4: Altered level of consciousness</b> Overall, would you rate this patient's level of consciousness as alert (normal), vigilant (hyperalert), lethargic (drowsy, easily aroused), stupor (difficulty to arouse), or coma (unarousable)?

RASS (Richmond Agitation Sedation Scale)		
4	Combative	Overtly combative, violent, immediate danger to staff
3	Very agitated	Pulls or removes tubes or catheters; aggressive
2	Agitated	Frequent non-purposeful mvmt, fights ventilator
1	Restless	Anxious but movements not aggressive or vigorous
0		Alert and calm
-1	Drowsy	Sustained awakening to voice (≥10sec)
-2	Light sedation	Briefly awakens with eye contact to voice (<10 sec)
-3	Moderate sedation	Movement or eye opening to voice but no eye contact
-4	Deep sedation	No response to voice but movement or eye opening to physical stimulation
-5	Cannot be aroused	No response to voice or physical stimulation

MINI MENTAL STATE EXAMINATION (MMSE)		Name:
		DOB:
		Hospital Number:
One point for each answer		DATE:
<b>ORIENTATION</b>	Year Season Month Date Time	...../5 ...../5 ...../5
	Country Town District Hospital Ward/Floor	...../5 ...../5 ...../5
<b>REGISTRATION</b>	Examiner names three objects (e.g. apple, table, penny) and asks the patient to repeat (1 point for each correct. THEN the patient learns the 3 names repeating until correct).	...../3 ...../3 ...../3
<b>ATTENTION AND CALCULATION</b>	Subtract 7 from 100, then repeat from result. Continue five times: 100, 93, 86, 79, 72, 65 (Alternative: spell "WORLD" backwards: DLROW).	...../5 ...../5 ...../5
<b>RECALL</b>	Ask for the names of the three objects learned earlier.	...../3 ...../3 ...../3
<b>LANGUAGE</b>	Name two objects (e.g. pen, watch).	...../2 ...../2 ...../2
	Repeat "No ifs, ands, or buts".	...../1 ...../1 ...../1
	Give a three-stage command. Score 1 for each stage. (e.g. "Place index finger of right hand on your nose and then on your left ear").	...../3 ...../3 ...../3
	Ask the patient to read and obey a written command on a piece of paper. The written instruction is: "Close your eyes".	...../1 ...../1 ...../1
	Ask the patient to write a sentence. Score 1 if it is sensible and has a subject and a verb.	...../1 ...../1 ...../1
<b>COPYING:</b>	Ask the patient to copy a pair of intersecting pentagons	...../1 ...../1 ...../1
		<b>TOTAL:</b> ...../30 ...../30 ...../30
<b>MMSE scoring</b> 24-30: no cognitive impairment 18-23: mild cognitive impairment 0-17: severe cognitive impairment		

## ◀ Lab and Other Tests

- Labs: Electrolytes, CBC, arterial blood gas analysis or oxygen saturation
- Urinalysis +/- culture and sensitivity
- Biochemistry: blood alcohol level, serum drug levels
- EKG, CXR, EEG (not usually necessary, can help if there is a confusion about the diagnosis)
- Urine drug screen, Serum drug levels (digoxin, theophylline, phenobarbital, cyclosporin, lithium, etc)
- Heavy metals, Lupus workup

## ◀ Differential Diagnosis (DDx)

- Major Neurocognitive Disorder (Dementia).
- Mild Neurocognitive Disorder.
- Depression.
- Schizophrenia

## ◀ Management

- **Goals of management:**
  - The primary goal is to **treat the underlying cause.**
  - The other important goal of treatment is to provide physical, sensory, and environmental support.
  - Discontinue or minimize dosing of nonessential medications. (especially anticholinergics) (they are hypersensitive to side effects [Anticholinergics cause confusion])
  - Coordinate with other physicians and providers.
  - Assess individual and family psychosocial characteristics, Establish and maintain an alliance with the family and other clinicians, Educate the family – temporary and part of a medical condition – not “crazy”.
  - Provide post-delirium education and processing for patient.
  - Increase observation and monitoring – (vital signs, fluid intake and output, oxygenation, safety).
  - Monitor and assure safety of patient and staff:
    - Suicidality and violence potential, fall & wandering risk.
    - Need for a sitter.
    - Remove potentially dangerous items from the environment.
    - Restrain ONLY when other means not effective (it may worsen delirium).

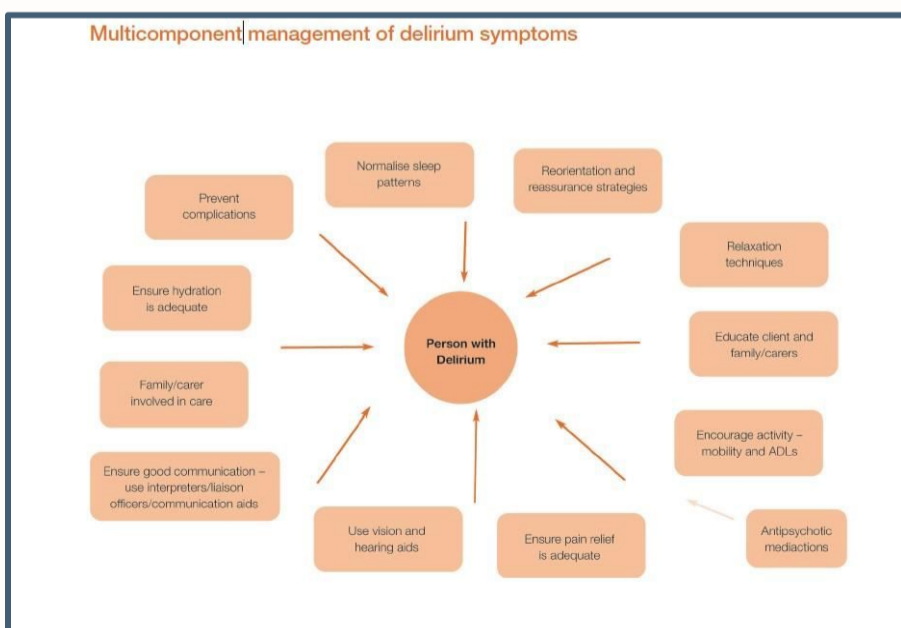


# Pharmacological Treatment (The Primary Treatment)

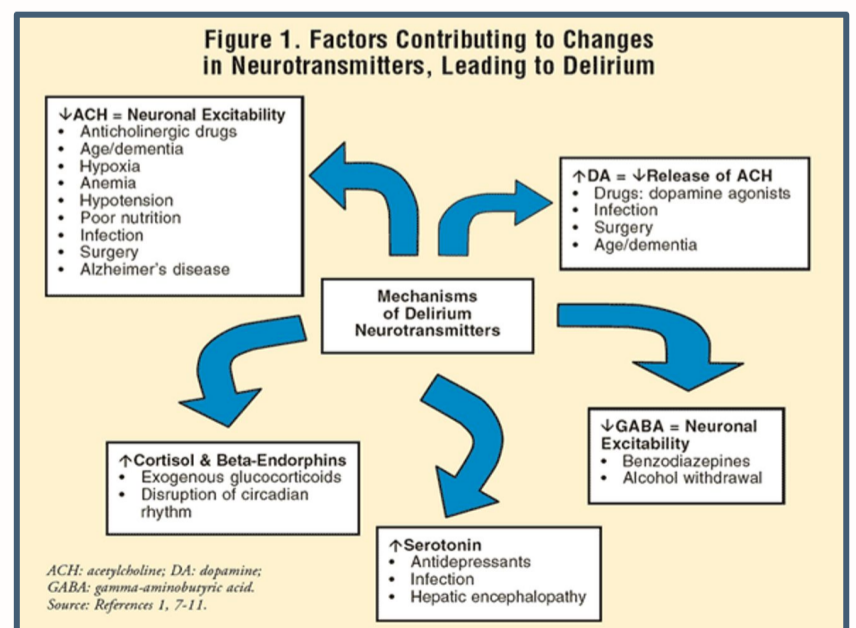
- Low doses of high potency antipsychotics (i.e. **haloperidol**) PO, IM or IV.
  - **Most often the preferred choice in treatment** (it is not preferred in alcoholic delirium)
- Atypical antipsychotics (risperidone, olanzapine, quetiapine, aripiprazole).
- **If alcohol withdrawal (delirium tremens) was the cause: benzodiazepines (e.g., lorazepam, oxazepam) can be used.**
- Benzodiazepines should be avoided in delirium; it makes it worse (except in alcoholic withdrawal)
- Rarely, some antipsychotics are associated with torsade de pointes arrhythmia by lengthening the QT interval; avoid or monitor this by ECG monitoring.

## Summary

- Delirium is common and is often –unfortunately– usher the way to death- especially in vulnerable populations.
- It is a sudden change in mental status, with a fluctuating course, marked by decreased attention.
- It is caused by underlying medical problems, drug intoxication/withdrawal, or a combination.
- Recognizing delirium and searching for the cause can save the patient's life



Dr: "Read it"



Scenario	Likely Diagnosis	Diagnostic Testing
Delirium + fever + cough + rales	Pneumonia	Chest x-ray
Delirium + dysuria + suprapubic tenderness	UTI	Urinalysis and urine culture
Delirium + constricted pupils (miosis) + bradypnea	Opioid intoxication	Urine toxicology screen
Cognitive impairment + fatigue + cold intolerance	hypothyroidism	TSH, free T4
Delirium + fever + nuchal rigidity + photophobia	Meningitis	Head CT and lumbar puncture
Delirium + tachycardia + tremor + thyromegaly	Thyrotoxicosis	TSH, free T4 and T3
Delirium + insulin use	Hypoglycemia	Blood glucose

Q from Doctor: You are on call in the surgical ward, you received an admission over the weekend of a 55 year old male admitted for an elective cholecystectomy. you did your investigations and everything was fine. the next day, you get a call from the surgical ward nurse telling you that the patient is agitated, confused, shouting at and hitting the staff. what goes through your mind while you are going to see the patient?

A: Delirium tremens

Explanation: the patient is 55 years old so if we assumed that he was an alcohol abuser for 30 years that would have been more than enough time to develop dependency and withdrawal symptoms, however if the patient was 25 years old with the same symptoms it wouldn't make sense.

# Major Cognitive Disorder (Dementia)

## ◀ Case Development 1

- Past history inquiry indicated that he has two years of deteriorating memory. He forgot mostly recent things. He has difficulty to name some familiar people to him. 6 months ago, he lost his ability to drive and to pray appropriately. However, his attention was well except of few days' prior current admission. There is positive family history of severe memory problem in his eldest brother.
- Analyze the symptoms (presented and expected) in this case and signs, including mood, thoughts, cognition, perception and physical aspects.
- Discuss other elements related to the case includes possible etiological reasons.
- Discuss the initial possible diagnosis of this case and different types of such clinical presentation.
- Discuss Cognitive disorders related psychopathology.

## ◀ Dementia

- **Global impairment of cognitive functions occurring in clear consciousness.**
- Aging populations.
  - The differentiating factor between mild cognitive impairment, major cognitive impairment and normal aging (also called benign senescent forgetfulness) is the degree of severity
  - Mild cognitive impairment can very well progress to major cognitive impairment, prompting its detection
- Difficulty with memory, attention, thinking, and comprehension.
- Other mental functions can often be affected, including mood, personality, judgment, and social behavior.
- Can be progressive or static.
- Permanent or **reversible (e.g., vitamin B12, folate, hypothyroidism, OSA?)**.
- **50-60%** have the most common type of dementia of the **Alzheimer's type**.
- **Vascular dementias account for 15-30%** of all dementia cases.

\*These are old numbers, it used to be Alzheimer's then Vascular as the most common causes now Alzheimer's is still number 1 but number 2 is Lewy body dementia.



Criterion	Mild NCD	Major NCD
<b>Functional decline in at least one cognitive domain relative to baseline as evidenced by</b>		
Concern (expressed by the patient or someone who knows them)	Mild decline	Significant decline
Objective findings on cognitive testing (preferably standardized neuropsychological testing)	Modest impairment	Substantial impairment'
Effect on functioning	Ability to perform IADLs preserved)(IADLs = instrumental activities of daily living)	Impaired performance of (IADLs/ADLs = activities of daily living)
Deficits do not occur exclusively in the context of a delirium		
Deficits are not better explained by another mental disorder		

## ◀ DSM-5 Criteria for Major Cognitive Disorder

- A. Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual-motor, or social cognition) based on:
1. Concern of the individual, a knowledgeable informant, or the clinician that there has been a significant decline in cognitive function.
  2. A substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.
- B. The cognitive deficits interfere with independence in everyday activities (i.e., at a minimum, requiring assistance with complex instrumental activities of daily living such as paying bills or managing medications).
- C. The cognitive deficits do not occur exclusively in the context of a delirium. (you cannot diagnose dementia in the context of delirium)
- D. The cognitive deficits are not better explained by another mental disorder (e.g., major depressive disorder, schizophrenia).

\*The Criteria was removed from the Dr slides this year (441).

In any case of dementia, you have to specify the cause, the behaviour status, and the severity:

Disease	Causes
Degenerative Dementias	<ul style="list-style-type: none"> <li>Alzheimer's disease.*</li> <li>Frontotemporal dementias (e.g., Pick's disease).*</li> <li>Parkinson's disease*. (delusions, hallucinations are more common, cognitive impairment occurs one year after after the onset of motor symptoms).</li> <li>Lewy body dementia.* (delusions, hallucinations are more common, cognitive impairment occurs in the first year of the disease)</li> </ul>
Miscellaneous	<ul style="list-style-type: none"> <li>Huntington's disease.*</li> <li>Wilson's disease.*</li> </ul>
Tumors	<ul style="list-style-type: none"> <li>Metastatic breast or lung cancer.</li> <li>Primary or metastatic brain tumor.</li> </ul>
Psychiatric	<ul style="list-style-type: none"> <li>Pseudodementia of depression. (needs to be differentiated from dementia. Treatable and can have a similar presentation.)</li> <li>Cognitive decline in late-life schizophrenia.</li> </ul>
Physiologic	<ul style="list-style-type: none"> <li>Normal pressure hydrocephalus.</li> </ul>
Metabolic	<ul style="list-style-type: none"> <li>Vitamin deficiencies (e.g., vitamin B12, folate).*</li> <li>Endocrinopathies (e.g., hypothyroidism).</li> <li>Chronic metabolic disturbances (e.g., uremia).</li> </ul>
Trauma	<ul style="list-style-type: none"> <li>Posttraumatic dementia.*</li> <li>Subdural hematoma.</li> <li>Dementia pugilistica (chronic traumatic encephalopathy, often seen in professional wrestlers)</li> </ul>
Infection	<ul style="list-style-type: none"> <li>Prion diseases (e.g., Creutzfeldt- Jakob disease, bovine spongiform encephalitis, Gerstmann-Straussler syndrome, kuru (in eaters of human flesh)).*</li> <li>Acquired immune deficiency syndrome (AIDS).*</li> <li>Syphilis.</li> </ul>
Cardiac, Vascular, and Anoxia	<ul style="list-style-type: none"> <li>Infarction (single or multiple or strategic lacunar).</li> <li>Binswanger's disease (subcortical arteriosclerotic encephalopathy).</li> <li>Hemodynamic insufficiency (e.g., hypoperfusion or hypoxia).</li> </ul>
Demyelinating Diseases	<ul style="list-style-type: none"> <li>Multiple sclerosis, neuromyelitis optica</li> </ul>
Drugs and Toxins	<ul style="list-style-type: none"> <li>Alcohol, Heavy metals, Carbon monoxide.</li> </ul>

\*Included in DSM-5 criteria as specifiers. Other specifiers include MND due to Another Medical Condition, Multiple Etiologies or Unspecified

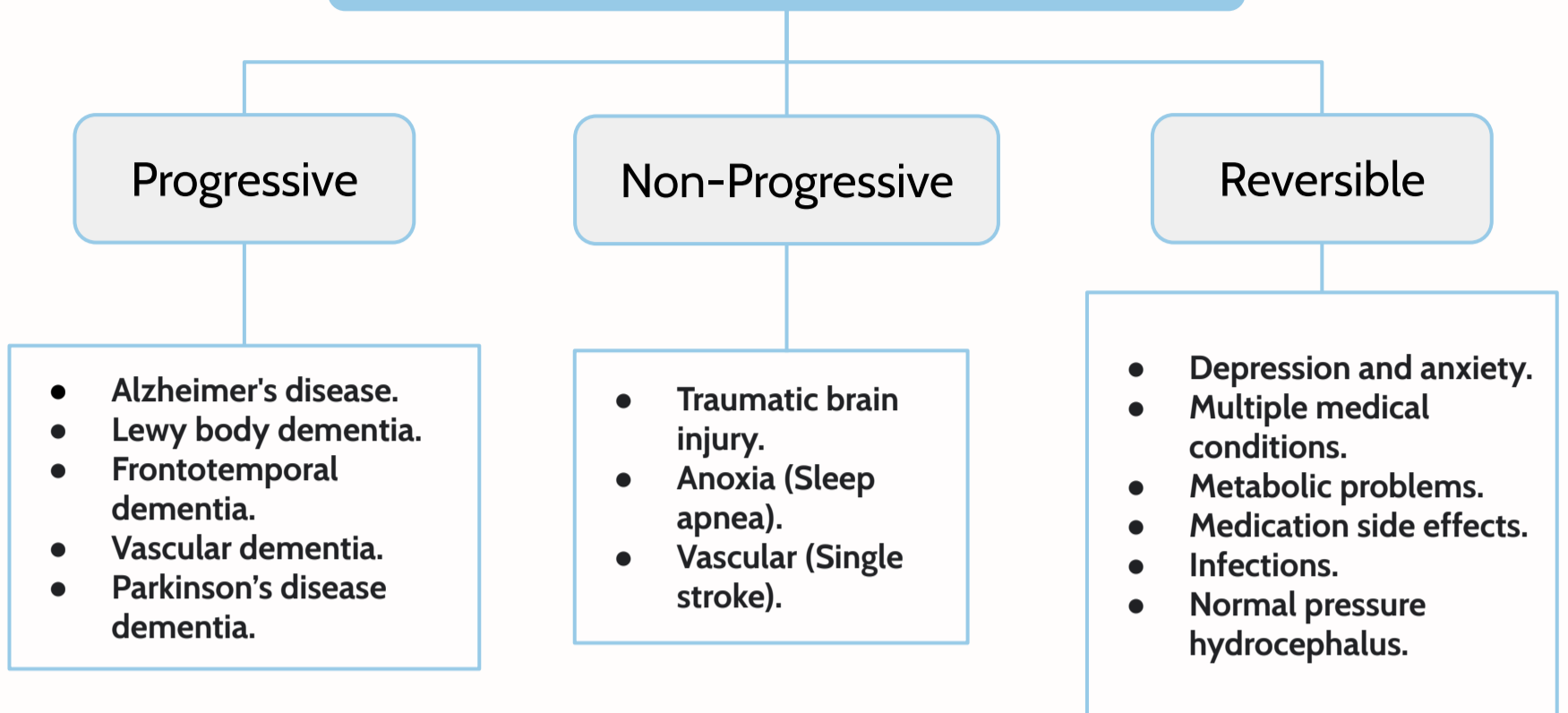
***Specify if:*****Behavioural Status**

With Behavioural Disturbance	<ul style="list-style-type: none"> <li>● If the cognitive disturbance is accompanied by a clinically significant behavioral disturbance (e.g., psychotic symptoms, mood disturbance, agitation, apathy, or other behavioral symptoms).</li> </ul>
Without Behavioural Disturbance	<ul style="list-style-type: none"> <li>● If the cognitive disturbance is not accompanied by any clinically significant behavioral disturbance.</li> </ul>

***Specify current severity:*****Severity**

Mild	<ul style="list-style-type: none"> <li>● Difficulties with instrumental activities of daily living (e.g., housework, managing money).</li> </ul>
Moderate	<ul style="list-style-type: none"> <li>● Difficulties with basic activities of daily living (e.g., feeding, dressing).</li> </ul>
Severe	<ul style="list-style-type: none"> <li>● Fully dependent. (e.g. double incontinence)</li> </ul>

## Cognitive Impairment and Dementia



### Diagnosis

- The diagnosis of dementia is based on the clinical examination.
- A comprehensive laboratory workup must be performed when evaluating a patient with dementia.
- The purposes of the workup are to detect **reversible** causes of dementia.

### Differential Diagnosis

- Delirium.
- Depression (pseudodementia).
- Schizophrenia.
- Normal Aging. (**benign senescent forgetfulness**)

## ◀ Clinical Features

- **Memory impairment is typically an early and prominent feature.**
- Orientation can be progressively affected.
- Early in the course of dementia, memory impairment is mild and usually most marked for recent events; As the course of dementia progresses, memory impairment becomes severe, and only the earliest learned information are intact.
- Personality change, intellectual impairment, forgetfulness, social withdrawal, anger and lability of emotions.
- **Hallucinations** 20-30% percent.
- **Delusions** 30-40% percent.
- **Physical aggression** & other forms of violence are common in demented patients with psychotic symptoms.
- **Depression and anxiety symptoms.**
- Pathological laughter or crying.
- Apraxia as a clinical feature.
- Hyper-sexuality.
- Aggression personality changes.
- Long-term memory usually intact

Scenario	Likely Diagnosis	Diagnostic Testing
Cognitive impairment with stepwise increase in severity + focal neurological signs	Vascular disease	Head CT /Brain MRI
Cognitive impairment + cogwheel rigidity + resting tremor	Lewy body disease parkinson disease	Clinical Exam
Cognitive impairment + gait apraxia + urinary incontinence	Normal pressure hydrocephalus	Head CT /Brain MRI
Cognitive impairment + fatigue + cold intolerance	hypothyroidism	TSH, free T4
Cognitive impairment + vegan diet + paresthesias + diminished position and vibration sensation	Vitamin B12 deficiency	Serum B12
Cognitive impairment + tremor + Kayser– Fleischer rings	Wilson's disease	Ceruloplasmin
Cognitive impairment + diminished position and vibration sensation + <b>Argyll Robertson Pupils</b> (Accommodation Response Present, response to light absent)	Neurosyphilis	CSF FTA-ABS and VDRL



# Major Cognitive Disorder (Dementia)

## ◀ Dementia of Alzheimer's Type

- The most common type of dementia.
- Progressive dementia.
- The final diagnosis of Alzheimer's disease requires a neuropathological examination of the brain (on autopsy)
- Genetic factors.
- Acetylcholine and norepinephrine, both of which are hypothesized to be hypoactive in Alzheimer's disease.
- **Clinical Manifestations:**
  - Gradual progressive decline in cognitive functions.
  - The primary cognitive domains affected are **memory, learning, and language**.
  - Personality changes, mood swings, and paranoia are very common.
  - Motor and sensory symptoms appear in advanced disease.
  - On average, death occurs 10 years after diagnosis.
- **Diagnosis (Alzheimer may be accompanied by major cognitive disorder or mild cognitive disorder)**
  - A diagnosis of a **major neurocognitive disorder due to probable AD** is made based on the presence of all these characteristic clinical findings or if there is evidence of a causative genetic mutation:
    - Insidious onset.
    - Gradual progression.
    - Impairment in one (mild NCD) or more (major MCD) cognitive domains.
  - If neither of the above are present, the diagnosis is **major neurocognitive disorder due to possible AD**
  - If the patient only meets the criteria for mild neurocognitive disorder, then Alzheimer is **probable** in the presence of a genetic mutation and **possible** if only the clinical features mentioned above are present.
  - Major NCD due to AD is **probable** if there is evidence of causation by one of several single-gene variants (ApoE ε4) the above characteristics.
  - The diagnosis of mild NCD due to Alzheimer is **probable** only in the presence of a genetic defect.
- **Treatment:**
  - **Cholinesterase inhibitors** (e.g., donepezil, rivastigmine, and galantamine): only slow the deterioration. (mild-to-moderate). **Insomnia is a prominent side effect.**
  - **NMDA receptor antagonist** (memantine)(severe, can be combined with with cholinesterase inhibitors)
  - **Antipsychotics:** they increase the mortality but helps with agitation, so you have to inform the patient/decision maker.



# Major Cognitive Disorder (Dementia)

## ◀ Vascular Dementia

- The primary cause of vascular dementia, formerly referred to as multi-infarct dementia, is presumed to be multiple areas of cerebral vascular disease.
- **Vascular dementia is more likely to show a **decremental, stepwise deterioration** than is Alzheimer's disease.**
- **Stepwise:** progression in appearance of clusters of new or worsening symptoms rather than individual gradual worsening and appearing of new symptoms (since symptoms are reflective of brain infarcts that may bear multiple functions)
- A lesion to the frontal lobe can manifest with a spectrum of symptoms including personality changes, disinhibition, inappropriate behavior, aggression, apathy, amotivation, and paranoia.
- **Risk Factors:**
  - Hypertension.
  - Diabetes.
  - Smoking.
  - Obesity.
  - Hyperlipidemia.
  - Atrial fibrillation.
  - Advanced age.
- **Clinical Manifestations:**
  - Presentation and progression of cognitive impairment are variable.
    - Classically demonstrates a stepwise deterioration corresponding with the occurrence of micro-infarcts (i.e., multi-infarct dementia).
    - May present with acute onset followed by partial improvement.
    - May have an insidious onset with gradual decline similar to AD.
  - **Complex attention** and **executive functions** are the cognitive domains typically affected in small vessel disease.
  - Confirmation of the diagnosis requires neuroimaging with findings that correlate to the clinical picture.
- **Treatment:**
  - No cure or truly effective treatment.
  - Atherosclerosis in major blood vessels is surgically correctable
  - Manage risk factors with a goal of preventing future strokes.
  - Symptomatic treatment is similar to AD.

# Major Cognitive Disorder (Dementia)

## Delirium Vs. Dementia

Features	Delirium	Dementia
Onset	Acute	Insidious
Course	Fluctuating	Progressive
Duration	Days to weeks	Months to years
Consciousness	Altered	Clear
Attention	Impaired	Normal, except in severe dementia
Psychomotor Changes	Increased or decreased	Often normal
Reversibility	Usually	Rarely

## ◀ Treatment of Dementia

- The first step in the treatment of dementia is verification of the diagnosis. (rule out reversible causes)
- Preventive measures are important.
- Establish a baseline.
- Supportive and educational psychotherapy.
- Any areas of intact functioning should be maximized by helping patients identify activities in which successful functioning is possible (brain plasticity is lifelong)
- Caregivers.
- **Primary treatments:**
- **Cognitive enhancers (slow but do not reverse cognitive decline)**
  - Cholinesterase inhibitors: Donepezil (Aricept), Rivastigmine (Exelon), Galantamine (Remiryl), and Tacrine (mild conditions)
  - NMDA glutamate receptors antagonist: Memantine. (severe conditions)
  - Drugs with high anticholinergic activity & Benzodiazepines should be avoided.
  - In treating patients with depression and dementia avoid TCAs and use SSRIs
  - Trazodone can be given at bedtime to reduce nighttime agitation or sundowning
  - Avoid benzodiazepines, except in conditions of acute agitations in patients not taking other agitation-relieving medications

# Major Cognitive Disorder (Dementia)

## Case Development 2

- Abdullah's son reluctantly reported that his father has current history of occasional alcohol drinking and using Diazepam to sleep well.
- He admits that he were heavy alcohol drinker 10 years ago. He had bouts of memory impairments and family problem secondary to his heavy drinking. He used to have tremors and craving for drinking at early morning. After searching patient's old medical notes, you found that the patient has been admitted to ICU 10 year ago with fever, sweating, tremor, dilated eyes, disorientation, confusion and seeing small animals.
- Discuss possible differential diagnosis.
- Discuss the acute use of antipsychotics and benzodiazepine.
- Discuss about Dementia treatments, indication, side effects, etc.
- Discuss about ability to give consent and take decision.

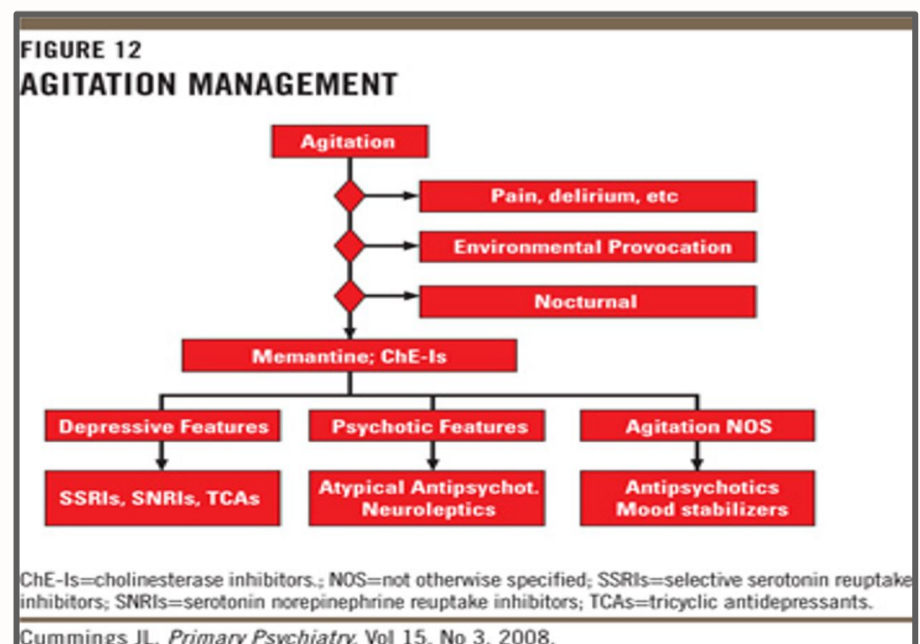
## Delirium Tremens (DTs)

(discussed extensively in Substance Use lecture)

- Delirium tremens is a dangerous form of alcohol withdrawal involving mental status and neurological changes.
- Symptoms include disorientation, agitation, visual and tactile hallucinations, and autonomic instability (increase in respiratory rate, heart rate, and blood pressure).
- It carries a 5% mortality rate but occurs in only 5% of patients that experience EtOH withdrawal. treatment includes supportive care and benzodiazepines.

Alcohol will cause inflammation of the GI tract leading to thickening of the mucosa and disturbance in the active transport of nutrients E.g. Thiamine.

ALCOHOL		IMIG
Wernicke's Encephalopathy		
<b>COMMON CAUSE</b> 50 – 75% of W.E. Alcohol ↓ dietary intake ↓ GI absorption ↓ hepatic storage impaired use	<b>CLINICAL TRIAD:</b> Only seen in ¼ pts W.E. is often under diagnosed	<b>Vitamin B1 (Thiamine) Deficiency</b>
<b>OTHER CAUSES</b> Malabsorption Poor Intake anorexia hyperemesis pregn IV feeding fasting GI surg bariatric surg Metabolic Req systemic illness transplant AID Loss of vitamins renal dialysis	<b>1. ENCEPHALOPATHY (82%)</b> Disorientation, Indifference, Inattentiveness. 5% have ↓ed LOC	<b>TREATMENT:</b> <i>If suspected</i> Thiamine & Thiamine Thiamine BEFORE Glucose Check Magnesium
	<b>2. OCCULOMOTOR DYSFUNCTION (29%)</b> Nystagmus, Lateral Rectus Palsy, Conjugate Gaze Palsy, INO, Unequal Pupils, Light near dissociation, Nonreactive pupils, etc	<b>KORSAKOFF'S SYNDROME</b> Chronic disease, progressed from untreated W.E. Severe <b>retrograde &amp; anterograde amnesia</b> with relatively <b>preserved</b> long term memory, cognitive, and social skills <b>Confabulation</b> sometimes present. Pt <b>unaware</b> of their illness
	<b>3. GAIT ATAXIA (23%)</b> Primarily: Stance & gait Unlike <i>Alcoholic Cerebellar Degeneration</i> W.E. has no upper limb ataxia	
	<b>OTHER:</b> peripheral neuropathy, hypothermia, cardiac, vestibular	



This diagram is very imp as the doctor focused on it extensively during the lecture however he mentioned that questions about it come in board exams so it might not be for our exams but we highly suggest that you read it

Confabulations: Filling up memory defects with made-up stories

*Important Note: This & the following few slides were found only in team 439 they were not in Dr. Slides this or the previous year, so we decided to include them just for you :)*



# Lewy Body Dementia

## ◀ Clinical Manifestations

- **Waxing and waning** of cognition, especially in the areas of **attention** and **alertness**.
- **Visual hallucinations**—usually vivid, colorful, well-formed images of animals or small people.
- **Rapid eye movement (REM) sleep behavior disorder** (not currently included in the DSM-5 core features)—violent movements during sleep in response to dreams, often of fighting.
- Development of **extrapyramidal signs** (Parkinsonism) at least 1 year after cognitive decline becomes evident

## ◀ Diagnosis

- Definitive diagnosis can only be made with autopsy.
- **Possible NCD with Lewy bodies**: Only one core feature without evidence from indicative biomarkers OR one or more indicative biomarker(s), but no core clinical features.
- **Probable NCD with Lewy bodies**: Two or more core features OR one core feature and one or more indicative biomarker(s).

## ◀ Treatment

- **Cholinesterase inhibitors** for cognitive and behavioral symptoms.
- **Quetiapine** or **clozapine** for psychotic symptoms.
  - Use the lowest effective dose for the shortest period of time possible.
  - Monitor closely for adverse effects, such as extrapyramidal signs, sedation, increased confusion, autonomic dysfunction, and signs of **Neuroleptic Malignant Syndrome (NMS)**.
- **Levodopa-carbidopa** for Parkinsonism.
  - Not as effective as in idiopathic Parkinson disease.
  - May exacerbate psychosis or REM sleep behavior disorder.
- **Melatonin** and/or **clonazepam** for REM sleep behavior disorder.

# Frontotemporal Degeneration

## ◀ Clinical Manifestations

- Cognitive deficits in **attention, abstraction, planning, and problem solving.**
- **Behavioral variant:**
  - **Disinhibited** verbal, physical, or sexual behavior.
  - Overeating or oral exploration of inanimate objects.
  - Lack of emotional warmth, empathy, or sympathy.
  - Apathy or inertia.
  - Perseveration, repetitive speech, rituals, or obsessions.
  - Decline in **social cognition** and/or **executive abilities.**
- **Language variant** (primary progressive aphasia):
- Difficulties with **speech** and **comprehension**

## ◀ Diagnosis

- Definitive diagnosis cannot be made until autopsy.
- FTD is **probable** if frontotemporal atrophy is evident on structural imaging or hypoactivity is visualized on functional imaging in context of the characteristic clinical signs

## ◀ Treatment

- Symptom-focused.
- Serotonergic medications (e.g., SSRIs, trazodone) may help reduce disinhibition, anxiety, impulsivity, repetitive behaviors, and eating disorders



# HIV Infection

## ◀ Clinical Manifestations

- Variable presentation depending on the part(s) of the brain affected.
- Decline may be observed in executive functioning, attention, working memory, and psychomotor activity.
- Psychiatric and neuromotor symptoms may also be present

## ◀ Diagnosis

- Mild or major NCD attributable to confirmed HIV infection.

## ◀ Treatment

- Antiretroviral therapy (ART) improves cognition in some patients.  
Psychostimulants target fatigue, apathy, and psychomotor retardation



# Huntington's Disease

## ◀ Clinical Manifestations

- Characterized by a triad of **motor**, **cognitive**, and **psychiatric** symptoms.
- Average age at diagnosis is 40 years.
- Cognitive decline and behavioral changes can precede onset of motor signs by up to 15 years.
- **Executive function** is the primary cognitive domain affected.
- Psychiatric manifestations include depression, apathy, irritability, obsessions, impulsivity, paranoia, delusions, and hallucinations.
- Patients are often aware of deteriorating mentation.
- Increased rate of suicide (7%).
- Movement disorders include **chorea** (jerky, dance-like movements) and **bradykinesia**.

## ◀ Diagnosis

- Extraparamidal movement disorder in an individual with either a **family history** of HD or **genetic testing** that confirms an increased number of CAG repeats in the HTT gene.
- Mild or major NCD may be diagnosed prior to onset of motor signs if an individual is determined to be at risk based on family history or genetic testing.

## ◀ Treatment

- Symptom-directed therapy with **tetrabenazine** or **atypical (second-generation) antipsychotics**.
- Amantadine
- SSRIs for depression



# Parkinson's Disease

## ◀ Clinical Manifestations

- Motor signs include rigidity, resting tremor, bradykinesia, and postural instability.
- Cognitive manifestations consist of executive dysfunction and visuospatial impairments.
- Depression, anxiety, personality changes, and apathy are common.
- Psychotic symptoms, including visual hallucinations and paranoid delusions, may result from the disease itself or from adverse effects of the medications used to treat the motor symptoms.

## ◀ Diagnosis

- Diagnosis of PD requires the presence of **bradykinesia** and either **tremor** or **rigidity**.
- Associated with asymmetry of motor symptoms and favorable response to dopaminergic therapy.
- Mild or major NCD is attributed to PD if **cognitive decline appears after the onset of motor symptoms** and no other underlying etiology is identified.

## ◀ Treatment

- Motor symptoms are most commonly treated with **carbidopa-levodopa** and/or **dopamine agonists**.
- Cholinesterase inhibitors are used to target cognitive symptoms and may also ameliorate some of the neuropsychiatric symptoms (hallucinations).
- Psychotic symptoms may respond to a reduction in the dose of dopamine agonists.
- **Low dose quetiapine** and **clozapine** are the preferred medications for treatment of psychotic symptoms. Avoid other antipsychotics since they can worsen the motor symptoms of PD.

## Capacity Vs. Competency

- Clinical vs. Legal term that denotes the ability to make rational and reasonably well-informed decisions by a particular patient (vs. person) in their treatment and/ or life decision/s.
- Capacity is a **clinical determination** that addresses the integrity of mental functions.
- Competency is a **legal determination** that addresses societal interest in restricting a person's right to make decisions or do acts because of incompetency. e.g. Bank.

## Valid Informed Consent

- Permission voluntarily given by a competent person without any elements of force, deceit, coercion after explanation and disclosure of:
  - Purpose and details of procedure or treatment.
  - Risks, benefits and available alternative treatment(s).
  - The right to withdraw consent verbally or in written forms at anytime.
- Possible Exceptions:
  - Life threatening situation.
  - Patient who waive their rights to disclose and consent (do not want to be informed).
  - Instances where “disclosure’ may be harmful to the patient“ Therapeutic privileges”.
    - Like severely depressed patients. The last two points are controversial and are not fully agreed upon.

## Rules of Capacity

- Being mentally ill doesn't in itself imply a loss of capacity or competency.
- Having Capacity or being Competent should be presumed until proven otherwise.

## Valid Informed Consent

- A.
  - General perspective or specific (Psychiatric hospitalization, ECT).
  - Find out the best language of communication.
  - Determine if patient has adequate information on which to base a decision.
  - MMSE: attention, concentration, memory.
  - Inform the patient about the nature of the disorder, AND the risk and benefit of the PROPOSED treatment, and of ALTERNATIVE treatments or of NO treatment.
- B.
  - Repeat information number of times and in different ways.
  - Let the patient paraphrase or restate the understanding.
  - Evaluate nature of questions that patient asks regarding treatment plan.
  - Periodical Re-assessment of capacity (if any change in clinical conditions or mental status such as in delirium or any modifications in treatment plan).
- C.
  - If patient has “severe deficit” in understanding information > No Capacity to make informed consent or make decision > Arrange a process for “a substitute decision maker”.

**Table 1. Legally Relevant Criteria for Decision-Making Capacity and Approaches to Assessment of the Patient.**

Criterion	Patient's Task	Physician's Assessment Approach	Questions for Clinical Assessment*	Comments
Communicate a choice	Clearly indicate preferred treatment option	Ask patient to indicate a treatment choice	Have you decided whether to follow your doctor's [or my] recommendation for treatment? Can you tell me what that decision is? [If no decision] What is making it hard for you to decide?	Frequent reversals of choice because of psychiatric or neurologic conditions may indicate lack of capacity
Understand the relevant information	Grasp the fundamental meaning of information communicated by physician	Encourage patient to paraphrase disclosed information regarding medical condition and treatment	Please tell me in your own words what your doctor [or I] told you about: The problem with your health now The recommended treatment The possible benefits and risks (or discomforts) of the treatment Any alternative treatments and their risks and benefits The risks and benefits of no treatment	Information to be understood includes nature of patient's condition, nature and purpose of proposed treatment, possible benefits and risks of that treatment, and alternative approaches (including no treatment) and their benefits and risks
Appreciate the situation and its consequences	Acknowledge medical condition and likely consequences of treatment options	Ask patient to describe views of medical condition, proposed treatment, and likely outcomes	What do you believe is wrong with your health now? Do you believe that you need some kind of treatment? What is treatment likely to do for you? What makes you believe it will have that effect? What do you believe will happen if you are not treated? Why do you think your doctor has [or I have] recommended this treatment?	Courts have recognized that patients who do not acknowledge their illnesses (often referred to as “lack of insight”) cannot make valid decisions about treatment Delusions or pathologic levels of distortion or denial are the most common causes of impairment
Reason about treatment options	Engage in a rational process of manipulating the relevant information	Ask patient to compare treatment options and consequences and to offer reasons for selection of option	How did you decide to accept or reject the recommended treatment? What makes [chosen option] better than [alternative option]?	This criterion focuses on the process by which a decision is reached, not the outcome of the patient's choice, since patients have the right to make “unreasonable” choices




\* Questions are adapted from Grisso and Appelbaum.<sup>31</sup> Patients' responses to these questions need not be verbal.



## Team leader

- Saleh Aloraini 

## Team members

- Abdulrahman Aljofan
- Faisal Alhusaini
- Alwaleed Bin shaya
- **Faisal Bin Moammar**  
- Mishari Alzoubi
- Abdulmajeed Namshah
- Abdulrahman bawazir
- Abdulmalik Alduraibi
- Hamad Alothman
- Sultan Alkassim
- Faisal Alshuaibi
- **Abdullah Alyamani**  
- Talal Alanazy
- Yahya Alghamdi
- Osama Alsaaid



Psychiatry team 441

Good luck!!



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