Neurocognitive Disorders

Dr. Rawan Masri

Cognitive disorders (formerly called organic mental syndromes) involve problems in memory, orientation, level of consciousness, and other intellectual functions.

a. These difficulties are due to abnormalities in neural chemistry, structure, or physiology originating in the brain or secondary to systemic illness.

b. Patients with cognitive disorders may also show psychiatric symptoms(e.g.,depression, anxiety, hallucinations, delusions, and illusions) which are secondary to the cognitive problems.

c. The major cognitive disorders are delirium, dementia, and amnestic disorder

Dementia

(Major Neurocognitive Disorder)

1. Dementia refers to a disease process marked by progressive cognitive impairment in clear consciousness. Dementia does not refer to low intellectual functioning or mental retardation because these are developmental and static conditions, and the cognitive deficits in dementia represent a decline from a previous level of functioning. Dementia involves multiple cognitive domains and cognitive deficits cause significant impairment in social and occupational functioning.

2. Dementia of Alzheimer type is the most common type of dementia (50%–65% of all dementias). Other types of dementia include vascular dementia (10%–15% of dementias), Lewy body dementia, and dementia caused by HIV infection .

Epidemiology

a. 5% of population older than 65
b. 20% older than 80
c. 15% of neurocognitive disorders are reversible.

Diagnosis and clinical features

- **Memory impairment** is typically an early and prominent feature in dementia.
- Early in the course , memory impairment is mild and usually most marked for recent events; people forget telephone numbers, conversations, and events of the day.
- As the course of dementia progresses, memory impairment becomes severe, and only the earliest learned information (e.g., a person's place of birth) is retained.
-

Reversible causes

Approximately **15%** of people with dementia have reversible illnesses if treatment is initiated before irreversible damage takes place.

Reversible causes:

- Metabolic abnormalities (e.g., hypothyroidism)
- Nutritional deficiencies(e.g., vitamin B12, folate)
- Dementia syndrome caused by depression.

DSM-5 Diagnostic Criteria for Major Neurocognitive 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;
and

2. substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment

B. 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)

- **Note:** if do not interfere in B, and impairments are mild-moderate in A, considered"mild neurocognitive disorder"

C. cognitive deficits do not occur exclusively in the context of a delirium

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

DSM-5 Diagnostic Criteria for Major Neurocognitive Disorder

Specify:
Without behavioral disturbance: If the cognitive disturbance is not accompanied by any clinically significant behavioral disturbance.
With behavioral disturbance (specify disturbance): If the cognitive disturbance is accompanied by a clinically significant behavioral disturbance (e.g., psychotic symptoms, mood disturbance, agitation, apathy, or other behavioral symptoms).

Specify current severity:

Mild: Difficulties with instrumental activities of daily living (e.g., housework, managing money).

Moderate: Difficulties with basic activities of daily living (e.g., feeding, dressing).
Severe: Fully dependent.

Alzheimer disease

- It is a neurodegenerative disorder that present with progressive memory loss.

- **The most common cause of dementia**

1. **Diagnosis and clinical features**

a. Patients with Alzheimer disease show a gradual loss of memory and intellectual abilities.

Their psychiatric symptoms include inability to control impulses and lack of judgment as well as depression and anxiety.

b. Later in the illness, symptoms include confusion and psychosis that progress to coma and death (usually within 8–10 years of diagnosis).

c. For patient management and prognosis, it is important to make the distinction between Alzheimer disease and both pseudodementia (depression that mimics dementia) and behavioral changes associated with normal aging .

Alzheimer disease

a. Ten warning signs of Alzheimer disease

i. Memory loss that affects job skills

ii. Difficulty performing familiar tasks

iii. Problems with language

iv. Disorientation to time and place

v. Poor judgment

vi. Problems with abstract thought

vii. Misplacing things

viii. Changes in mood or behavior

ix. Changes in personality

Mr. J, a 70-year-old retired businessman, was brought to psychiatric services on referral by the family physician. His wife claimed that Mr. J had become so forgetful that she was afraid to leave him alone, even at home. Mr. J retired at age 62 years after experiencing a decline in work performance during the previous 5 years. He also slowly gave up hobbies he once enjoyed (photography, reading, golf) and became increasingly quiet. However, his growing forgetfulness went basically unnoticed at home. Then one day while walking in an area he knew well, he could not find his way home. From then on his memory failure began to increase. He would forget appointments, misplace things, and lose his way around the neighborhood he resided in for 40 years. He failed to recognize people, even those he knew for many years. His wife had to start bathing and dressing him because he forgot how to do so himself.

On examination, Mr. J was disoriented in time and place. He was only able to recall his name and place of birth. Mr. J seemed lost during the interview, only responding to questions with an occasional shrug of his shoulders. When asked to name objects or to recall words or numbers, Mr. J appeared tense and distressed. Mr. J had difficulty following instructions and was unable to dress or undress himself. His general medical condition was good. Laboratory examinations showed abnormalities on Mr. J's EEG and CT scans

Alzheimer disease

2. Genetic associations in Alzheimer disease include:

a. Abnormalities of chromosome 21 (Down syndrome patients ultimately develop Alzheimer disease).

b. Abnormalities of chromosomes1 and 14 (sites of the presenilin 2 and presenilin 1genes, respectively) implicated particularly in early onset Alzheimer disease (i.e., occurring before the age of 65).

c. Possession of at least one copy of the apolipoprotein E4 (apoE4) gene on chromosome19. (People with one copy of the gene have Alzheimer's disease three times more frequently than do those with no E4 gene, and people with two E4 genes have the disease eight times more frequently than do those with no E4 gene)

d. Gender—there is a higher occurrence of Alzheimer disease in women.

Alzheimer disease

2. Neurophysiological factors include:

a. Decreased activity of acetylcholine (Ach) and reduced brain levels of choline acetyl-transferase (i.e., the enzyme needed to synthesize Ach).

b. Abnormal processing of amyloid precursor protein.

c. Overstimulation of the N-methyl-D-aspartate (NMDA) receptor by glutamate leading to an influx of calcium, nerve cell degeneration and cell death .

3. Gross anatomical brain changes include:

a. Enlargement of brain ventricles.

b. Diffuse atrophy and flattening of brain sulci.

Alzheimer disease

4. Microscopic anatomical brain changes include:

A. Senile plaques, neurofibrillary tangles, neuronal loss(particularly in the cortex and the hippocampus).

➢ Extracellular **Aβ amyloid** deposition : in brain (senile plaques) & in vessel wall (Amyloid angiopathy)

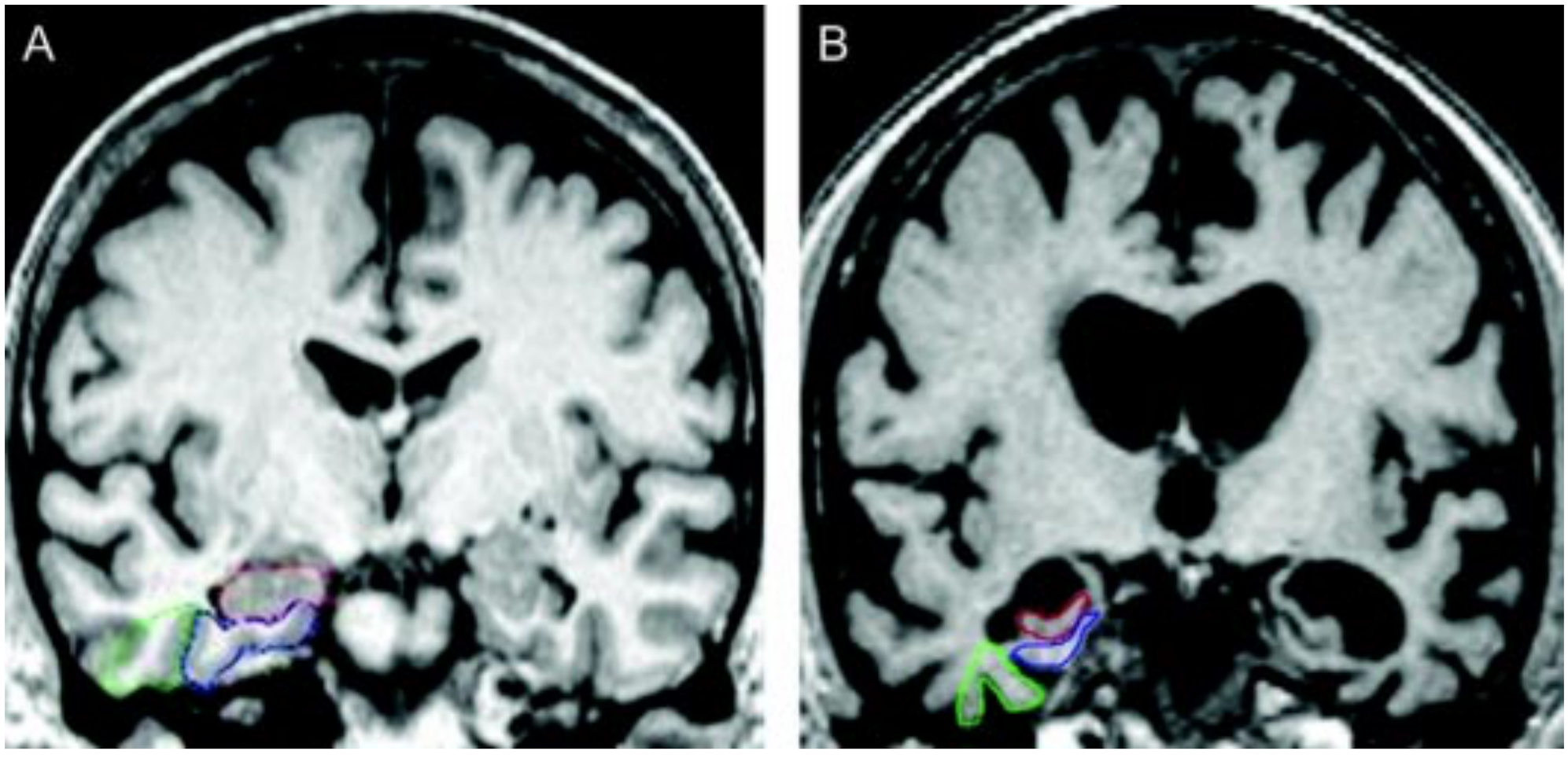
➢ Intracellular **Tau prottein** deposition : Neurofibrillary tangles (within neurons).

- *Amyloid plaques and neurofibrillary tangles (also seen in other neurodegenerative diseases, Down syndrome and, to a lesser extent, in normal aging).*

b. Loss of cholinergic neurons in the basal forebrain.

c. Neuronal loss and degeneration in the hippocampus and cortex.

Alzheimer disease



Alzheimer disease

2. Alzheimer disease has a progressive, irreversible, downhill course. The most effective initial interventions involve providing a structured environment, including visual-orienting cues. Such cues include labels over the doors of rooms identifying their function; daily posting of the day of the week, date, and year; daily written activity schedules; and practical safety measures (e.g., disconnecting the stove).

3. **Pharmacologic interventions include:**
   a. Acetylcholinesterase inhibitors(e.g., Tacrine, Donepezil, Rivastigmine, and Galantamine) to temporarily slow the progression of the disease. However, these agents cannot restore function that has already been lost.

   b. Memantine, an NMDA antagonist, decreases the influx of glutamate and thus slows deterioration in patients with moderate to severe Alzheimer disease.

   c. Psychotropic agents are used to treat associated symptoms of anxiety, depression, or psychosis. Since antipsychotics are associated with increased mortality in elderly demented patients (particularly those with Lewy body dementia), they should be used with extreme caution.

Vascular Dementia

a. It is caused by multiple, small cerebral infarctions usually resulting from cardiovascular disorders such as hypertension or atherosclerosis.

b. In contrast to Alzheimer disease, vascular dementia has a higher risk for men and is more likely to cause motor symptoms.

c. The primary intervention is the management of the cardiovascular disorder(e.g.,antihypertensives, anticoagulants) to prevent further infarcts leading to deterioration in cognitive functioning.

Neurocognitive Disorder, Alzheimer Type versus Vascular Neurocognitive Disorder

Neurocognitive Disorder, Alzheimer Type	Vascular Neurocognitive disorder
General deterioration	Patchy deterioration
More in women	More in men
Later onset	Earlier onset
Most common, 65% of neurocognitive disorders	Less common, 15% of neurocognitive disorders
Etiology unknown	Etiology features hypertension
Progressive onset	Quick onset
No lateral signs	Lateralizing neurologic signs

Lewy Body Dementia

a. Gradual, progressive loss of cognitive abilities as well as hallucinations (often visual) and the motor characteristics of Parkinson disease. Also associated with REM sleep behavior disorder.

b. Pathology includes amyloid plaques but, in contrast to Alzheimer disease, few neurofibrillary tangles.

c. Patients typically have adverse responses to antipsychotic medications.

Clinical Criteria for Dementia with Lewy Bodies (DLB)

The patient must have sufficient cognitive decline to interfere with social or occupational functioning. Of note early in the illness, memory symptoms may not be as prominent as attention, frontosubcortical skills, and visuospatial ability.

Probable DLB requires two or more core symptoms, whereas possible DLB only requires one core symptom.

Core features

Fluctuating levels of attention and alertness

Recurrent visual hallucinations

Parkinsonian features (cogwheeling, bradykinesia, and resting tremor)

Supporting features

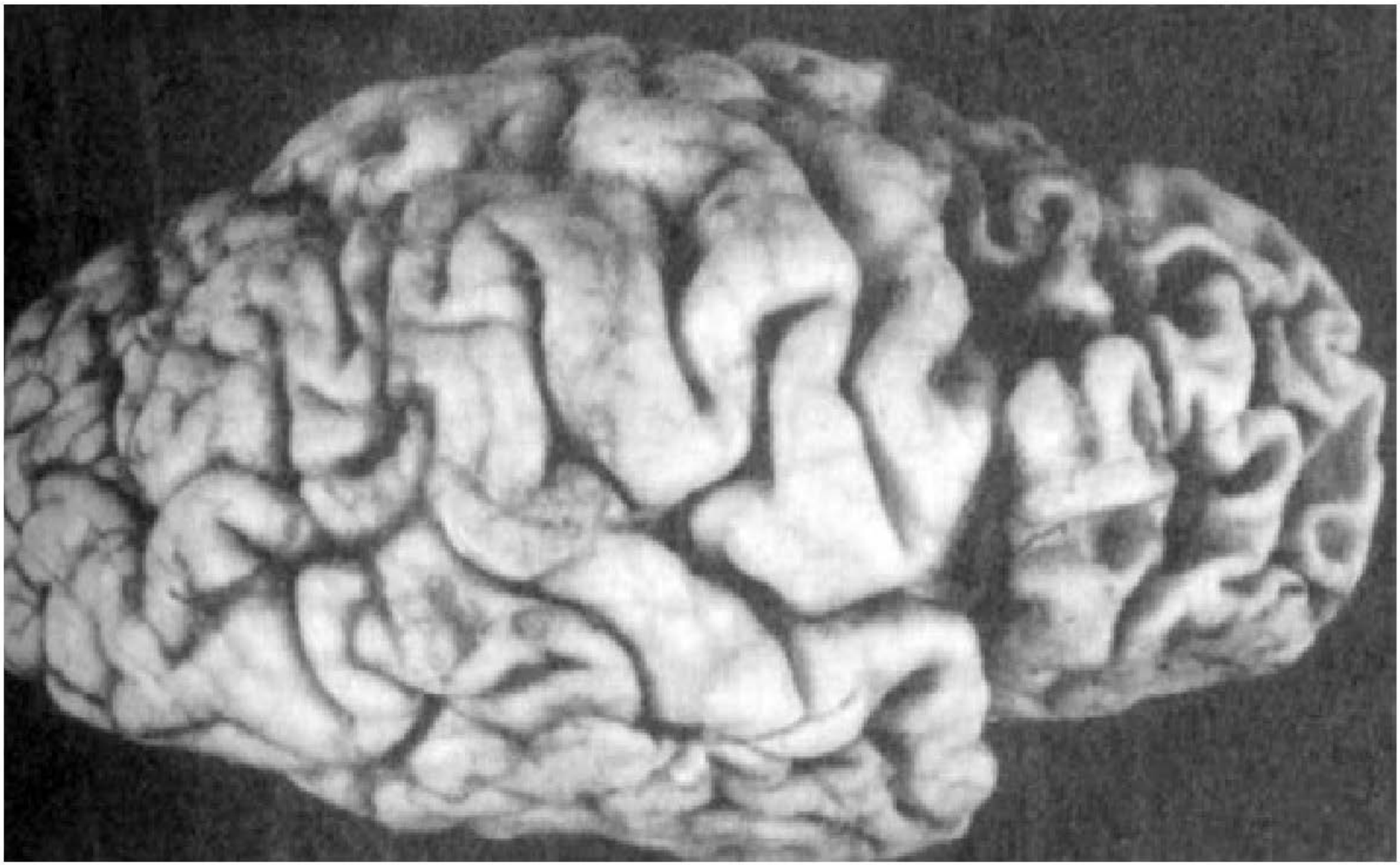
Repeated falls
Syncope
Sensitivity to neuroleptics
Systematized delusions
Hallucinations in other modalities (e.g. auditory, tactile)

Frontotemporal Dementia (Pick's Disease)

In contrast to the parietal-temporal distribution of pathological findings in Alzheimer's disease, Pick's disease is characterized by a preponderance of atrophy in the frontotemporal regions. These regions also have neuronal loss; gliosis; and neuronal Pick's bodies, which are masses of cytoskeletal elements. The cause of Pick's disease is unknown, but the disease constitutes approximately 5 percent of all irreversible dementias. It is most common in men, especially those who have a first-degree relative with the condition. Pick's disease is difficult to distinguish from dementia of the Alzheimer's type, although the early stages of Pick's disease are more often characterized by personality and behavioral changes, with relative preservation of other cognitive functions, and it typically begins before 75 years of age. Familial cases may have an earlier onset, and some studies have shown that approximately half of the cases of Pick's disease are familial .

- CT or MRI sometimes shows frontal lobe involvement but definitive diagnosis is only at autopsy

Frontotemporal Dementia (Pick's Disease)



Prion disease

Prion disease is a group of related disorders caused by a transmissible infectious protein known as a prion. Included in this group are Creutzfeldt-Jakob disease (CJD), Gerstmann-Straussler Scheinker disorder (GSS), fatal familial insomnia (FFI), and kuru. A variant of CJD (vCJD), also called "mad cow disease," appeared in 1995 in the United Kingdom and is attributed to the transmission of bovine spongiform encephalopathy (BSE) from cattle to humans. Collectively, these disorders are also known as subacute spongiform encephalopathy

CREUTZFELDT-JAKOB DISEASE. First described in 1920, CJD is an invariably fatal, rapidly progressive disorder that occurs mainly in middle-aged or older adults. It manifests initially with fatigue, flulike symptoms, and cognitive impairment. As the disease progresses, focal neurological findings such as aphasia and apraxia occur. Psychiatric manifestations include emotional lability, anxiety, euphoria, depression, delusions, hallucinations, or marked personality changes. The disease progresses over months, leading to dementia, akinetic mutism, coma, and death.

The rates of CJD range from one to two cases per 1 million persons a year worldwide. The infectious agent self-replicates and can be transmitted to humans by inoculation with infected tissue and sometimes by ingestion of contaminated food. Iatrogenic transmission has been reported via transplantation of contaminated cornea or dura mater or to children via contaminated supplies of human growth hormone derived from infected persons.

Prion disease

Prion disease

a. Neurocognitive disorder caused by prion (no DNA or RNA)

b. Rapidly progressive

c. Generally onset between ages 40 and 50

d. Initially, vague somatic complaints and unspecified anxiety, followed by ataxia, choreoathetosis, and dysarthria

e. Fatal in 2 years (usually sooner)

f. CT demonstrates atrophy in cortex/cerebellum

g. No treatment

Huntington chorea

a. Autosomal dominant

b. Defect in chromosome 4

c. Males = females

d. Basal ganglia and caudate atrophy

e. Choreoathetoid movements, neurocognitive disorder, psychosis, depression

f. Onset between ages 30 and 40

g. Progressive deterioration

h. Neurocognitive disorder, later with psychosis progressing to infantile state

i. Death in 15–20 years

j. Suicide is common.

Parkinson’s disease

a. Decreased dopamine in substantia nigra

b. Annual prevalence is 200 in 100,000

An estimated 20 to 30 percent of patients with Parkinson's disease have dementia, and an additional 30 to 40 percent have measurable impairment in cognitive abilities.

c. **Symptoms**

i. Bradykinesia ii.Resting tremor iii. Pill-rolling tremor

iv. Masklike facies v. Cogwheel rigidity vi. Shuffling gait

d. 40% to 80% develop neurocognitive disorder

e. Depression is common; treat with antidepressants or electroconvulsive therapy (ECT)

f. Treatment: L-dopa or Selegiline

HIV Dementia

a. Dementia due to cortical atrophy, inflammation, and demyelination resulting from direct infection of the brain with HIV. Supportive measures are the primary management.

b. Must be differentiated, in HIV patients, from delirium caused by cerebral lymphoma or opportunistic brain infection. Such delirium is often reversible with chemotherapeutic or antibiotic agents.

Delirium

1. **Delirium is a syndrome which includes confusion and clouding of consciousness that result from central nervous system impairment.**

2. **It usually occurs in the course of an acute medical illness such as encephalitis or meningitis but is also seen in drug abuse and withdrawal, particularly withdrawal from alcohol ("delirium tremens").**

3. **It is common in surgical and coronary intensive care units and in elderly debilitated patients.**

Hallmark >>>> Impaired consciousness

Occurrence

More common in children and the elderly

Most common etiology of psychiatric symptoms in medical and surgical hospital units

In delirium, the EEG characteristically shows a generalized slowing of activity and may be useful in differentiating delirium from depression or psychosis.

DSM-5 **Diagnostic Criteria for 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, 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

Predisposing Factors for Delirium

Demographic characteristics

Age 65 years and older

Male sex

Cognitive status

Dementia
Cognitive impairment

History of delirium

Depression

Functional status

Functional dependence

Immobility
History of falls
Low level of activity

Sensory impairment

Hearing / Visual

Decreased oral intake

Dehydration / Malnutrition

Predisposing Factors for Delirium

Drugs

Treatment with psychoactive drugs
Treatment with drugs with anticholinergic properties

Alcohol abuse

Coexisting medical conditions

Severe medical diseases
Chronic renal or hepatic disease
Stroke
Neurological disease
Metabolic derangements
Infection with human immunodeficiency virus

Fractures or trauma
Terminal diseases

Precipitating Factors for Delirium

Drugs

Sedative-hypnotics/ Narcotics/Anticholinergic drugs /Treatment with multiple drugs/ Alcohol or drug withdrawal

Primary neurologic diseases

Stroke,/ lntracranial bleeding/ Meningitis or encephalitis

lntercurrent illnesses

Infections/ latrogenic complications / Severe acute illness / Hypoxia/Shock/ Anemia/ Fever or hypothermia / Dehydration
Poor nutritional status/ Low serum albumin levels / Metabolic derangements

Surgery

Orthopedic surgery/ Cardiac surgery/ Prolonged cardiopulmonary bypass / Noncardiac surgery

Environmental

Admission to intensive care unit/ Use of physical restraints/ Use of bladder catheter/Use of multiple procedures

Pain/ Emotional stress/ Prolonged sleep depravation

Delirium

Associated psychological findings

Impaired consciousness Illusions, delusions (often paranoid) or hallucinations (often visual and disorganized)

“Sundowning” (symptoms much worse at night)
Anxiety with psychomotor agitation

Course

Develops quickly Fluctuating course with lucid intervals

Delirium

- In treating delirium, the primary goal is to treat the underlying cause.

- Rooms should be kept well lit to minimize misperceptions; a room with a window can assist with day/ night orientation.

- Patients should be frequently reoriented to their surroundings-for example, clocks and calendars should be provided.

- Staff members should reintroduce themselves each time they visit.
- Two major symptoms of delirium that may require pharmacological treatment are: **psychosis and insomnia.**

✓ A commonly used drug for psychosis is **haloperidol.**

✓ Insomnia is best treated with **benzodiazepines** with short or intermediate half-lives (e.g., lorazepam).

•

Delirium versus Neurocognitive Disorder

History	Delirium	Neurocognitive Disorder
Onset	Rapid	Insidious
Duration	Days to weeks	Months to years
Course	Fluctuating	Chronically progressive
Level of consciousness	Fluctuating	Normal
Orientation	Impaired periodically	Disorientation to time → place → person
Memory	Recent markedly impaired	Recent impaired then remote
Perception	Visual hallucinations	Hallucinations, sundowning
Sleep	Disrupted sleep-wake cycle	Less sleep disruption
Reversibility	Reversible	Most not reversible
Physiologic changes	Prominent	Minimal
Attention span	Very short	Not reduced

A 72-year-old woman is brought to the emergency department from a nursing home for poor oral intake. She is afebrile, has a pulse of 95, and a blood pressure of 90/ 60. Mental status examination (MSE) reveals an awake and alert, but frail, malnourished and dehydrated woman who is oriented to person only. She reports that the president is George Bush. She is easily distracted and cannot recall any of three items after a few minutes. She is irritable and swings at the staff when they try to insert an IV. The team starts IV fluids as blood and urine are sent to the laboratory. A chest x-ray is unremarkable, as is the head CT. One hour later, she is calmer and reports the correct day, time, and place; she is less distractible.

Labs are remarkable for leukocytosis and dirty urinalysis. Aside from cystitis, what is the diagnosis?

Amnestic Disorders

The amnestic disorders are coded in the DSM-5 as "**major or minor neurocognitive disorders due to another medical condition**." All of these disorders cause impairment in memory as the major sign and symptom, although other signs of cognitive decline may coexist.

The syndrome is defined primarily by impairment in the ability to create new memories. Three different etiologies exist: amnestic disorder caused by a general medical condition (e.g., head trauma), substance-induced persisting amnestic disorder (e.g., caused by carbon monoxide poisoning or chronic alcohol consumption), and amnestic disorder not otherwise specified for cases in which the etiology is unclear.

The major neuroanatomical structures involved in memory and in the development of an amnestic disorder are particular diencephalic structures such as the dorsomedial and midline nuclei of the thalamus and midtemporal lobe structures such as the hippocampus, the mamillary bodies, and the amygdala .

Amnestic Disorders

Hallmark >>> Loss of memory with few other cognitive problems

Etiology

Thiamine deficiency due to long-term alcohol abuse, leading to destruction of mediotemporal lobe structures (e.g., mammillary bodies)

Temporal lobe trauma, vascular disease, or infection (e.g., herpes simplex encephalitis)

Occurrence

More common in patients with a history of alcohol abuse

Associated physical findings

No medical illness
Little autonomic dysfunction

Normal EEG

Associated psychological findings

Normal consciousness

Psychotic symptoms uncommon in early stages
Depressed mood
Little diurnal variability

Confabulation (untruths told to hide memory loss)

Amnestic Disorders

Course

Develops slowly
Progressive downhill course if drinking continues

Management and prognosis

No effective treatment, rarely reversible

Pharmacotherapy and supportive therapy to manage associated psychiatric symptoms

Vitamin B1 for acute symptoms

The End