Cognitive disorders
Dementia / Delirium

Cognitive disorders

- Cognitive disorders affect memory, orientation, attention, and judgment. They result from primary or secondary abnormalities of the central nervous system.
- The main categories of cognitive disorders are:
  - Dementia
  - Delirium
  - Amnestic disorders

[Wernicke-Korsakoff Syndrome]

Amnesia is loss of memory, but with preservation of motor/ executive functions

able to recognize daily objects, able to speak, have motor skills
⇒ problem just in loss of memory

MINI MENTAL STATE EXAM (MMSE)

- The MMSE is used to assess a patient's current state of cognitive functioning. It can be used as a daily barometer to evaluate interval changes but should not be used to make a formal diagnosis. It tests orientation, registration, attention and calculation, recall, and language.
- MMSE scoring:
  - Perfect score: 30
  - Dysfunction: < 25

Performing the Mini Mental State Exam

1. **Orientation**:-
   - What is the date, month, year? 5 points
   - Where are we (state, city, hospital)? 5 points
2. **Registration**:-
   - Name three objects and repeat them. 3 points
3. **Attention and calculation**
   - Serial 7s (subtract 7 from 100 and continue subtracting 7 from each answer) or spell "world" backward. 5 points
4. **Recall**
   - Name the three objects above 5 minutes later. 3 points
5. **Language**
   - Name a pen and a clock. 2 points
   - Say, "No ifs, ands, or buts." 1 points
   - Three-step command: 3 points

Take a pencil in your right hand, put in your left hand, then put it on the floor.

6. **Read and obey the following:**
   - Close your eyes. 1 point
   - Write a sentence. 1 point
   - Copy design. 1 point

TOTAL 30 points

DEMENTIA

- Dementia is an impairment of memory and other cognitive functions without alteration in the level of consciousness. -- Most forms of dementia are progressive and irreversible. Dementia is a major cause of disability in the elderly. It affects memory, cognition, language skills, behavior, and personality.
- **EPIDEMIOLOGY:-**
- Incidence increases with age.
- Twenty percent of people > age 80 have a severe form of dementia.
- *Associations: Delusions and hallucinations occur in approximately 30%* of demented patients. Affective symptoms, including depression and anxiety, are seen in 40 to 50% of patients. Personality changes are also common.

ETIOLOGY

- The *most common causes of dementia are:*

1. **Alzheimer's disease (50 to 60%)**
2. **Vascular dementia (10 to 20%)**
3. **Major depression ("pseudodementia")**

- Patient will often reply "I don't know" to MMSE questions, whereas a patient with a true dementia will confabulate
- Patient will usually be able to state approximate onset of symptoms and will elaborate on deficits

↓ appetite
depressed mood

- good appetite
- good mood

15% of demented patients have a treatable and potentially reversible condition.

DIFFERENTIAL DIAGNOSIS

- 1. **Psychiatric:-**

✔ Depression (pseudodementia).

✔ Delirium.

✔ Schizophrenia.

✔ Malingering.

- 2. **Organic:-**

- *Structural:* *Benign forgetfulness of normal aging*, *Parkinson's disease*, Huntington's disease, Down's syndrome, head trauma, brain tumor, normal pressure hydrocephalus, multiple sclerosis, subdural hematoma
- *Metabolic:* *Hypothyroidism, hypoxia, malnutrition (B12, folate, or thiamine* deficiency), Wilson's disease, lead toxicity.
- *Infectious:* *Lyme disease, HIV dementia, Creutzfeldt–Jakob disease*, neurosyphilis, meningitis, encephalitis

- 3. **Drugs:-** Alcohol (chronic and acute), phenothiazines, anticholinergics, sedatives.

Alzheimer's Disease

just dementia and the patient otherwise healthy (not HTN, No Hyper-cholesterolemia)

declining (slowly but surely).

* in general → healthy patients but they are starting to forget things as they get older → forget thing + losing orientation, cognitive process

- Most common dementia (80% of all dementias).
- EPIDEMIOLOGY
- Incidence: 5% of all people > 65; 15 to 25% of all people > 85
- More common in women than men
- Average life expectancy: 8 years after diagnosis
- Forty percent of patients have a family history of Alzheimer's.

CLINICAL MANIFESTATIONS

- **Hallmarks: Gradual progressive decline of cognitive functions, especially** memory and language. Personality changes and mood swings are very common.

DIAGNOSIS AND DSM-IV CRITERIA

- **Memory impairment plus at least one of the following:**

✔ **Aphasia—disorder of language affecting speech *and understanding*.**

✔ **Apraxia—inability to perform purposeful movements (e.g., copying a** picture)

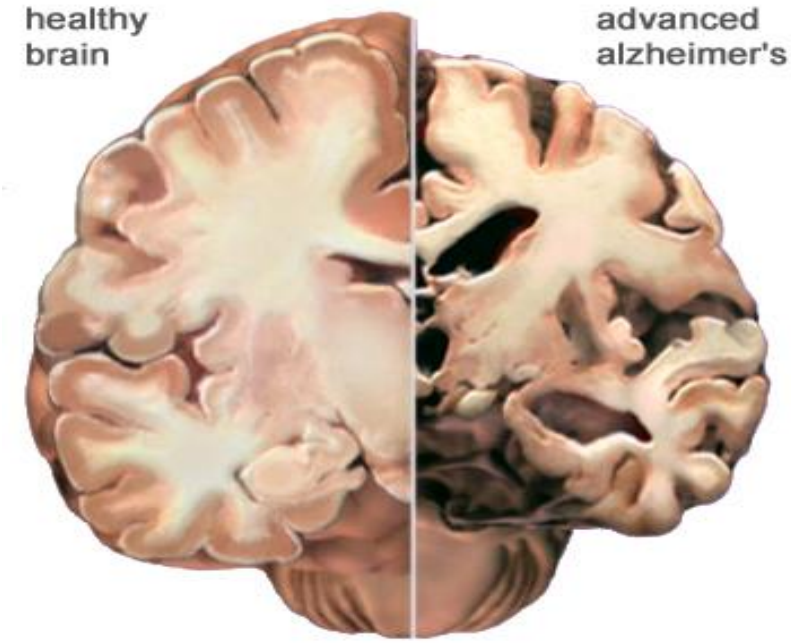
✔ **Agnosia—inability to interpret sensations correctly (*visual agnosia—inability*** to recognize a previously known object)

✔ **Diminished executive functioning—problems with planning, organizing,** and abstracting.

✔ *Personality/mood changes: Depression, anxiety, anger, and suspiciousness are* common. Psychotic symptoms such as paranoia are common.

※ patho physiology ⟶ Cortical atrophy, reduction in Ach + NE Synthesis and deposition of amyloid plaques.

- **NEUROPHYSIOLOGY:-**
  Alzheimer's patients have decreased levels of acetylcholine (due to loss of noradrenergic neurons in the locus ceruleus of the brainstem) and of norepinephrine (due to preferential loss of cholinergic neurons in the basal nucleus of Meynert of the midbrain).
- **PATHOLOGY:-**
- **Gross**
  Diffuse atrophy with enlarged ventricles and flattened sulci
- **Microscopic**
  Senile plaques composed of amyloid protein / Neurofibrillary tangles derived from Tau proteins/ Neuronal and synaptic.



TREATMENT

- No cure or truly effective treatment
- Physical and emotional support, proper nutrition, exercise, and supervision
- NMDA(n.methyl.d.aspartate) receptor antagonists: memantine

Cholinesterase inhibitors to help slow progression:

- Tacrine (Cognex)
- Donepezil (Aricept)
- Rivastigmine (Exelon)

Treatment of symptoms as necessary:

- Low-dose, short-acting benzodiazepines for anxiety
- Low-dose antipsychotics for agitation/psychosis (e.g., quetiapine)
- Antidepressants for depression (if the patient fulfills criteria for major depression)

Vascular Dementia

demented symptoms + Focal neurologic deficits

+ due to multiple small, sub clinical infracts of various part of the brain.

→ non-linear progression → Small strokes happen at different time.

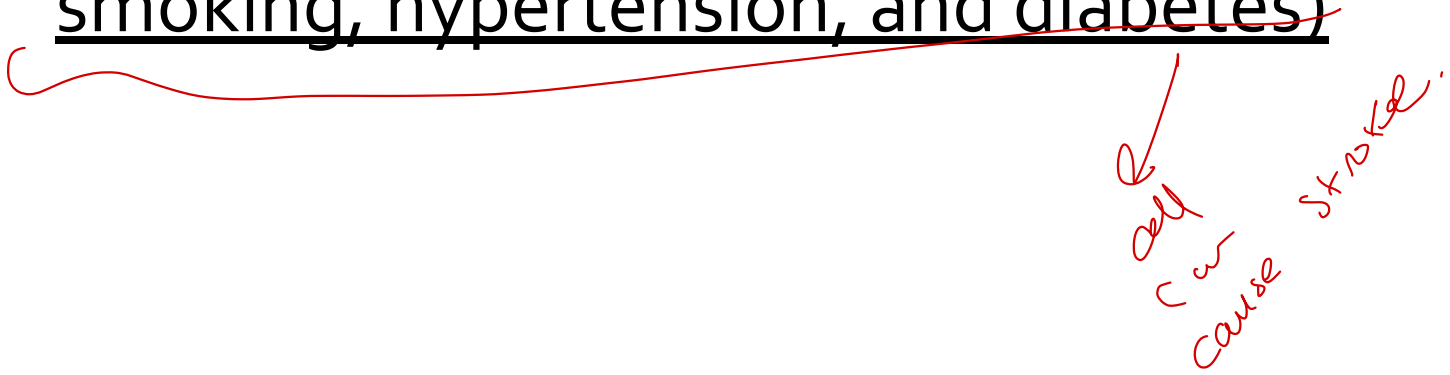
- Caused by <u>microvascular disease in the brain</u> that <u>produces multiple small infarcts</u>. A substantial infarct burden must accumulate before dementia develops.
- **CLINICAL MANIFESTATIONS**
- Disease manifestations of vascular dementia are identical to Alzheimer's.

Memory impairment and at least one of the following must be present:

- **1. Aphasia**
- **2. Apraxia**
- **3. Agnosia**
- **4. Diminished executive functioning**
- *Personality changes: Depression, anger, and suspiciousness are common. Psychotic* symptoms such as paranoia are also common.

VASCULAR DEMENTIA VERSUS ALZHEIMER'S

- Since vascular dementia is caused by small brain infarcts, patients also have focal neurological symptoms (such as hyperreflexia or paresthesias).
- Onset usually more abrupt than Alzheimer's
- Greater preservation of personality
- Can reduce risk by modifying risk factors (such as smoking, hypertension, and diabetes)



- DIAGNOSIS

Can be diagnosed readily by MRI.

- TREATMENT
  - No cure or truly effective treatment
  - Physical and emotional support, proper nutrition, exercise, and supervision
  - Treatment of symptoms as necessary

Pick's Disease/Frontotemporal Dementia (FTD)

كثير صعب تميزه عن الزهايمر Clinical

- A rare cause of slowly progressing dementia.
- CLINICAL MANIFESTATIONS:-

Aphasia, apraxia, agnosia; difficult to distinguish from Alzheimer's clinically, but personality and behavioral changes are more prominent early in the disease. ✗ prior to onset of memory changes.

- PATHOLOGY
- Atrophy of frontotemporal lobes
- **Pick bodies—intraneuronal inclusion bodies (not necessary for diagnosis** of FTD)
- TREATMENT
- No effective treatment
- Physical, emotional, and nutritional support
- Treat emotional/behavioral symptoms as needed.

Huntington's Disease

- Autosomal dominant genetic disorder that results in progressively disabling cognitive, physical, and psychological functioning, ultimately resulting in death after approximately 15 years.
- CLINICAL MANIFESTATIONS

Onset: 35 to 50 years of age

Hallmarks:

- Progressive dementia
- Bizarre **choreiform movements (dancelike flailing of arms and legs)**
- Muscular hypertonicity
- Depression and psychosis very common.

PATHOLOGY

- Trinucleotide repeat on short arm of chromosome 4; primarily affects basal ganglia.

DIAGNOSIS

- MRI shows caudate atrophy (and sometimes cortical atrophy). Genetic testing and MRI are diagnostic.

TREATMENT

- There is no effective treatment available (supportive only).

Parkinson's Disease

[lewy body dementia]

dementia in patient with parkinson's

- Progressive disease with prominent neuronal loss in substantia nigra, which provides dopamine to the basal ganglia, causing physical and cognitive impairment.

Approximately 30% of patients with Parkinson's disease develop dementia.

CLINICAL MANIFESTATIONS

Characterized by:

1. **Bradykinesia**
2. **Cogwheel rigidity**
3. **Resting tremor—"pill-rolling" tremor most common**
4. **Masklike facial expression**
5. **Shuffling gait**
6. **Dysarthria (abnormal speech).**

Fifty percent of patients will suffer from depression.

ETIOLOGY

- Idiopathic (most common)
- Traumatic (e.g., Muhammad Ali)
- Drug- or toxin-induced
- Encephalitic (as in the book/movie *Awakenings)*
- Familial (rare)

PATHOLOGY AND PATHOPHYSIOLOGY

- Loss of cells in the substantia nigra of the basal ganglia, which leads to a decrease in dopamine and loss of the dopaminergic tracts.

TREATMENT

- **Pharmacologic**
- Levodopa
- Carbidopa

→ Replacement of dopamine (due to dopaminergic neuronal destruction)

- Amantadine → [Not First choice]
- Anticholinergics—help relieve tremor
- Dopamine agonists (bromocriptine, etc.)
- Monoamine oxidase (MAO)-B inhibitors (selegiline)—inhibit breakdown of dopamine.

Surgical

- Thalamotomy or pallidotomy may be performed if no longer responsive to pharmacotherapy.

Creutzfeldt–Jakob Disease (CJD)

- A rapidly progressive, degenerative disease of the central nervous system (CNS) caused by a *prion*. *CJD may be inherited, sporadic, or acquired. A* small percentage of patients have become infected through corneal transplants.
- CLINICAL MANIFESTATIONS
- **Hallmarks: Rapidly progressive dementia 6 to 12 months after onset of symptoms.**
- More than 90% of patients have myoclonus (sudden spasms of muscles).
- Extrapyramidal signs, ataxia, and lower motor neuron signs are also common.
- There is a long latency period between exposure and disease onset.

10 months ago the patient was fine and they've been rapidly quickly developing the symptoms for forgetfulness, inability to remember objects, inability to perform activities of daily life and so it's going to resemble alzheimer's but it's like compressing into like 1-year period opposed to 10-year.

Huntington's disease → gait disturbance, chorea

Fast (Fast the onset of death from diagnosis onset of symptoms) is within month

PATHOLOGY

- Spongiform changes of cerebral cortex, neuronal loss, and hypertrophy of glial cells.

DIAGNOSIS

- *Definitive—pathological demonstration of spongiform changes of brain tissue*
- *Probable—the presence of both rapidly progressive dementia and periodic* generalized sharp waves on electroencephalogram (EEG) *plus at least two of* the following clinical features:
  - Myoclonus
  - Cortical blindness
  - Ataxia, pyramidal signs, or extrapyramidal signs
  - Muscle atrophy
  - Mutism

3M → myoclonus, mutism, muscle atrophy
* cortical blindness
* pyramidal + extrapyramidal signs, Ataxia
+ rapidly progressive dementia

TREATMENT AND COURSE

- No treatment; relentless course, progressing to death usually within a year

Normal Pressure Hydrocephalus (NPH)

- NPH is a reversible cause of dementia. Patients have enlarged ventricles with increased CSF pressure. The etiology is either idiopathic or secondary to obstruction of CSF reabsorption sites due to trauma, infection, or hemorrhage.
- CLINICAL MANIFESTATIONS

Clinical triad:

1. Gait disturbance (often appears first)

2. Urinary incontinence

3. Dementia (mild, insidious onset)

TREATMENT

- Relieve increased pressure with shunt. Of the clinical triad, the dementia is least likely to improve.

DELIRIUM

+ any intra or extra cranial pathological process affecting CNs
+ alter level of consciousness, impaired cognitive function (usually hallucination)
+ due to organic causes → CNs dz
+ acute/ reversible + ttt → treat the underlying cause.

+ uremia
+ ICU

+ behavioral hallucination

- Delirium is an acute disorder of cognition related to impairment of cerebral metabolism.
- Unlike demented patients, delirious patients have a **rapid onset** of symptoms, periods of **altered levels of consciousness**, **and potential reversal** of symptoms with treatment of the underlying cause.
- Delirious patients appear confused and have a fluctuating course with **lucid intervals. They may be either stuporous or agitated, and perceptual disturbances** (e.g., **hallucinations) are common. Patients are often anxious, incoherent,** and unable to sleep normally.
- It can be caused by virtually any medical disorder, and there is a high mortality rate if untreated.
- It can last from days to weeks, and can also be chronic.

ETIOLOGY

- *Common causes of delirium include:*
- CNS injury or disease
- Systemic illness
- Drug abuse/withdrawal
- Hypoxia

Additional causes of delirium include:

- Fever
- Sensory deprivation
- Medications (anticholinergics, steroids, antipsychotics, antihypertensives,
- insulin, etc.)
- Postop
- Electrolyte imbalances

- DSM-IV TREATMENT CRITERIA

The two types of delirium are:

- **1. *Quiet: patient may seem depressed or exhibit symptoms similar to failure*** to thrive; an MMSE must be done to distinguish from depression and other diagnostic criteria
- **2. *Agitated: obvious pulling out lines; may hallucinate.***

- DIFFERENTIAL DIAGNOSIS

Dementia, fluent aphasia (Wernicke's), acute amnestic syndrome, psychosis, depression, malingering.

TREATMENT

- First and foremost: Treat the underlying cause!
- Provide physical and sensory support.
- Treat drug withdrawal.
- Treat symptoms of psychosis (low-dose antipsychotic) and insomnia
- (sedative-hypnotic).

Delirium Versus Dementia

Delirium	Dementia
Clouding of consciousness	Loss of memory/intellectual ability
Acute onset	*Insidious onset*
Lasts 3 days to 2 weeks	Lasts months to years
Orientation impaired	Orientation often impaired
Immediate/recent memory impaired	Recent and remote memory impaired
Visual hallucinations common	Hallucinations less common
Symptoms fluctuate, often worse at night	Symptoms stable throughout day
Usually reversible	15% reversible
Awareness reduced	Awareness clear