



Introduction to Neurocognitive/Neuropsychiatric Disorders

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Objectives:

- ✓ Delirium.
- ✓ Major Neurocognitive Disorders (MCD):
 - ✓ Dementia.
 - ✓ Amnestic syndrome.
- ✓ Traumatic Brain Injury (TBI).



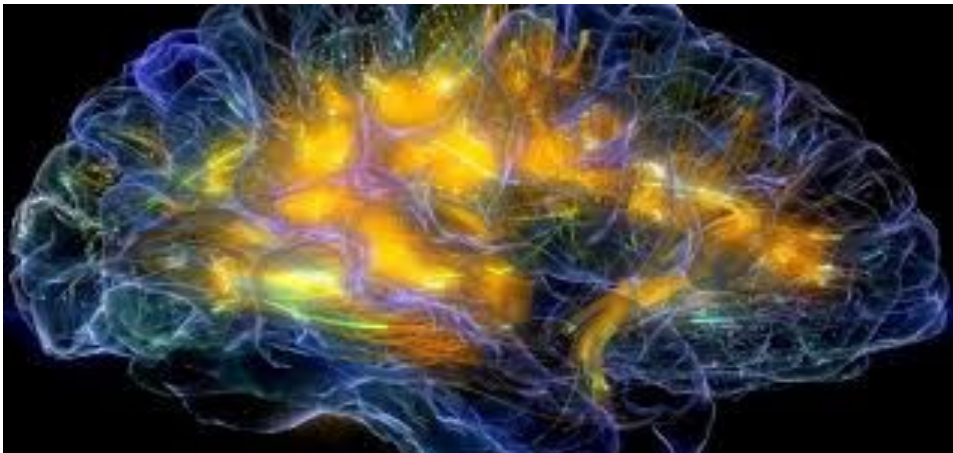
Introduction:

- Cognition Functions Vs Cognitive Disorders.



Cognitive functions Vs Cognitive disorders

✓ **Cognitive functions:** is the **mental action or process** of acquiring knowledge and understanding through **thought**, **experience**, and the **senses**.



✓ It **encompasses** many aspects of **intellectual functions and processes:**

- ✓ Attention.
- ✓ Concentration.
- ✓ Memory.
- ✓ Processing speed.
- ✓ Orientation.
- ✓ Impulse control.
- ✓ Language processing.
- ✓ Executive function.

Perceptual-motor function
Visual perception
Visuoconstructional reasoning
Perceptual-motor coordination

Language
Object naming
Word finding
Fluency
Grammar and syntax
Receptive language

Neurocognitive domains

Learning and memory
Free recall
Cued recall
Recognition memory
Semantic and autobiographical long-term memory
Implicit learning

Executive function
Planning
Decision-making
Working memory
Responding to feedback
Inhibition
Flexibility

Complex attention
Sustained attention
Divided attention
Selective attention
Processing speed

Social cognition
Recognition of emotions
Theory of mind
Insight

Cognitive functions Vs Cognitive disorders



Cognitive functions Vs Cognitive disorders

- ✓ Cognitive/Neurocognitive disorders characterized by:
 - ✓ **Cognitive deficits:**
 - ✓ That present in many mental/neurological disorders.
 - ✓ Were not present from birth or very early in life.
 - ✓ Represent a decline from a previously attained level of functioning.
 - ✓ **Different than cognitive function/Processes:**
 - ✓ (our ways of thinking and conclusion formations).
 - ✓ **Cognitive Therapy:**
 - ✓ Type of psychotherapy that concerned with detection of:
 - ✓ Wrong thoughts and thinking process.
 - ✓ It is not treatment for cognitive disorders.



Cognitive functions vs Cognitive disorders

✓ *In the Diagnostic and Statistical Manual of Mental Disorders, fifth edition DSM-5:*

✓ **Neurocognitive disorders:**

✓ *Delirium.*

✓ *Mild Neurocognitive Disorders.*

✓ *Major Neurocognitive Disorder*

✓ **Dementias**

✓ **Amnestic syndromes**



Cognitive functions vs Cognitive disorders

✓ ***Delirium:***

- ✓ Short-term confusion and changes in cognition
- ✓ Acute global cognitive disorder WITH disturbed consciousness.

✓ **Major Neurocognitive Disorder:**

✓ **Dementias:**

- ✓ Severe impairments in memory, judgment, orientation, and cognition.
- ✓ Chronic global cognitive decline WITHOUT disturbed consciousness.

✓ **Amnestic syndrome:**

- ✓ Major neurocognitive disorder caused by other medical condition.
- ✓ Marked primarily by memory impairment or specific disorder of short-term memory caused by:
 - ✓ Medical condition.
 - ✓ Toxins or medications.
 - ✓ Unknown causes.

Delirium



Case number 1



- A 75-year-old male known to have a long-standing history of HTN, DM type 2, hypercholesterolemia, and BPH.
- He was brought to the ER by his family with three days history of high-grade fever, lethargy, and dysuria.
- He also started to have poor sleep for the last three days and therefore, his daughter gave him unknown medication that she bought from the pharmacy.
- On the same day of ER presentation, he started to have a high-grade fever, and he started to be *confused.*
- His daughter stated that he was *talking nonsense* and it seems that he saw *unobserved images on different occasions.* There was *a history of fluctuating consciousness,* and he was *disoriented to place, person, and time.*

- There were periods where her father was less confused and less disoriented. and it seems that he went back to his usual self. And there were periods of complete confusion and disorientation.
- Past medical history: HTN, DH, Hypercholesterolemia, and BPH.
- Personal/social history: smoke tobacco.
- Patient was admitted to the hospital and diagnosed to have *UTI and mild urinary retention*.
- Few hours later, after hospital admission:
 - He started to be aggressive and agitated.
 - He pulled out his IV lines.
 - Insisted to be discharged from hospital because he thought that nursing staff want to kill him.

Hallucination • Agitated • Distracted
Disoriented • Rambling • Withdrawn
Restless **Delirium** sense of place
bewildered • Confused • Incoherent
Hallucination • Agitated • Distracted
Disoriented • Rambling • Withdrawn
Loss of sense of time

Delirium (الهذيان):

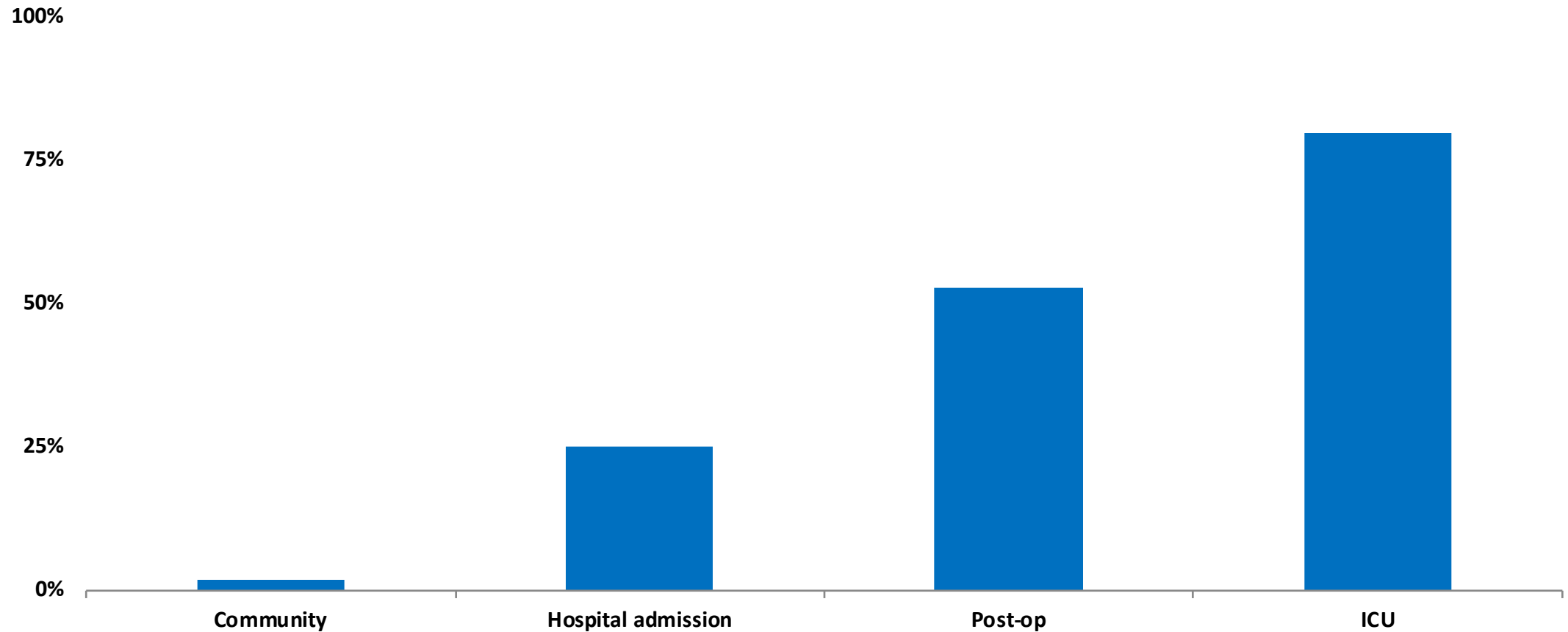
- ✓ Acute transient reversible global cognitive impairment with impaired consciousness due to a medical problem.
- ✓ *Many terms are used to describe delirium:*
 - ✓ Acute confusional state
 - ✓ Acute organic syndrome
 - ✓ Acute brain failure.
 - ✓ Acute brain syndrome.
 - ✓ Acute cerebral insufficiency.
 - ✓ Exogenous psychosis.
 - ✓ Metabolic encephalopathy.
 - ✓ ICU psychosis
 - ✓ Toxic encephalopathy.



Epidemiology:

- ✓ It may occur at **any age** but more in elderly and children.
- ✓ Community Prevalence: **General: 1-2 %** > 85yr: ~ 14 %.
- ✓ 10-30 % Medically Ill Hospitalized patients.
 - ✓ ~ 10 to > 50 % Post-Operative Patients.
 - ✓ > 90 % Post-cardiotomy Patients.
 - ✓ ~ 70-85 % ICU.
- ✓ **60 %** in nursing homes or post-acute care settings.
 - ✓ ~ 80 % at end of life.
- ✓ **Underdiagnosed when patient is hypoactive and somnolent.**
 - ✓ Such cases may be misdiagnosed as depression.

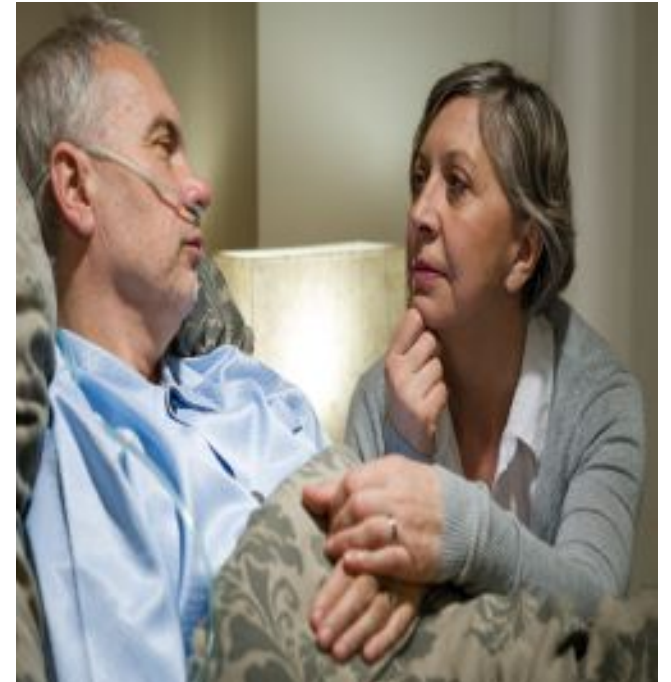
Delirium complicates at least 25% of all hospitalizations in the elderly



Delirium:

✓ Clinical features:

- ✓ **Acute onset** of mental status change with **fluctuating** course.
- ✓ **Attention** deficits.
- ✓ **Confusion** or **disorganized** thinking.
- ✓ **Perceptual** disturbances.
- ✓ Disturbed sleep/wake cycle. (**Sundowning phenomena**)
- ✓ **Altered** psychomotor activity.
- ✓ **Disorientation** and **memory impairment**.
- ✓ **Behavioral** and **emotional** abnormalities.
- ✓ Other cognitive deficits.



(DSM-5) diagnostic criteria for delirium is as follows:

A) Disturbance in:

- ✓ Attention (Reduced ability to direct, focus, sustain, and shift attention)
- ✓ Awareness (Reduce orientation to the environment).

B) The disturbance:

- ✓ Develops over a short period (usually hours to days)
- ✓ Represent a change in the baseline attention and awareness.
- ✓ Tends to fluctuate in severity during the course of a day.

C) An additional disturbance in cognition:

- ✓ Memory deficit, disorientation, language, perceptual disturbance.

(DSM-5) diagnostic criteria for delirium is as follows:

D) Disturbance in criteria A and C:

- ✓ Not due to another preexisting, established, or evolving dementia.
- ✓ Do not occur in the context of a severely reduced level of arousal (e.g. coma)

E) There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by a direct physiologic consequence of:

- ✓ General medical condition
- ✓ An intoxicating substance
- ✓ Medication use
- ✓ More than one cause

Diagnostic criteria (Simplified) (Reference)



- A) **Consciousness is disturbed** (e.g. awareness of the environment is impaired but patient not in coma).
- B) Cognitive functions are **impaired +/- perceptual disturbance** (illusions or hallucinations)
- C) **Acute onset with fluctuating symptoms** (within hours during the day) & **transient course** (few days).
- D) Caused by a **physical problem** (e.g. hypoxia, hypoglycemia, infection..etc.)

Type of delirium (DSM-5 specifiers):

1) Hyperactive 30% (most clear and least controversial)

- ✓ Hyperactive psychomotor activity.
- ✓ May have mood lability, agitation, refusal to cooperate with medical care.

2) Hypoactive 24% (most difficult type to identify)

- ✓ Hypoactive psychomotor activity.
- ✓ May be have sluggishness or lethargy that approaches stupor.
- ✓ Inappropriately diagnosed and treated as depression.

3) Mixed level of activity 46% (Classic wax and waning pattern)

- ✓ Normal psychomotor activity with disturbed attention and awareness.
- ✓ May have rapidly fluctuating activity level.

Why it is important to discover delirium?

✓ It is a very *serious medical and psychiatric condition* and that due to high risk of:

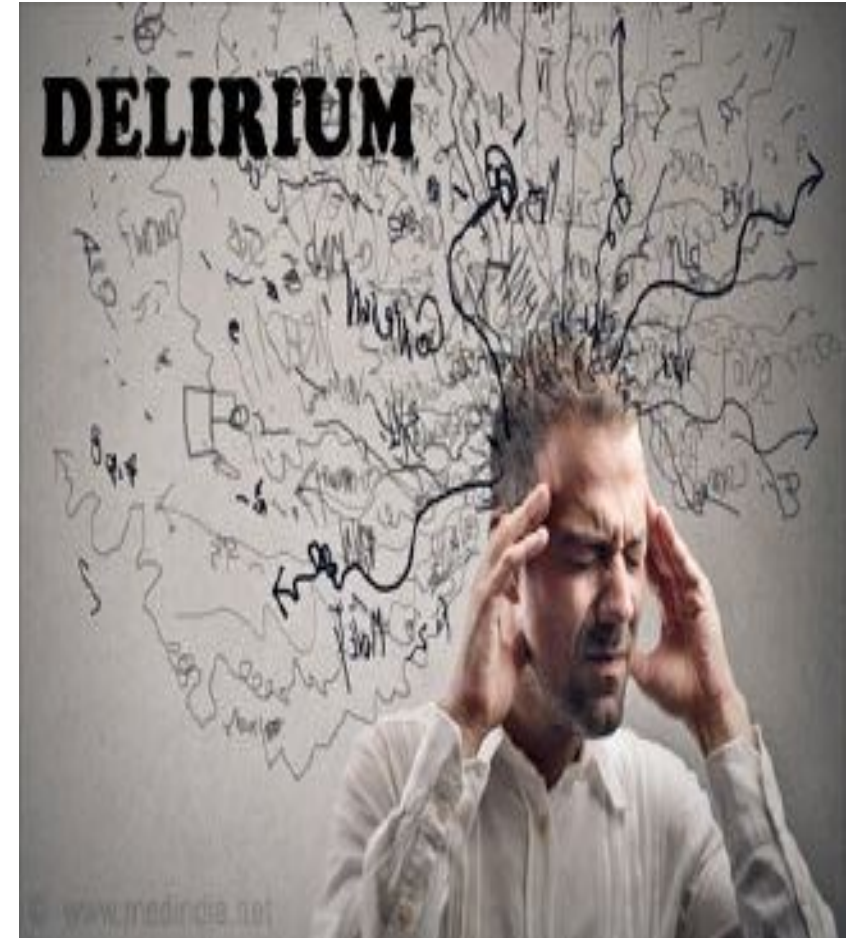
- 1) Death (*due to associated serious medical condition*)
- 2) Violence toward medical staff.
- 3) Self-harm or suicidal risk.
- 4) Impaired judgment.
- 5) Psychosis



Why it is important to discover delirium?

- ✓ Delirium is associated with:
 - ✓ ↑ **morbidity** and **mortality**.
 - ✓ ↑ **length** of hospital stay.
 - ✓ ↑ **Rates of admission** to long term care facilities
 - ✓ **20% of patients discharged** post hip # still had **evidence of delirium**.

(Journal of American Geriatric Society 2001
May;49(5):678-9).



Why dose a delirious patient become suicidal or aggressive?

- ✓ Due to **severe disturbance** in the patient's perception, mood, judgment, thinking, and behavior.
- ✓ Patient may act on **hallucinations, illusions or delusional thoughts** as *if they were genuine dangers* (e.g., blood extraction by a nurse might be perceived as an attack).



Delirium Risk factors/Predisposing Factors:

- ✓ > 60 years of age
- ✓ Male sex
- ✓ Visual/hearing impairment
- ✓ Underlying brain pathology such as stroke, tumor, vasculitis, trauma, or dementia
- ✓ Major medical illness.
- ✓ Recent major surgery.
- ✓ Depression
- ✓ Functional dependence
- ✓ Dehydration
- ✓ Substance abuse/dependence
- ✓ Hip fx
- ✓ Metabolic abnormalities
- ✓ Polypharmacy

Delirium Risk factors/Predisposing Factors: (Reference)

Demographics General Medical Hx	Psychiatric Hx	Current Medical Problem	Medications	Current Status
<ul style="list-style-type: none"> ✓ Male ✓ Age >75 ✓ Functional Impairment ✓ Immobility ✓ Low levels of activity ✓ Sensory Impairment ✓ Fall Hx 	<ul style="list-style-type: none"> ✓ Hx of Delirium ✓ Dementia ✓ Depression ✓ Bipolar ✓ Schizophrenia ✓ Drug/ETOH/Toxins 	<ul style="list-style-type: none"> ✓ Severe Illness ✓ Multiple Illnesses ✓ Abn. Blood Work ✓ Metabolic D/O ✓ CNS pathology ✓ Trauma ✓ Burns ✓ Post-Op ✓ Poor O2 States 	<ul style="list-style-type: none"> ✓ > 3 drugs ✓ Psychoactive Meds ✓ Anticholinergic ✓ Meds 5HT Meds ✓ Examples: ✓ Opioids* ✓ Corticosteroids* ✓ Benzodiazepines* ✓ NSAIDS ✓ Chemo Meds 	<ul style="list-style-type: none"> ✓ Dehydration ✓ Malnutrition ✓ Sleep Deprivation ✓ Over Sedation ✓ Pain ✓ Abnormal VS ✓ Catheters IV ✓ Restraints

Etiology (Delirium Precipitating Factors):

I watch death

- *I*: Infections.
- *W*: Withdrawal.
- *A*: Acute metabolic.
- *T*: Trauma.
- *C*: CNS pathology.
- *H*: Hypoxia.
- *D*: Deficiencies.
- *E*: Endocrinopathies.
- *A*: Acute vascular.
- *T*: Toxins.
- *H*: Heavy metal.



Etiology (Delirium Precipitating Factors): (Reference)

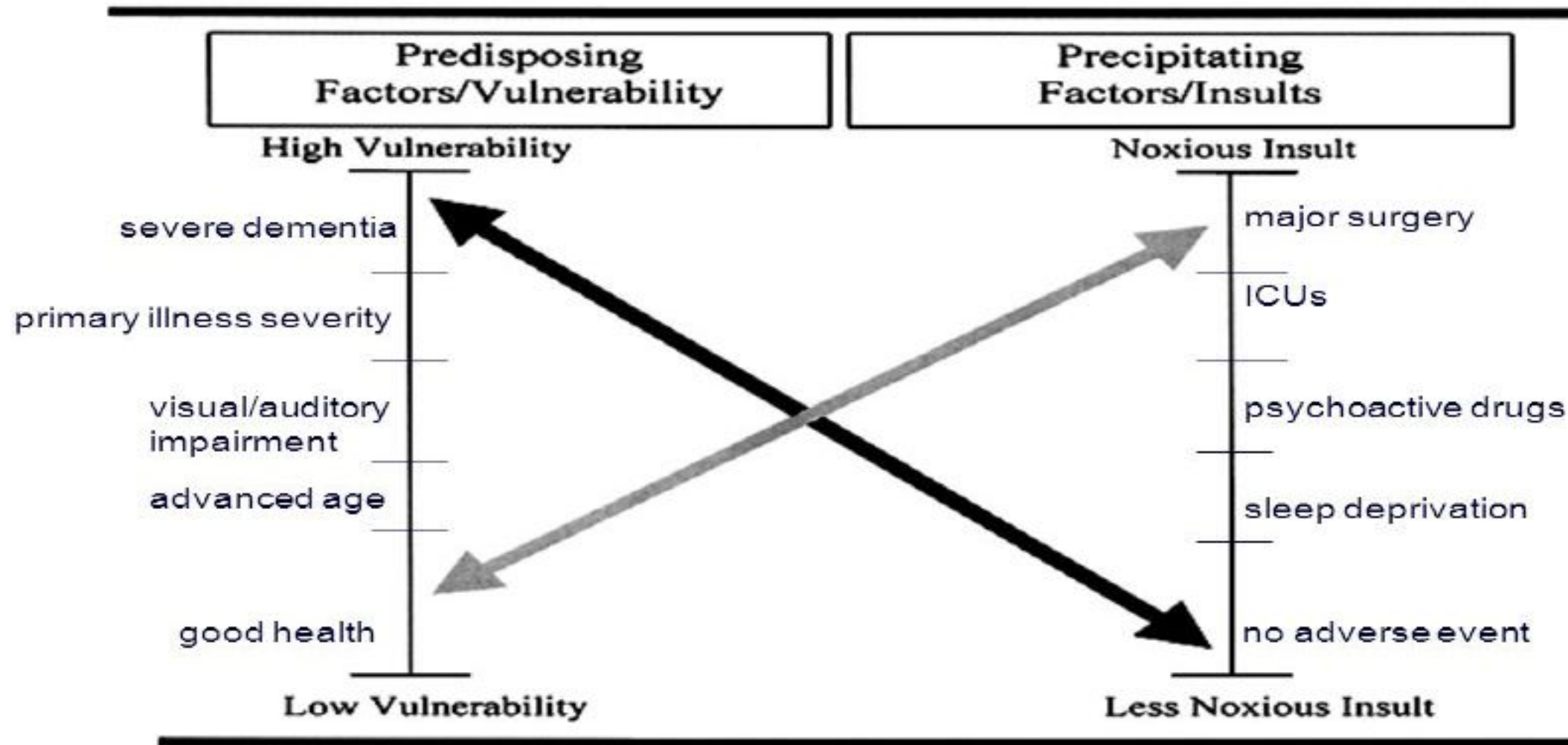
- ✓ Infections (encephalitis, meningitis, HIV, syphilis, sepsis, typhus, malaria)
- ✓ Withdrawal from substance of the abuse (alcohol, sedative-hypnotic, barbiturates)
- ✓ Acute metabolic (acidosis, alkalosis, liver/kidney failure)
- ✓ Trauma (closed head trauma, heatstroke, recent surgery, severe burns)
- ✓ CNS pathology (abscess, tumor, seizures, hydrocephalus)
- ✓ Hypoxia (anemia, hypoperfusion due to heart/lung failure, CO poisoning)
- ✓ Deficiencies of vitamins (B12, folate, thiamine, niacin)
- ✓ Endocrinopathies (Hyper/Hypoglycemia, Hypo/Hyperadrenocorticism, Hyperparathyroidism)
- ✓ Acute vascular (hypertension, stroke, TIA, arrhythmia)
- ✓ Toxins (medications, illicit drugs, pesticides, solvents)
- ✓ Heavy metal (lead, manganese, mercury)

Life threatening causes of delirium:

- 1) *Wernicke's encephalopathy.*
- 2) *Alcohol/Benzodiazepine withdrawal*
- 3) *Hypoxia.*
- 4) *Hypoglycemia.*
- 5) *Hypertensive encephalopathy.*
- 6) *Intra-cerebral hemorrhage.*
- 7) *Meningitis/encephalitis.*
- 8) *Poisoning*



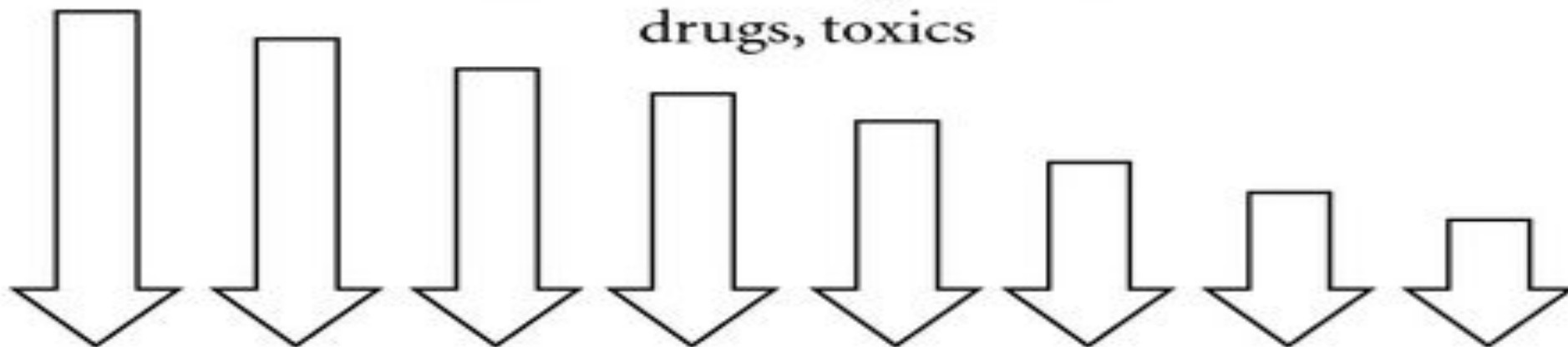
MULTIFACTORIAL MODEL OF DELIRIUM IN OLDER PERSONS



Precipitating factors

Acute medical or surgical conditions
drugs, toxics

Insult intensity



Protective factors

Age Cognitive impairment Frailty

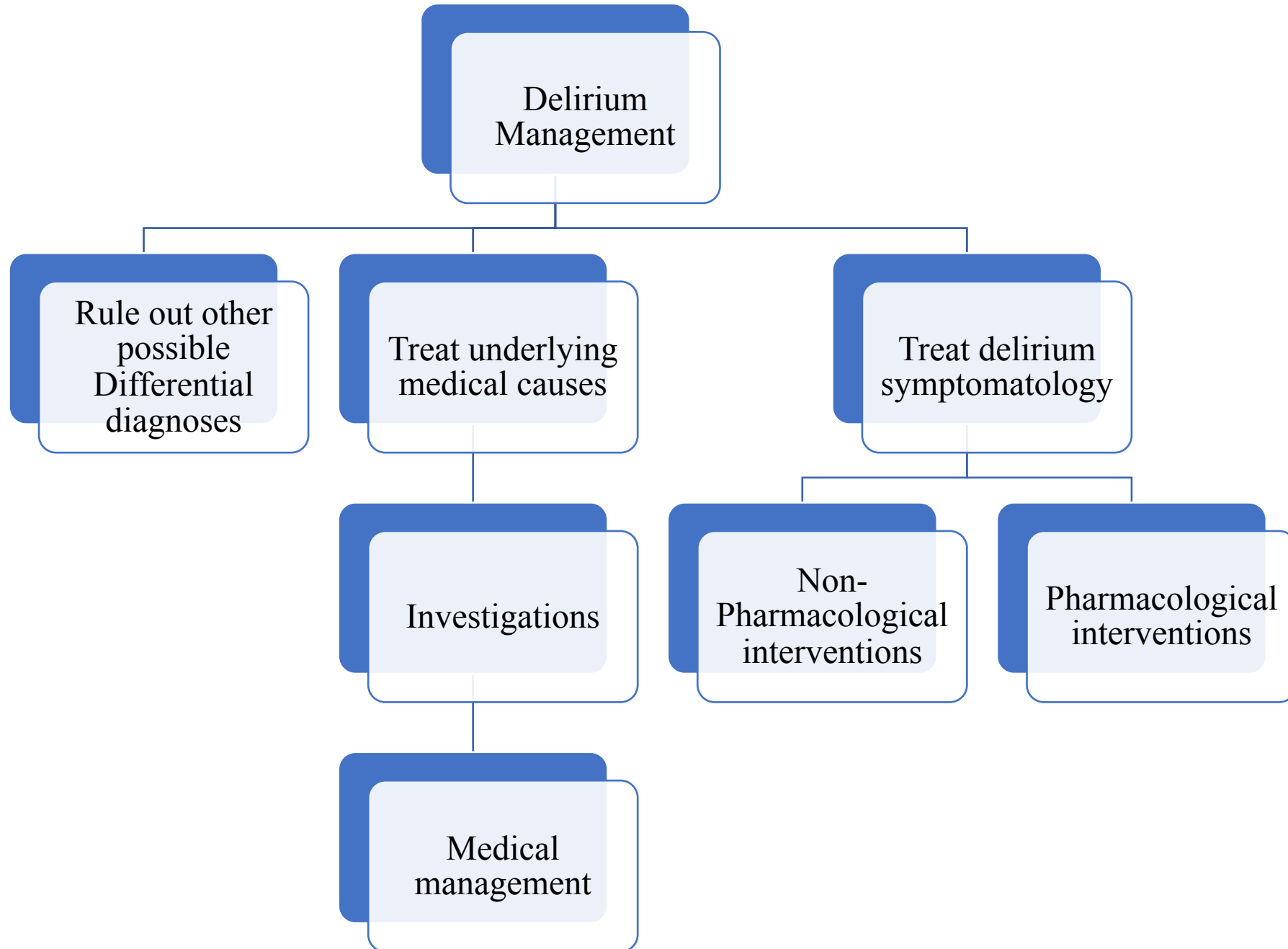
Predisposing factors



Delirium

Delirium Management/Interventions:

Ensure patient / staff safety and then
treatment of the underlying medical
causes



Delirium differential diagnoses

1) Dementia:

- ✓ In many Occasions, **delirium occurs in a patient with dementia**, a condition known as beclouded dementia. However, a dual diagnosis (i.e., delirium in top of dementia) can only be made when there is a definite history of pre-existing dementia.

2) Substance abuse:

- ✓ Alcohol, inhalants, sedatives, and opioids

3) Amnestic syndrome (see later)



Delirium differential diagnoses

4) Acute functional psychosis (brief psychosis, mania, exacerbation of schizophrenia)

- ✓ Patients usually experience no change in their level of consciousness or their orientation. The hallucination and delusions are more constant and better organized than those of patients with delirium.

5) Severe depression:

- ✓ Patients with hypoactive symptoms of delirium may appear somewhat similar to severely depressed patients, but can be distinguished on the basis of EEG (normal in depression).

QuickBooks



Differential Diagnosis
Revisited

Delirium differential diagnoses

Proper assessment of mental functions

➤ Mini-Mental state exam (MMSE)


- Tests orientation, short-term memory, attention, concentration, constructional ability.
- 30 points is perfect score.
- < 20 points suggestive of problem
- Not helpful without knowing patient's baseline

➤ MoCA (Montreal Cognitive Assessment)

Mini-Mental State Examination (MMSE)

Patient's Name: _____ Date: _____

Instructions: Ask the questions in the order listed.
Score one point for each correct response within each question or activity.

Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day of the week? Month?"
5		"Where are we now: State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible. Number of trials: _____
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, ...) Stop after five answers. Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.) 
30		TOTAL

Treat underlying medical causes

➤ Investigation

➤ There is no specific diagnostic investigation for delirium.

✓ A) Good clinical skills are essential:

✓ 1) Careful History and physical examinations:

- ✓ Acute onset + review medical conditions/diseases + cognitive & consciousness disturbances.

✓ 2) Collateral history:

- ✓ Baseline cognition
- ✓ Presence of sensory impairments
- ✓ Exposure to risk factors
- ✓ **Review medications**, procedures, tests,...etc.



Treat underlying medical causes

➤ *First line investigations:*

- ✓ Complete blood count (CBC) and differentials WBCs
- ✓ Electrolytes, Mg, ca, and po4 tests.
- ✓ Liver function tests.
- ✓ Renal function tests
- ✓ Urinalysis + cultures & sensitivity
- ✓ Blood cultures & sensitivity
- ✓ Thyroid function test
- ✓ Electrocardiogram (ECG)
- ✓ Blood glucose
- ✓ Chest x-rays

➤ *Second line investigations:*

- ✓ Drug screen.
- ✓ Cardiac enzymes
- ✓ Blood gas (ABG)
- ✓ Serum folate / B12
- ✓ Electroencephalography (EEG)
- ✓ Cerebrospinal fluid examinations.
- ✓ Brain CT scan
- ✓ Brain MRI

Treatment of delirium symptomatology

1) Non-Pharmacological interventions

- ✓ Symptomatic measures involving attention to fluid and electrolyte balance, nutritional status, and early treatment of infections.
- ✓ Environmental interventions:
 - ✓ Reduce unfamiliarity by providing a calendar, a clock, family pictures, and personal objects.
 - ✓ Maintain a moderate sensory balance in the patient by avoiding sensory overstimulation or deprivation.
 - ✓ Minimize staff changes, limit noise and the number of visits, a nightlight, and where necessary, eyeglasses and hearing aids.
 - ✓ Proper communication and support are critical with these patients

Treatment of delirium symptomatology

2) Pharmacological interventions:

- ✓ All the patient's medications should be reviewed, and any unnecessary drugs should be discontinued. (especially anticholinergic)
- ✓ These patients should receive the lowest possible dose and should not get drugs such as phenobarbital or benzodiazepine.
 - ✓ Their effects may increase disorientation, drowsiness, ataxia, and possible falls, head trauma and fractures
- ✓ For agitation or aggressive behaviour: Haloperidol 5 mg oral/IV/IM or olanzapine 5 mg oral/IM.
 - ✓ Intramuscular administration may be preferable for some patients with delirium who are poorly compliant with oral medications or who are too sedated

Delirium course and Prognosis:

- ✓ The course usually **short** (7-10 days)
- ✓ Symptoms of **delirium usually persist** as long as the **causally relevant factors are present**.
- ✓ The **longer** the patient **has been delirious** and the **older the patient**, The **longer the delirium takes to resolve**.
- ✓ Delirium may **spontaneously resolved** or **progress rapidly** into death because of the serious nature of the associated medical conditions.
- ✓ *When underlying cause treated, it usually resolves rapidly.*
 - ✓ *Some residual deficit may persist.*
- ✓ Some patients may **develop depression symptoms** or **Post Traumatic Stress Disorder (PTSD)**

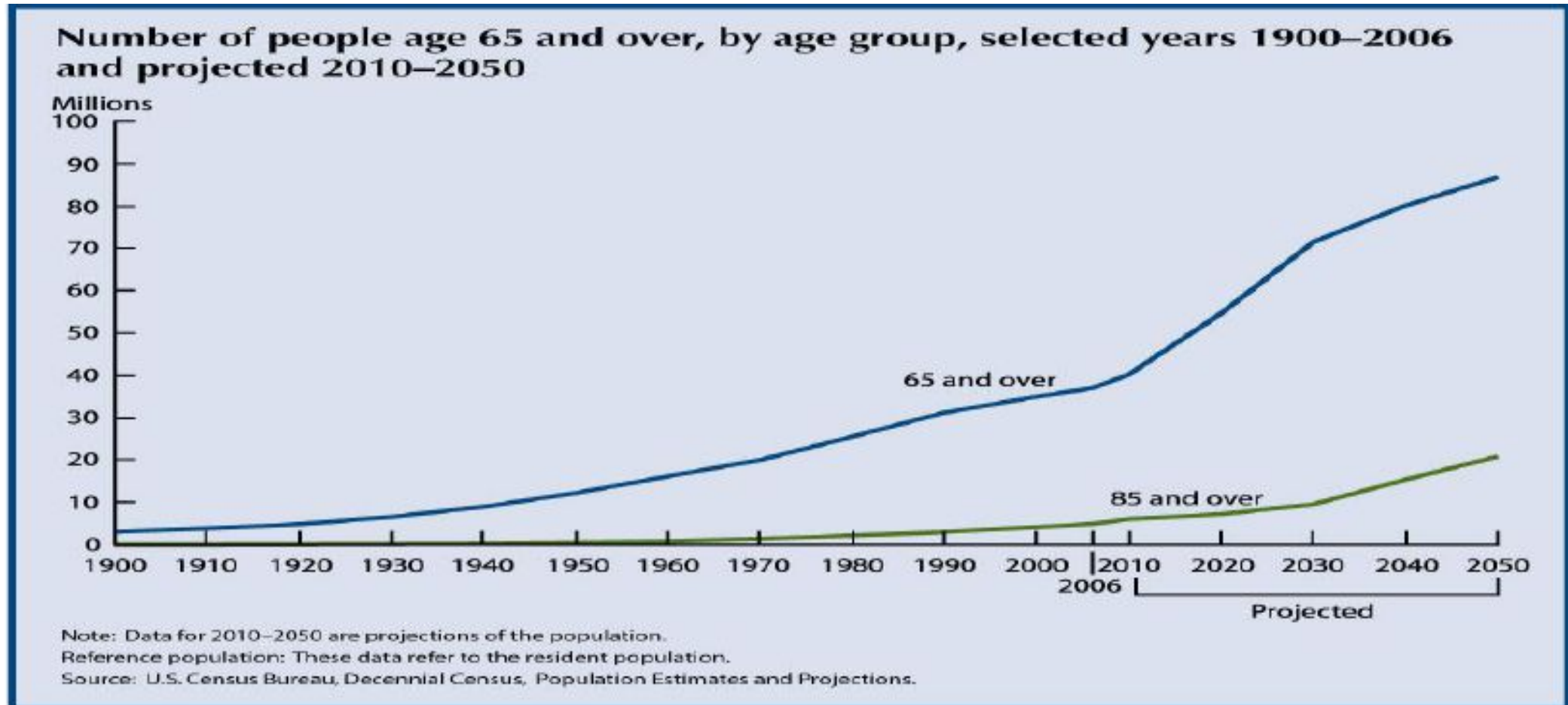
Major Neurocognitive Disorders



Introduction:

- ✓ Aging is a normal part of development.
- ✓ **Unlike childhood development**, there are **NO** specific motor, speech or cognitive milestone for adults **to meet** as they enter old age.
- ✓ Instead, aging is often accompanied by **accumulating losses** in functioning that **gradually increase the risk of mortality**.
- ✓ Many of these changes (**including some degree of memory loss**) **are considered to be completely within the realm of normalcy**.
- ✓ However, there are also a variety of conditions associated with old age that **cause distress** and **dysfunction** not only for the **patient** themselves but also for **their family and caregivers**.

People > 65 make up one of the fastest growing segment of population



A dramatic photograph of a massive tsunami wave crashing over a beach. The water is a deep, dark blue-green, and the crest of the wave is curling over, creating a thick wall of white foam. The sky is filled with heavy, grey clouds, suggesting a storm or a very large-scale event. The overall mood is one of immense power and potential destruction.

The Silver Tsunami

**By 2030 there will be
72.1 million older Americans**

Case number 2



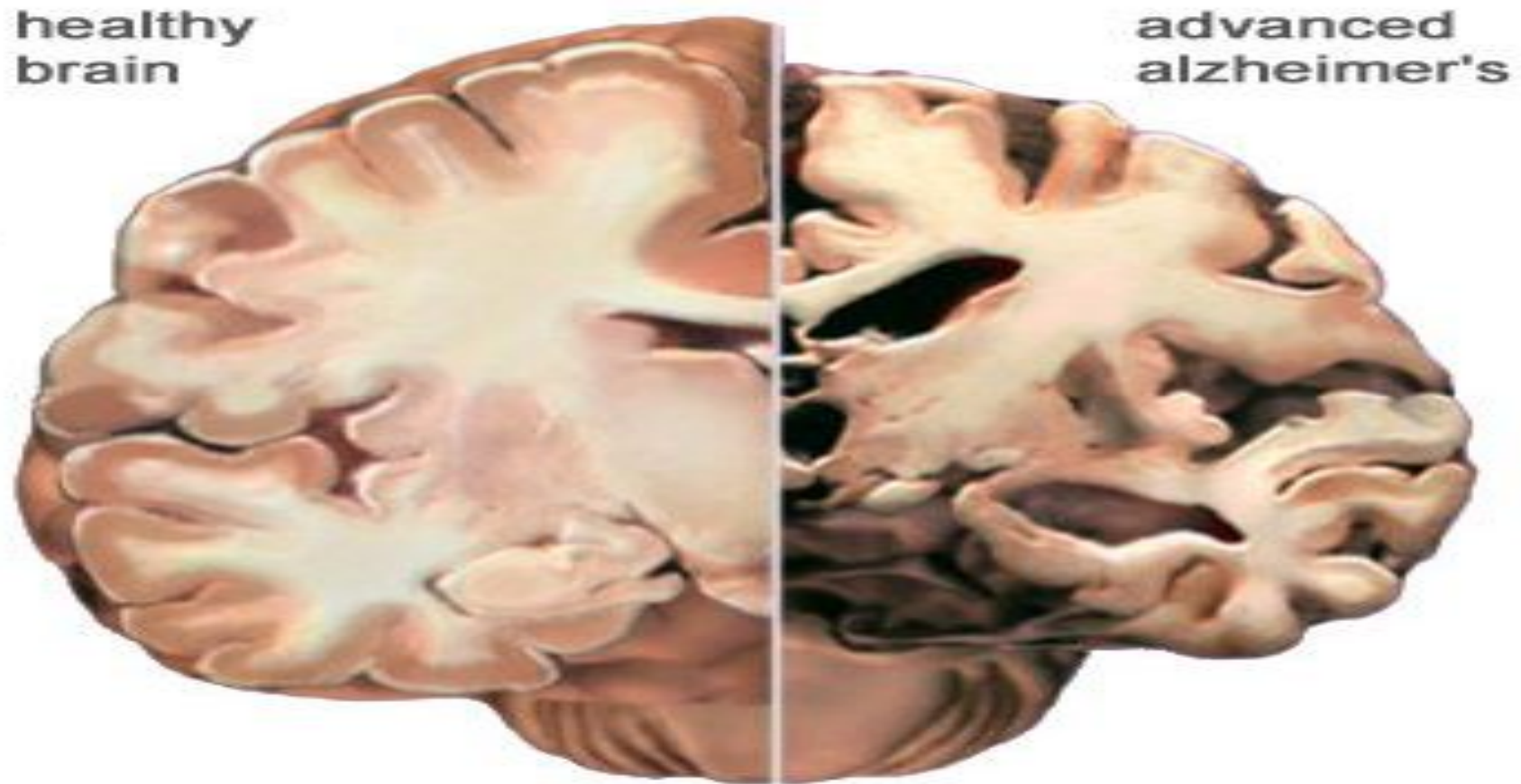
- 73 year-old-lady, she was diagnosed for many years to have DM, HTN, Hypercholesterolemia, and Osteoporosis.
- Her family noticed in the last year that she start to be more isolated and not socially engaged.
- She started to be more forgetful and repeating the same questions over and over. More recently, she started to misplace things like her keys and her items. Also, there were a few occasions where she left the refrigerator open.



- More recently, the patient's family discovered that the patient is *either not taking her oral medications or taking her medications wrongly*. In addition, she started to be more *irritable and sometimes aggressive* towards her family. She has *poor insight into her current situation*.
- Throughout the patient's history, there is *no history of loss of consciousness*. And there is *no motor abnormality*. There is no history of abnormal perception or unusual thinking; however, more recently, patient started to be more suspicious.



Dementia



Perceptual-motor function
Visual perception
Visuoconstructional reasoning
Perceptual-motor coordination

Language
Object naming
Word finding
Fluency
Grammar and syntax
Receptive language

Neurocognitive domains

Learning and memory
Free recall
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Complex attention
Sustained attention
Divided attention
Selective attention
Processing speed

Social cognition
Recognition of emotions
Theory of mind
Insight

Dementia

- ✓ Dementia refers to a disease process marked by:
 - ✓ Progressive cognitive impairment in clear consciousness.
 - ✓ Does NOT refer to low intellectual functioning or mental retardation because these are developmental conditions.
 - ✓ Cognitive deficits represent a decline from a previous level of functioning.
 - ✓ Involves multiple neurocognitive domains.
 - ✓ Cognitive deficits cause significant impairment in social or occupational functioning or both.

The Dementia Syndrome (Reference)

A) **Global deterioration** of intellectual function (learning & memory, complex attention, language, executive function, perceptual-motor abilities, social cognition).

B) **Clear** consciousness (rule out delirium).

C) Impairment in **performance** of personal activities of *daily living and social or occupational activities* due to the decline in intellectual function.

D) Noncognitive psychopathological symptoms and/or deterioration in emotional control, motivation, or personality frequently present but not necessary for diagnosis.

E) Duration of at least 6 months.

Epidemiology:

- ✓ No gender difference.
- ✓ Increasing age is the most important risk factor (It is primarily a disorder of the elderly).
- ✓ The prevalence of moderate to severe dementia:
 - ✓ In the general population is 5 % > 65 years.
 - ✓ 20-40 % in > 85 years.
 - ✓ 15-20 % In outpatient general medical practice.
 - ✓ 50 % in chronic care facilities.
- ✓ Affective symptoms, including depression and anxiety are seen in 40 to 50 % of demented patients.
- ✓ Delusion and hallucination occur in 30 %

Dementia Presentation:

- ✓ In early stage cognitive impairment may not be apparent:
 - ✓ Gradual loss of social and intellectual skills (first noticed in work setting where high performance is required)
 - ✓ Mild memory impairment.
 - ✓ Subtle changes in personality.
 - ✓ Changes in affect (irritability, anger,...)
 - ✓ Multiple somatic complaints and vague psychiatric symptoms.



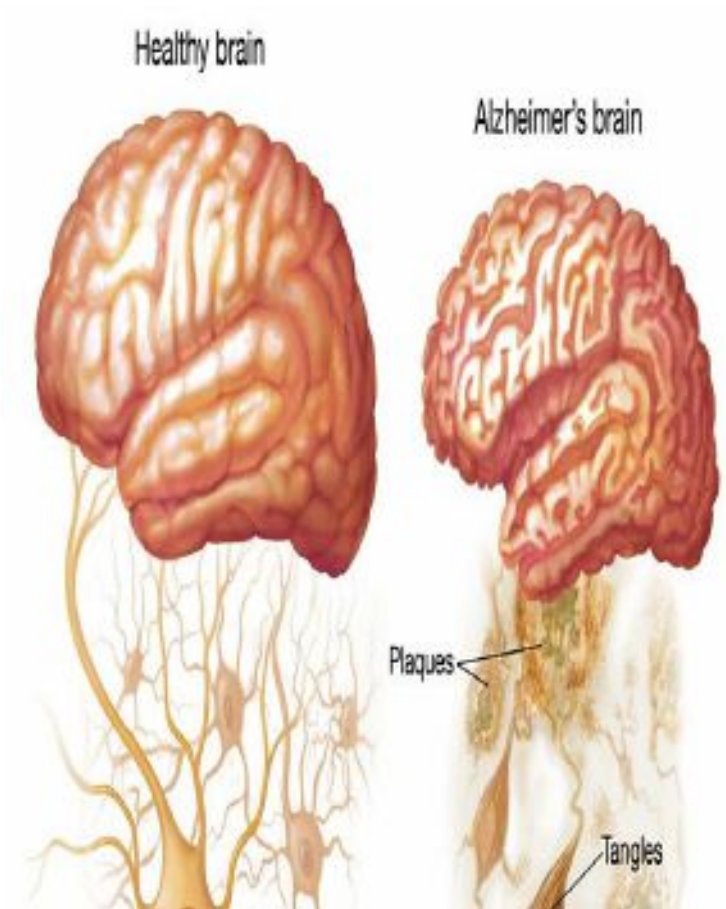
Dementia Presentation:

- ✓ In the late stages cognitive disturbances emerge:
 - ✓ Increasing memory impairment (esp. recent memory)
 - ✓ Attention impairment.
 - ✓ Disorientation (particularly to time, and when severe to place and person).
 - ✓ Language: vague and imprecise speech with inappropriate repetition of the same thoughts (Perseveration).
 - ✓ Impaired judgment.
 - ✓ Potential aggression (verbal & physical).
 - ✓ Psychotic features (hallucination & delusions).
 - ✓ Emotional lability.
 - ✓ Catastrophic reaction (marked by agitation secondary to subjective awareness of intellectual deficits under stressful circumstances).

Causes of dementia:

1) Alzheimer's disease (AD) (50-60 %)

- ✓ Gradual onset and a continuous slow but steady decline in prior intellectual and functional capacities, especially memory.
- ✓ Age of onset:
 - ✓ Before age 65 (5%)
 - ✓ After age 65 (95%)
- ✓ Live an average of 10 years following diagnosis.
- ✓ Risk factors:
 - ✓ *Old age, female, low education, first-degree relative with AD, cigarette smoking, depression, mild cognitive impairment, and social isolation.*



**SYMPTOMS BECOME MORE PRONOUNCED
IN THE MODERATE STAGE, CREATING A
GREATER NEED FOR CAREGIVER SUPERVISION^{3,4}**

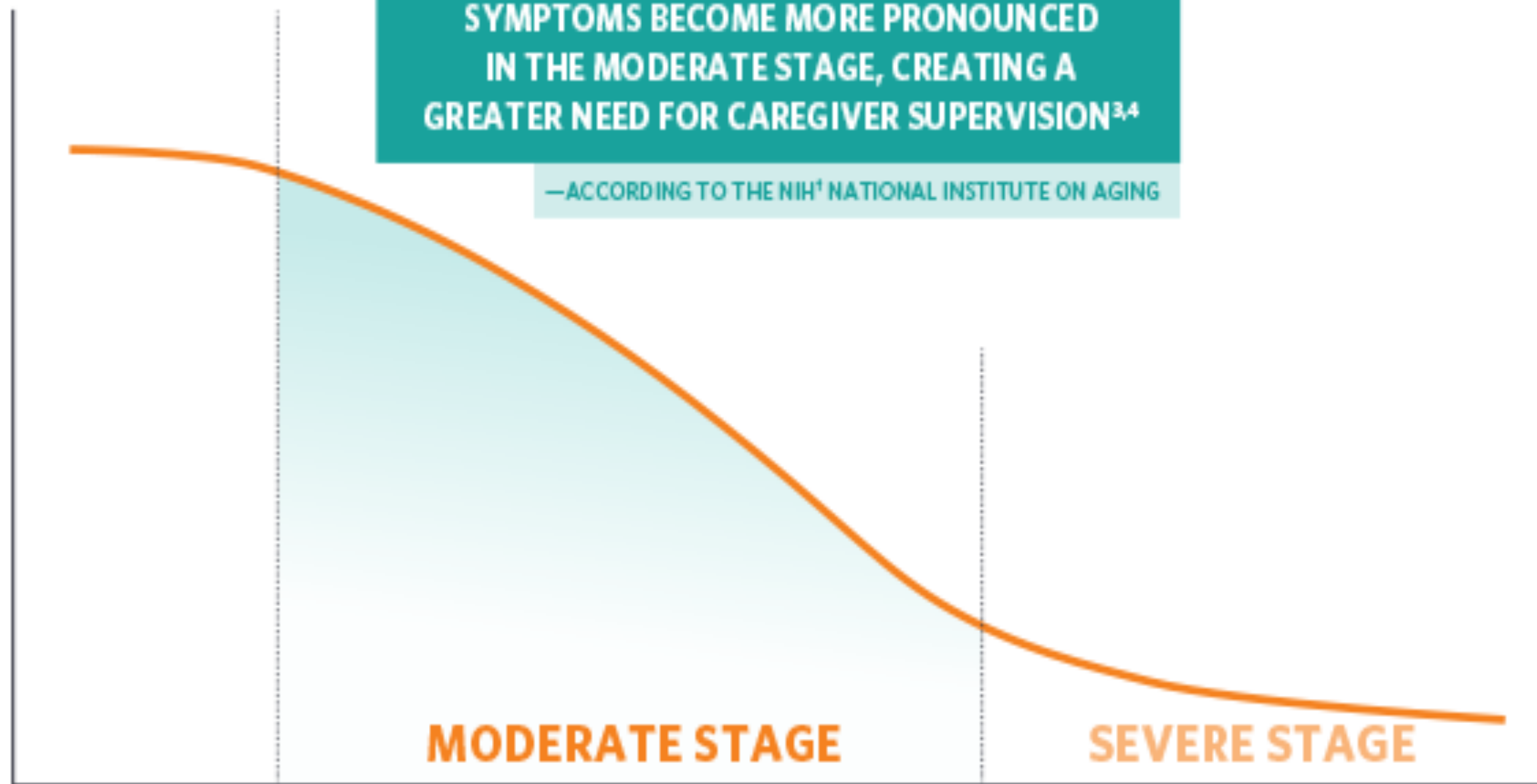
—ACCORDING TO THE NIH¹ NATIONAL INSTITUTE ON AGING

MODERATE STAGE

SEVERE STAGE

STAGES OF ALZHEIMER'S DISEASE (AD)

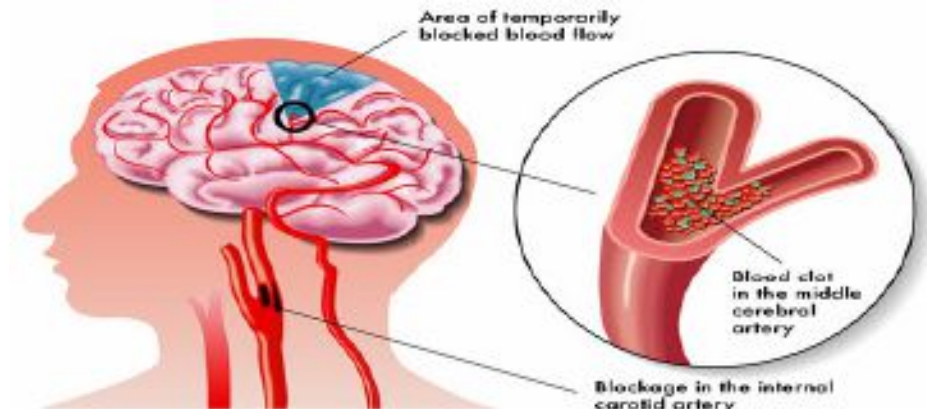
COGNITIVE AND
FUNCTIONAL DECLINE



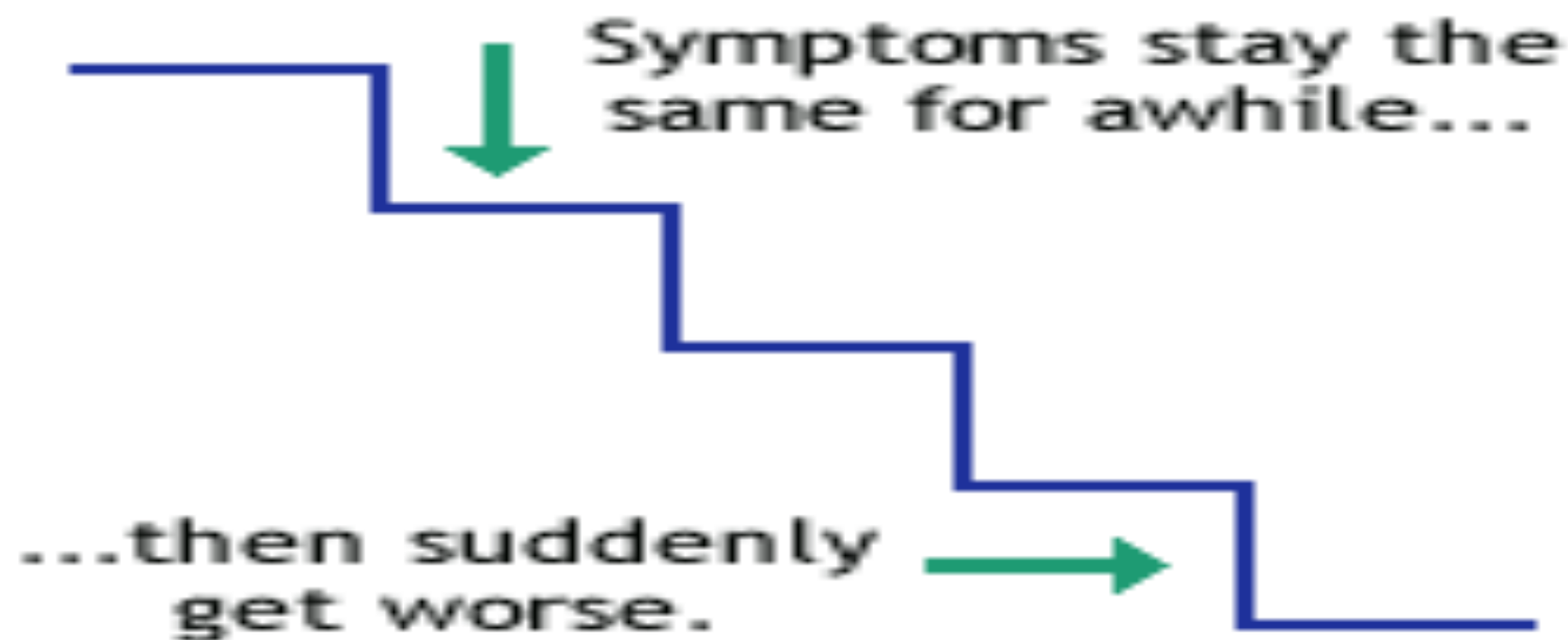
Causes of dementia:

2) Vascular (multi-Infarct) dementia (10-20 % of dementias):

- ✓ Declining Stepwise deterioration of intellectual functioning due to multiple infarcts of varying sizes or arteriosclerosis in the main intracranial vessels.
- ✓ Risk factors for vascular dementia:
 - ✓ Age > 60
 - ✓ Male
 - ✓ Previous stroke
 - ✓ Stroke risk factors: (HTN, heart disease/atrial fibrillation, DM, Smoking, obesity, and hypercholesterolemia)



Typical Progression of Multi-Infarct Dementia



Causes of dementia:

3) Medical conditions (reversible conditions; 15 % of dementias):

- ✓ A variety of non-psychiatric, non-neurologic conditions can cause cognitive symptoms which can strongly resemble dementia.
- ✓ Referred as reversible dementias, as treating the underlying condition can effectively restore cognitive function back to its previous state.
- ✓ Common causes of reversible dementia:
 - ✓ Drugs (Benzodiazepines, anticonvulsants, anticholinergics...) , alcohol/substance abuse.
 - ✓ Sensory impairments (Vision, hearing loss)
 - ✓ Metabolic abnormalities (Poorly treated DM)
 - ✓ Endocrinological problems (Hypothyroidism)
 - ✓ Nutritional deficiency (Vitamin B12 deficiency)
 - ✓ Infections (HIV, neurosyphilis)

Causes of dementia:

4) **Lewy Body dementia:** characterized by fluctuating in cognition, vivid visual hallucinations, parkinsonian features (tremor, rigidity, gait problems/falls)

5) **Frontotemporal dementia:** degeneration of the frontal and temporal lobe and characterized by inappropriate behavior (hypersexuality), personality changes, and loss of impulse control.

6) **Other type of dementia:**

- ✓ Parkinson's disease (20-30 % of patients with Parkinson's disease have dementia).
- ✓ Normal-pressure hydrocephalus (Progressive memory impairment, slowness and marked unsteady gait (+ urine incontinence in the late stage)
- ✓ Huntington's disease (intellectual impairments with extrapyramidal features).
- ✓ Creutzfeldt-Jakob's disease (CJD).
- ✓ Traumatic Brain Injury (TBI).
- ✓ Prion disease.

Dementias are classified as: (Reference)

✓ Cortical:

- ✓ Alzheimer's disease.
- ✓ Frontotemporal dementia.
- ✓ Dementia with Lewy Body.

✓ Subcortical:

- ✓ Huntington's disease.
- ✓ Parkinson's disease.
- ✓ Normal-pressure hydrocephalus.
- ✓ *Subcortical dementias are associated with psychomotor retardation, movement disorders, gait incoordination, apathy, and akinetic mutism.*



Dementia workup:

1) Comprehensive history and physical examination.

2) Investigations:

- ✓ Essential workup to detect treatable causes:
 - ✓ Blood work (CBC with differential, TSH, blood glucose, electrolytes, Ca, Mg, vitamin B12, folate, liver and renal function tests).
 - ✓ Other tests (serum HIV).
 - ✓ Neuropsychological testing (MoCA)
 - ✓ Neuroimaging (CT scan and MRI)



Dementia workup:

✓ Neuroimaging:

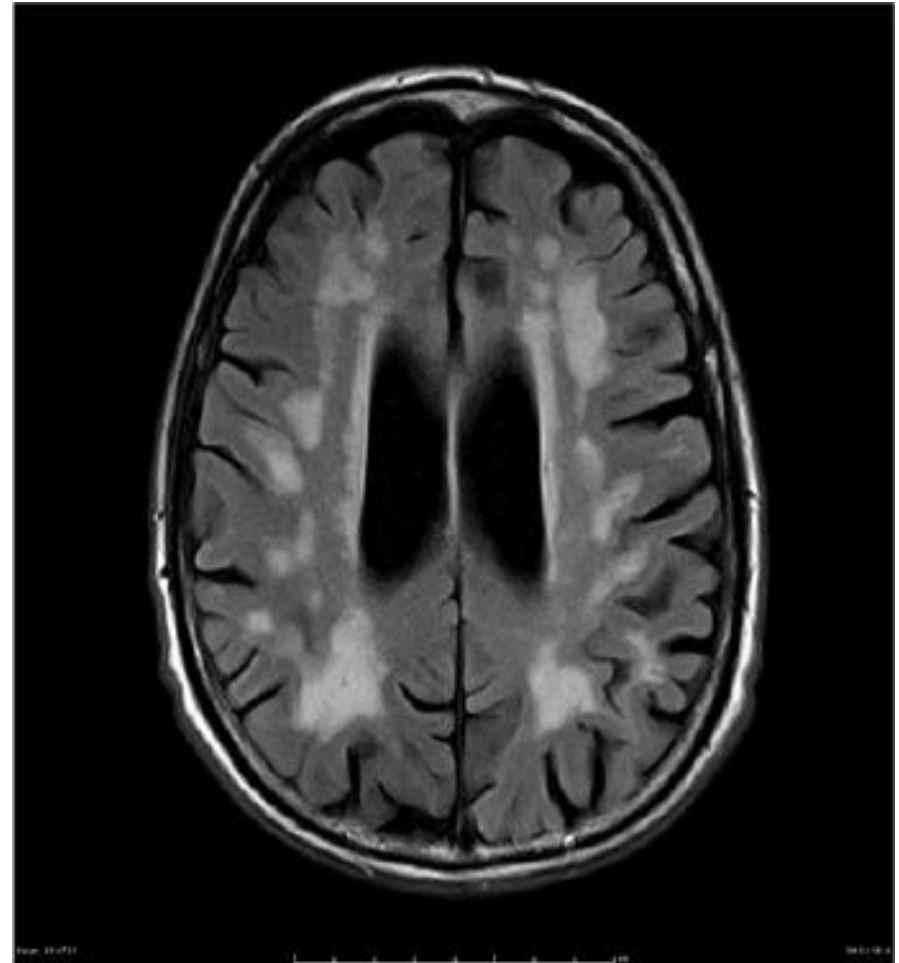
- ✓ Alzheimer's dementia:
 - ✓ Cortical atrophy
 - ✓ Wide sulci & gyri
 - ✓ Wide ventricles



Dementia workup:

✓ Neuroimaging:

- ✓ Vascular dementia:
 - ✓ Lesions and atrophy of cortical and/or subcortical structures corresponding to infarcts.



Dementias Differential Diagnoses:

1) Normal aging:

- ✓ Age-related cognitive decline (the course is not progressively deteriorating), NO loss of social or occupational functioning.

2) Depression in the elderly (Pseudo-dementia):

- ✓ Cognitive disturbance is relatively of rapid onset and preceded by depressive features.
- ✓ The differentiation is sometimes difficult as demented patients may also become depressed as they begin to comprehend their progressive cognitive impairment.
- ✓ EEG and CT scan are normal in pseudo-dementia.

3) Delirium:

- ✓ The onset is rapid and consciousness is impaired.
- ✓ Some demented patients may develop delirium.
- ✓ Diagnosis of dementia cannot be made before delirium clears.

Delirium Vs Dementia

Feature	Dementia	Delirium
onset	Slow/gradual (except for vascular dementia)	Rapid
Duration to develop	months to years	hours to weeks
Attention	Preserved	Fluctuates
Awareness	Unchanged	Reduced
Consciousness	intact	impaired
Course	Chronic/deteriorating	transient/clears within 7-10 days

Delirium vs. Dementia vs. Depression

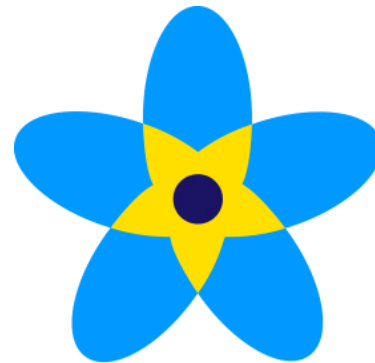
Features	Delirium	Dementia	Depression
<i>Onset</i>	Acute (hours to days)	Insidious (months to years)	Acute or Insidious (wks to months)
<i>Course</i>	Fluctuating	Progressive	May be chronic
<i>Duration</i>	Hours to weeks	Months to years	Months to years
<i>Consciousness</i>	Altered	Usually clear	Clear
<i>Attention</i>	Impaired	Normal except in severe dementia	May be decreased
<i>Psychomotor changes</i>	Increased or decreased	Often normal	May be slowed in severe cases
<i>Reversibility</i>	Usually	Irreversible	Usually

Dementias Treatment/Management:

1) Supportive measures:

- a) Ensure patient safety
- b) Provide good meals & hygiene.
- c) Encourage family's involvement.
- d) Support

✓ *Keep patient in familiar settings (if possible) to avoid accidents and possible agitation*



**Dementia
Friends**

An Alzheimer's Society initiative

Dementias Treatment/Management:

2) Specific measures:

a) Identify and correct any treatable or controllable condition

✓ Hypothyroidism, Vitamin B12 deficiency, hypertension, diabetes.

3) Symptomatic treatment:

a) Agitation/aggression: (small dose of antipsychotics (e.g. olanzapine 5mg, risperidone 2mg, or quetiapine 25mg)).

b) Insomnia

c) Depression: (give a small dose of antidepressant (e.g. escitalopram 5 mg or sertraline 25mg))

✓ Be aware of possible side effects (over-sedation, fall risk “head trauma/fractures”, central anticholinergic activity that may cause delirium)

Dementias Treatment/Management:

4) Cognitive-enhancing medications (mainly for Alzheimer's dementia):

a) Cholinesterase inhibitors:

- ✓ Donepezil (Aricept): 5 mg at night & can be increased gradually to 10 mg. It is well tolerated (S/E: diarrhea, weight loss, bradycardia, and syncope).
- ✓ Rivastigmine (Exelon): 1.5 mg twice/day & can be increased gradually to maximum 6mg twice/day (S/E: anorexia, fatigue, somnolence, and dizziness)
- ✓ Galantamine (Reminyl): 4mg twice/day & can be increased gradually to 12mg twice/day (S/E: similar to rivastigmine)



Dementias Treatment/Management:

b) NMDA receptor antagonist:

- ✓ Memantine (Epixa, Akatinol):
 - an N-methyl-D-aspartate (NMDA) receptor antagonist , protects neurons from neurodegenerative process induced by glutamate excitotoxicity.
 - Memantine has been shown to have a modest effect in moderate to severe Alzheimer's disease and in dementia with Lewy body. In general, well tolerated.
 - Adverse drug reactions include confusion, dizziness, drowsiness, headache, insomnia, agitation, and/or hallucination. Less common adverse effects include vomiting, anxiety, hypertonia, cystitis, and increased libido.



Course and prognosis:

- ✓ The course and prognosis depend on the cause
- ✓ Alzheimer's dementia:
 - ✓ Shows a progressive slow deterioration.
 - ✓ The patient may become incontinent of urine and/or stool.
- ✓ Vascular dementia:
 - ✓ Shows stepwise deterioration.



Case number 3



- A 48-years-old male. Has a long-standing history of:
 - Hypertension.
 - DM type 2.
 - Hypercholesterolemia
- Presented with significant cognitive and behavioural problems.
- He had difficulty with learning new information and making appropriate plans.
- Personal/social history: smoke tobacco and consume alcohol on an almost daily basis for many years.



Amnestic syndrome



✓ Definition:

- ✓ Impairment in short term memory (retention of new information; temporal lobe function) due to a specific organic cause, in the absence of generalized intellectual impairment.
- ✓ Impairment in the ability to create new memories.
- ✓ It leads to social and occupational dysfunctioning.
- ✓ The patient may show confabulation (filling memory gaps with incorrectly retrieved information).
- ✓ The insight is partially impaired.
- ✓ In contrast to delirium, the immediate memory is usually intact. (i.e. digit span test “frontal lobe function” is normal).
- ✓ In contrast to dementia, the remote memory is intact.

Etiology (major causes of amnestic disorders):

✓ Head injury lesions:

(Hippocampus, Posterior Hypothalamus and nearby midline structures)

✓ Thiamine (B1) Deficiency

- ✓ Thiamine is essential for the enzyme transketolase, which essential for glucose metabolism.
- ✓ Associated with alcohol abuse, poor nutrition (e.g., starvation), gastric carcinoma, persistent vomiting, hemodialysis.

Major Causes of Amnestic Disorders

□ **Systemic medical conditions**

- Thiamine deficiency (Korsakoff's syndrome)

- Hypoglycemia

- Primary brain conditions

 - Seizures

 - Head trauma (closed and penetrating)

 - Cerebral tumors (especially thalamic and temporal lobe)

 - Cerebrovascular diseases (especially thalamic and temporal lobe)

 - Surgical procedures on the brain

 - Encephalitis due to herpes simplex

 - Hypoxia (including nonfatal hanging attempts and carbon monoxide poisoning)

 - Transient global amnesia

 - Electroconvulsive therapy

 - Multiple sclerosis

□ **Substance-related causes**

- Alcohol use disorders

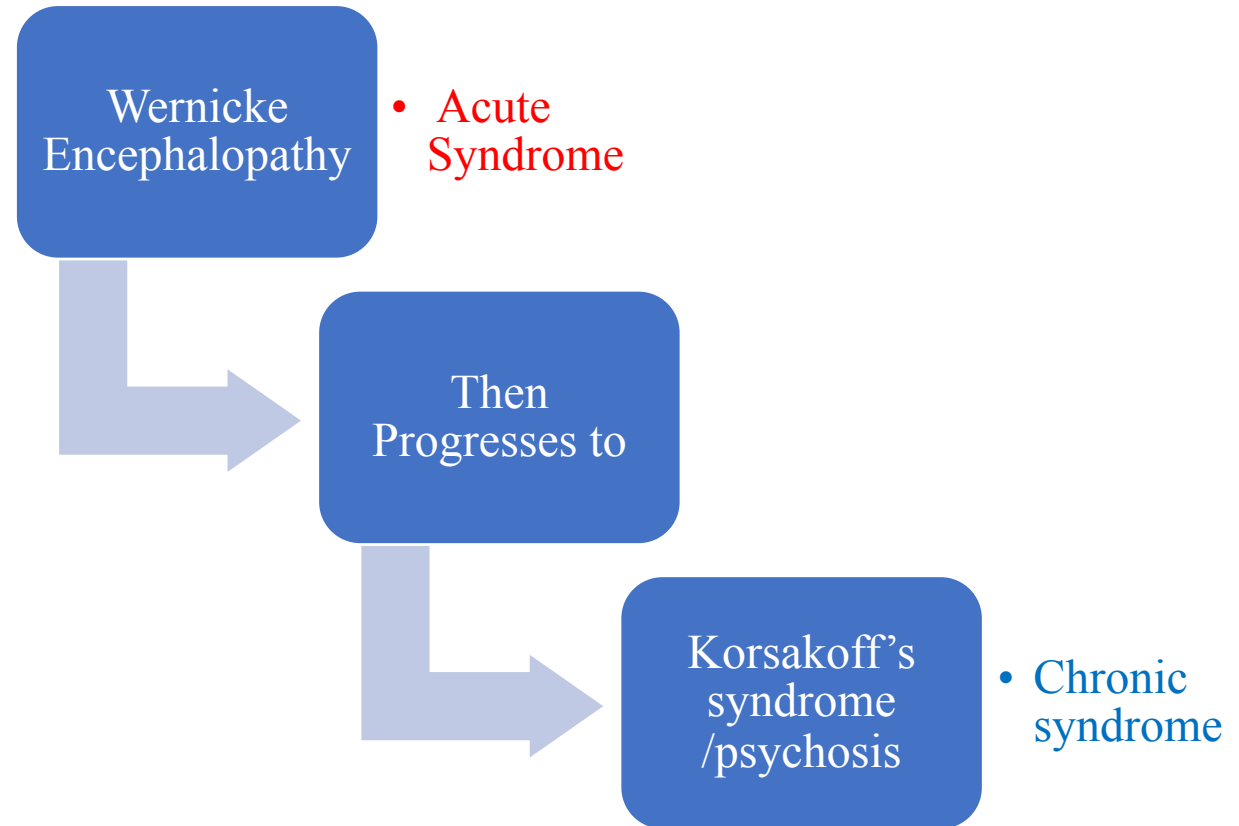
- Neurotoxins

 - *Benzodiazepines (and other sedative-hypnotics)

 - Many over-the-counter preparations

Wernicke-Korsakoff's syndrome

- ✓ Is an **amnestic syndrome** caused by **thiamine deficiency**.
- ✓ Most commonly associated with **poor nutritional habits** of people with **chronic alcohol use**.



✓ Wernicke encephalopathy

✓ Acute syndrome

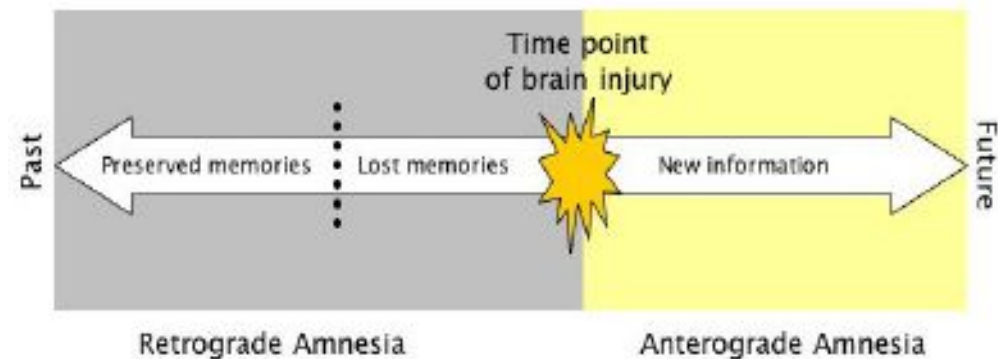
- ✓ Impaired consciousness (confusion)
- ✓ Ophthalmoplegia.
- ✓ Ataxia
- ✓ Memory impairment



✓ Korsakoff's syndrome

✓ Chronic syndrome

- ✓ Peripheral neuropathy
- ✓ Irritability and personality changes.
- ✓ Apathy
- ✓ Profound anterograde amnesia and inability to form a new memories.
- ✓ Confabulate or make up information when asked questions



✓ Treatment:

- ✓ Identify and reverse the cause if possible.
- ✓ Thiamine supply (if due to thiamine deficiency)
- ✓ Supportive medical measures; fluids & nutrition.

✓ Prognosis:

- ✓ If it is due to thiamine deficiency and thiamine is provided promptly.
 - ✓ *Prognosis is good*
- ✓ Otherwise, the course is usually chronic and may be progressive.



Case number 4



- A 19-year-old male involved in a road traffic accident. He lost his consciousness for 5 days and remained 3 weeks in the hospital.

- After discharge, his parents noticed that he become
 - Impulsive
 - Disinhibited
 - And sometimes aggressive
 - More recently they noticed that he started to be more depressed and sometimes feeling so anxious

Traumatic Brain Injury (TBI)



If the head hits a hard surface or if the person is severely shaken or jerked, the brain can strike the skull and become damaged.



Traumatic Brain Injury (TBI)

✓ Definition:

- ✓ An insult to the brain from an external mechanical force, possibly leading to permanent or temporary impairment of cognitive, physical, and psychosocial functions
- ✓ Associated diminished or altered state of consciousness.

✓ Area of function affected:

1. Cognitive
2. Sensory/perceptual
3. Seizures
4. Other physical changes
5. Social-emotional



Traumatic Brain Injury (TBI)

✓ Acute consequences:

- ✓ Impaired consciousness in varying duration (hours, days, weeks or months). long duration suggests poor prognosis.
- ✓ Delirium (after severe head trauma).
- ✓ Memory defects (on recovery of consciousness, defects of memory are usually present).

✓ Anterograde (post-traumatic) amnesia:

- ✓ Amnesia for events in the time between the trauma and the resumption of normal continuous memory.
- ✓ It is a good prognostic factor: probably full recovery when anterograde amnesia was less than 12 hours.

✓ Retrograde amnesia:

- ✓ Amnesia for events in the time between the trauma and the last clearly recalled memory before the injury. It is not a good predictor of outcome.

Traumatic Brain Injury (TBI)

✓ Chronic Consequences:

✓ Lasting cognitive impairment:

- ✓ When the injury has caused a prolonged post traumatic amnesia (of more than 24 hours).
- ✓ Parietal and temporal damage, especially on the left side.
- ✓ Recovery of function may be very slow and may continue over the years.

✓ Emotional disturbances:

- ✓ Depressive, anxiety and phobic features are common
- ✓ Somatic complaints such as headache, fatigue and, dizziness.

✓ Personality changes:

- ✓ Irritability.
- ✓ Reduced control of aggressive impulses.
- ✓ Sexual disinhibition and some coarsening of behaviour (particularly after frontal lobe injury).

✓ Psychotic features:

- ✓ Psychotic features related to depression (non-dominant frontal damage).
- ✓ Paranoid psychosis (temporal lobe damage)

Traumatic Brain Injury (TBI)

✓ Social consequences:

- ✓ Many patients and their relatives experience severe distress of head injury, and have to make substantial changes in their way of life.

✓ Medico-legal aspects:

- ✓ The compensation issue is more likely to contribute to disability if the patient feels someone else is at fault, financial compensation is possible, low social status and in industrial injury.



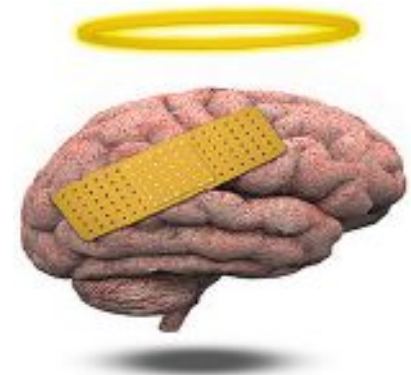
Factors affecting the outcome of head trauma:

- 1) Duration of loss of consciousness.
- 2) Duration of anterograde (Post-traumatic) amnesia.
- 3) Amount and location of brain damage.
- 4) Premorbid personality and past psychiatric history.
- 5) Development of seizures.
- 6) Medico-legal factors e.g. compensation.



Treatment:

- ✓ A plan for long-term treatment should be made as early as possible after head trauma.
- ✓ The treatment of the cognitive and behavioral disorders is similar to the treatment approaches used in other patients.
 - ✓ Head trauma patients may be particularly susceptible to the side effects associated with psychotropics/antipsychotics medications.
 - ✓ Drugs should be initiated in lower dosages than usual.
 - ✓ Should be titrated upward more slowly than usual.



Treatment:

- ✓ Aggression and impulsivity can be treated with antipsychotics or anticonvulsants.
- ✓ Treatment should include physical and psychological rehabilitation.
- ✓ Continuing psychosocial help should be provided to patients and caregiver by a special team.



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 incapacity.

Valid Informed Consent

- ✓ Permission voluntary 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 withdrawal consent verbally or in written forms at anytime

Exceptions

- ✓ Life threatening situation.
- ✓ Patient who waive their rights to disclose and consent (do not want to be informed).



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.**

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.³¹ Patients' responses to these questions need not be verbal.

Thank you