# DELIRIUM- ETIOPATHOLOGY, CLINICAL FEATURES AND MANAGEMENT

# OUTLINE

- DEFINITON
- HISTORY
- PRECIPITATING, PREDISPOSING FACTORS
- ETIOLOGY
- PATHOGENESIS
- CLINICAL FEATURES
- CLINICAL CRITERIA
- DIAGNOSIS- EXAMINATION, INVESTIGATION AND DIFFRENTIAL DIAGNOSIS
- MANAGEMENT
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# DEFINITON

- Deliro- ‘to be crazy’ in Latin
- Delirium is defined as a relatively acute decline in cognition and attention that fluctuates over hours or days.

‘Erasinus, who lived near the Canal of Bootes, was seized with fever after supper; passed the night in an agitated state. During the first day quiet, but in pain at night. On the second, symptoms all exacerbated; at night [mad]. On the third, was in a painful condition; great incoherence. On the fourth, in a most uncomfortable state; had no sound sleep at night, but dreaming and talking; then all the appearances worse, of a formidable and alarming character; fear, impatience. On the morning of the fifth, was composed, and quite coherent, but long before noon was furiously mad, so that he could not constrain himself; extremities cold, and somewhat livid; urine without sediment; died about sunset.’

# HISTORY

- Hippocrates's observations outline core symptoms of delirium
- Celsus coined the term 'Delirium' in 1st AD
- Aretaeus of Cappadocia- Delirium: phrenitis and lethargus
- Phillip Barrough in1583- derangement of some combination of three main internal senses, including imagination, cognition, and memory.

# HISTORY

- Darwin- dream state
- John Hunter-defined delirium as “a cessation of consciousness” of one's own existence.
- James Sims argued that delirium was distinctly different from general insanity and that it constituted an “alienation of the mind.”
- Engel and John Romano-demonstrated that delirium is due to a reduction in the metabolic activity of the brain through the use of electroencephalograms (EEGs),

# PREDISPOSING FACTORS

- The two most consistently identified risks are **older age** and **baseline cognitive dysfunction.**
- Male
- Dementia
- History of delirium
- Depression
- **Functional status**
  1. Functional dependence
  2. Immobility
  3. History of falls
  4. Low level of activity
  5. Sensory impairment Hearing Visual
- **Decreased oral intake**
  1. Dehydration
  2. Malnutrition
- **Drugs**

# PREDISPOSING FACTORS

1. Treatment with psychoactive drugs
2. Treatment with drugs with anticholinergic properties
3. Alcohol abuse

**Coexisting medical conditions**

1. Severe medical diseases
2. Chronic renal or hepatic disease
3. Stroke
4. Neurological disease
5. Metabolic derangements
6. Infection with human immunodeficiency virus
7. Fractures or trauma
8. Terminal diseases

# PRECIPITATING FACTORS

- **Drugs**
1. Sedative-hypnotics
2. Narcotics
3. Anticholinergic drugs
4. Treatment with multiple drugs
5. Alcohol or drug withdrawal

- **Primary neurologic diseases**
1. Stroke, nondominant hemispheric
2. Intracranial bleeding ,
3. Meningitis or encephalitis

- **Intercurrent illnesses Infections**
1. Iatrogenic complications
2. Severe acute illness
3. Hypoxia
4.

# PRECIPITATING FACTORS

5. Anemia
6. Fever or hypothermia
7. Dehydration
8. Poor nutritional status
9. Low serum albumin levels
10. Metabolic derangements

- **Surgery**

1. Orthopedic surgery
2. Cardiac surgery
3. Prolonged cardiopulmonary bypass
4. Non-cardiac surgery

- **Environmental**

1. Admission to intensive care unit
2. Use of physical restraints
3. Use of bladder catheter
4. Use of multiple procedures
5. Emotional stress
6. Prolonged sleep deprivation

# ETIOLOGY

**Systemic conditions**

- Cardiac failure, arrhythmia, myocardial infarction, cardiac assist device, cardiac surgery
- Pulmonary disease
- Uremia
- Hepatic encephalopathy
- Electrolyte disturbances
- Hypoglycemia
- Inflammatory disorders
- Anemia
- Porphyria
- Carcnoid syndrome

# ETIOLOGY

## Endocrinopathies

- Thyroid dysfunction
- Parathyroid dysfunction
- Adrenal dysfunction
- Pituitary dysfunction

## Nutritional deficiencies

- Thiamine (Wernicke's encephalopathy)
- Niacin
- $B_{12}$
- Folic acid

# ETIOLOGY

## Intoxications

- Iatrogenic drugs (Serotonin syndrome)
- Self-administered drugs
- Alcohol
- Metals
- Industrial agents
- Biocides
- Antibiotics, antivirals, and antifungals
- Steroids
- Anesthesia
- Cardiac medications
- Antihypertensives
- Antineoplastic agents
- Anticholinergic agents
- Neuroleptic malignant syndrome
- Herbals, teas, and nutritional supplements
- jimsonweed, oleander, foxglove, hemlock, dieffenbachia, and Amanita

# ETIOLOGY

## Withdrawal syndromes

- Drugs
- Alcohol

## Infections

- Systemic infections with fever
- Meningitis

## Miscellaneous conditions

- Heatstroke
- Radiation
- Nutritional deficiency Burns
- High altitude (usually >5,000 m)
- Electrocution
- Hypersensitivity reaction
- [redacted]
- Postoperative [redacted]ion

# ETIOLOGY

## Intracranial disorders

- Head trauma
- Cerebral edema
- Epilepsy (ictal and postictal confusion)
- Hypertensive encephalopathy
- Intracranial inflammatory disease
- Cerebrovascular accident (acute phase)
- Migraine
- Subdural hematoma
- Focal cerebral lesions
- Right parietal lesions
- Bilateral occipitotemporal lesions

# ETIOLOGY

**Idiopathic psychiatric disorders**

- Mania (particularly in elderly individuals)
- Schizophrenia
- Depression

# PATHOGENESIS

- The leading hypotheses for the pathogenesis of delirium focus on the **roles of neurotransmission, inflammation, and chronic stress.**
- Dysfunction in the prefrontal cortex, subcortical structures, thalamus, basal ganglia, frontal and temporoparietal cortex, fusiform cortex, and lingual gyri, particularly on the nondominant side.
- Delirium results from **widespread disturbances in cortical and subcortical regions** rather than a focal neuroanatomic cause.

# PATHOGENESIS

- Electroencephalogram (EEG) data in persons with delirium usually show symmetric slowing, a nonspecific finding that supports diffuse cerebral dysfunction.
- The quantitative electroencephalogram may be more sensitive than the conventional electroencephalogram to changes in slow-wave power during the course of delirium.
- The quantitative EEG signal correlates with the severity and duration of the delirium whereas the normalization of the signal parallels and occasionally precedes the course of recovery

# PATHOGENESIS

- **Neurochemical factors**

1. Acetylcholine- cholinergic deficiency  involved in rapid eye movement (REM) sleep, attention, arousal, and memory.
2. Dopamine- excess dopamine
3. Glumate disturbances- wernicke's encephalopathy
4. GABA- Increased GABA levels in hepatic encephalopathy
5. Nor-epinephrine, melatonin, serotonin
6. Impaired oxidative metabolism
7. Blood-brain barrier: CNS response to systemic inflammation during a state of blood-brain barrier compromise.
8. Ammonia- Hepatic encephalopathy (astrocyte swelling )
9. Cytokines- increase BBB permeablity and alter neurotransmission

# PATHOGENESIS

- Chronic stress brought on by illness or trauma activates the sympathetic nervous system and hypothalamic–pituitary–adrenocortical axis, resulting in increased cytokine levels and chronic hypercortisolism.

- The **concept of delirium developing as the result of an insult in predisposed individuals** is currently the most widely accepted [redacted]nstruct

# CLINICAL FEATURES

- Rapid onset
- Variable and intermittent symptoms
- Cardinal feature- reduced alertness
- Impaired memory- registration and retrieval
- Decline in higher integrative functions- incoherent speech and diminished ability to sequence actions properly
- Brief and fragmented sleep, reversal of sleep pattern

# CLINICAL FEATURES

- Hallucinations, misperceptions, illusions, and delusions
- somatic features such as urinary incontinence, gait impairment, tremor, and language disorders (including receptive and expressive aphasias)
- Behavioural disturbances-

1. Patients with hypoactive delirium may appear sluggish and lethargic as well as confused.
2. Patients with hyperactive delirium may exhibit agitation, psychosis, and mood lability and may refuse to cooperate with medical care, may demonstrate disruptive behaviors

# CLINICAL FEATURES

| Factor | Characteristics |
|---|---|
| Alertness | `Clouded or fluctuating |
| Attention | Impaired attention, distractibte |
| Language | Incoherent spontaneous speech |
| | Anomia |
| | Agraphia |
| | Nonaphasic misnaming |
| Memory | Disoriented, poor recent memory |
| Constructions | Visuospatial deficits |
| Cognition | Incoherent thought |
| | Concrete thinking |
| | Dyscalculia |

# CLINICAL FEATURES

| | |
|---|---|
| Other behavioral alterations | Perseveration and/or persistence |
| | Occupational pantomime |
| Neuropsychiatric disorders | Hallucinations |
| | Delusions |
| | Mood alterations |
| Motor system abnormalities | Psychomotor retardation and/or hyperactivity |
| | Action tremor |
| | Asterixis |
| | Myoclonus |
| | Dysarthria |
| | Tone and reflex abnormalities |
| Miscellaneous | Sleep disturbances |
| | Autonomic dysfunction |

# CLINICAL CRITERIA

## DSM-IV Criteria for Delirium

- Disturbance of consciousness
- Reduced awareness of environment
- Reduced ability to focus attention
- Reduced ability to sustain attention
- Reduced ability to shift attention
- Cognitive change not resulting from dementia
- Quickly evolving (hours or days) with fluctuations
- There is evidence that the disturbance is caused by the direct physiological consequences of a general medical condition

# CLINICAL CRITERIA

## ICD-10

**F05: Delirium, not induced by alcohol and other psychoactive substances**

An etiologically nonspecific organic cerebral syndrome characterized by concurrent disturbances of consciousness and attention, perception, thinking, memory, psychomotor behaviour, emotion, and the sleep-wake schedule. The duration is variable and the degree of severity ranges from mild to very severe.

# CLINICAL CRITERIA

**Includes:** acute or subacute:

1. brain syndrome
2. confusional state (nonalcoholic)
3. infective psychosis
4. organic reaction
5. psycho-organic syndrome

**Excludes:** delirium tremens, alcohol-induced or unspecified (F10.4)

# CLINICAL CRITERIA

**F05.0 Delirium not superimposed on dementia, so described**

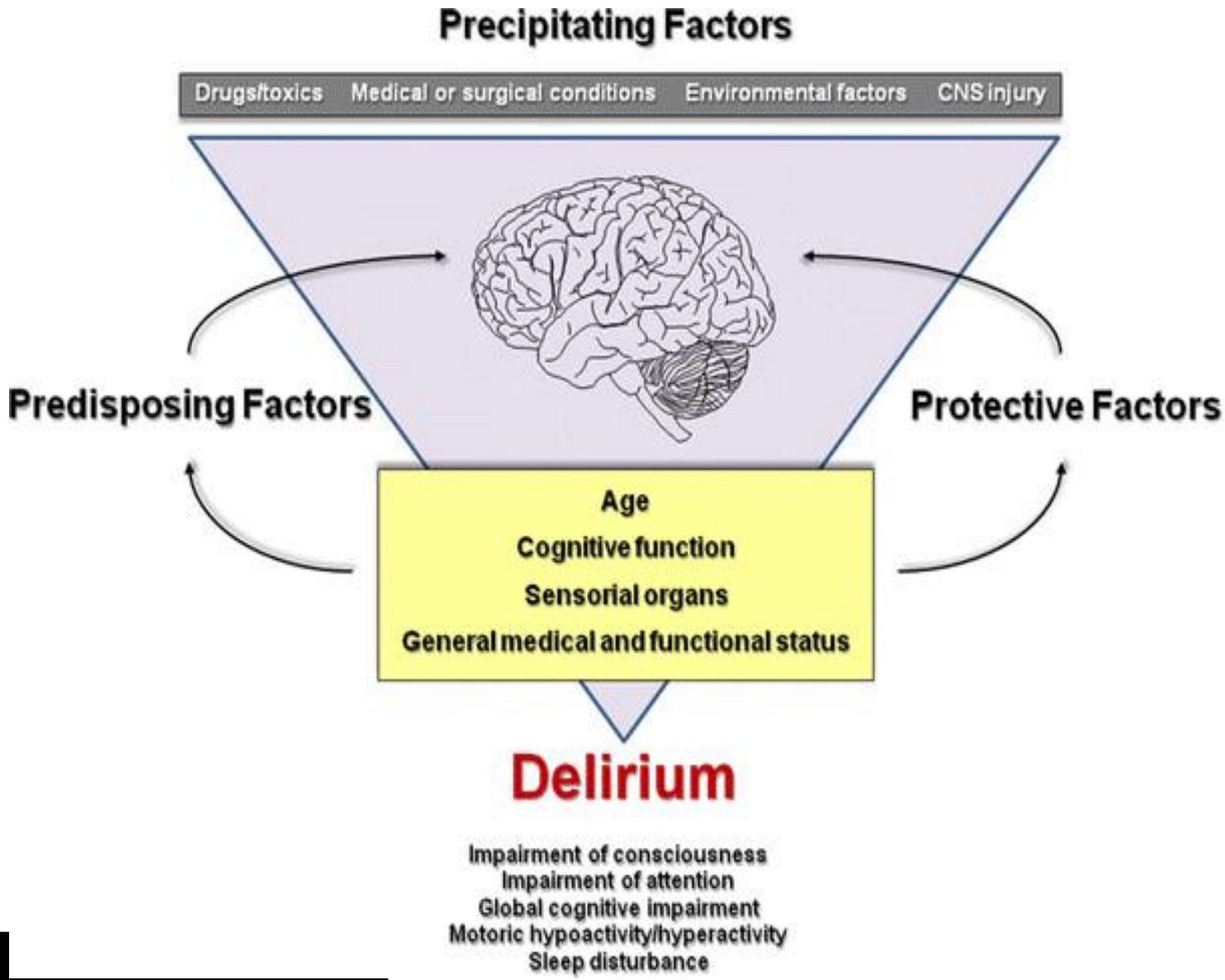
**F05.1 Delirium superimposed on dementia**

Conditions meeting the above criteria but developing in the course of a dementia (F00–F03).

**F05.8 Other delirium**

Delirium of mixed origin

**F05.9 Delirium, unspecified**


Precipitating Factors
Drugs/toxics
Medical or surgical conditions
Environmental factors
CNS injury
Predisposing Factors
Protective Factors
Age
Cognitive function
Sensorial organs
General medical and functional status
Delirium
Impairment of consciousness
Impairment of attention
Global cognitive impairment
Motoric hypoactivity/hyperactivity
Sleep disturbance

# DELIRIUM ASSESSMENT

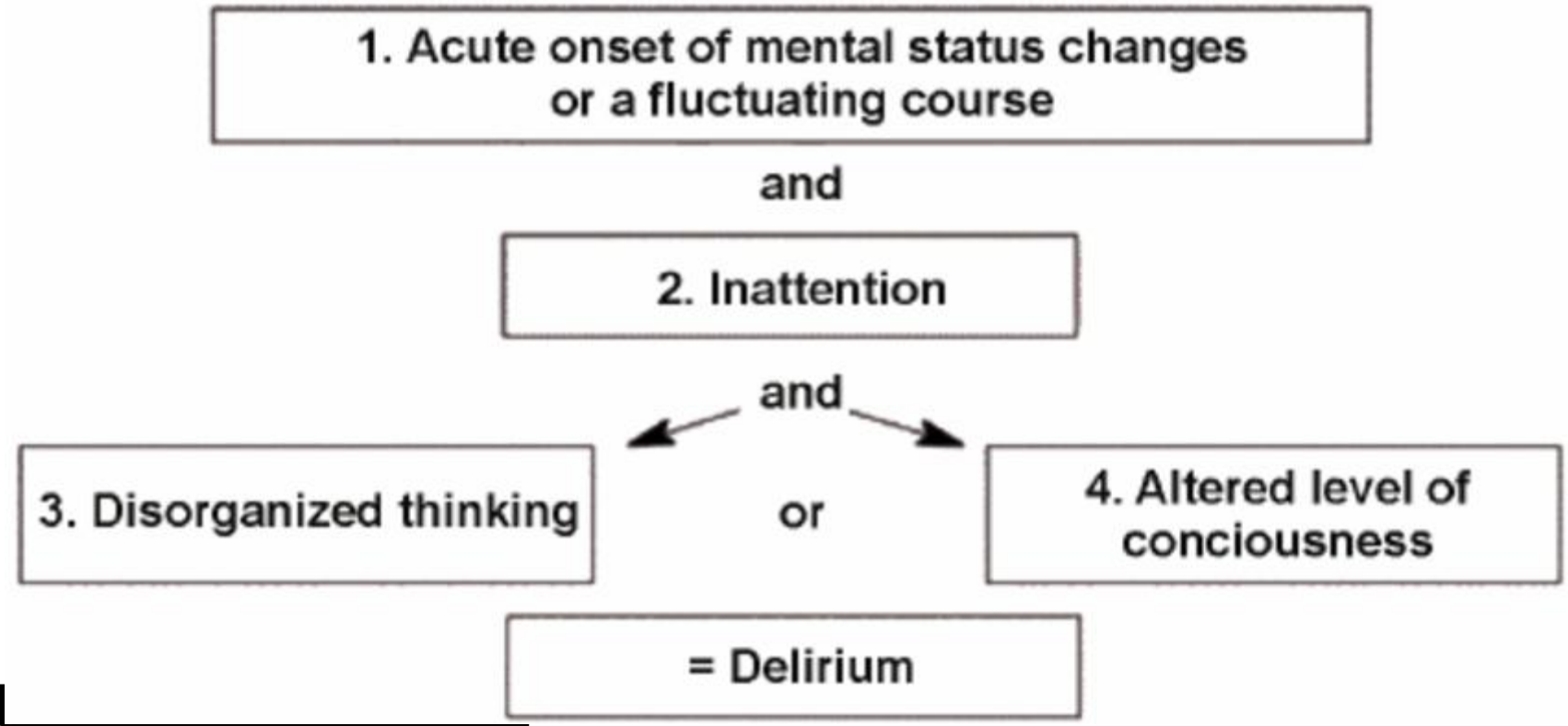
- Confusion Assessment Method

1. Acute onset
2. Inattention
3. Disorganized Thinking
4. Altered level of consciousness
5. Disorientation
6. Memory impairment
7. Perceptual disturbances
8. Psychomotor agitation
9. Psychomotor retardation
10. Altered sleep-wake cycle

# DELIRIUM ASSESSMENT

- Memorial delirium rating scale
- Delirium Rating Scale-revised version (DRS-R-98)
- Saskatoon delirium checklist
- Paediatrics CAM
- Clinical assessment of confusion-A and B
- Confusional state evaluation scale
- Delirium assessment scale
- Delirium severity scale

# CONFUSION ASSESSMENT METHOD



# PHYSICAL EXAMINATION

| PARAMETER | FINDING | CLINICAL IMPLICATION |
|---|---|---|
| 1. PULSE | Bradycardia | • Hypothyroidism<br>• Stokes-Adams syndrome<br>• ICT |
| | Tachycardia | • Hyperthyroidism<br>• Infection<br>• Heart Failure |
| 2. TEMPERATURE | Fever | • Sepsis<br>• Thyroid Storm<br>• Vasculitis |
| 3. BLOOD PRESSURE | Hypotension | • Shock<br>• Hypothyroidism<br>• Addison's disease |
| | Hypertension | • Encephalopathy<br>• Intracranial mass |

| PARAMETER | FINDING | CLINICAL IMPLICATIONS |
|---|---|---|
| 4. RESPIRATION | Tachypnea | • Diabetes<br>• Pneumonia<br>• Cardiac failure<br>• Fever<br>• Acidosis |
| | Shallow | • Alcohol or substance intoxication |
| 5. CAROTID VESSELS | bruit/ decreased pulse | Transient cerebral ischaemia |
| 6. SCALP & FACE | Trauma | |
| 7. NECK | Nuchal rigidity | • Meningitis<br>• SAH |
| 8. EYES | Papillodema | • Tumor<br>• Hypertensive encephalopathy |
| | Pupillary dilatation | • Anxiety<br>• Autonomic overactivity |

| PARAMETER | FINDING | CLINICAL IMPLICATION |
|---|---|---|
| 9. MOUTH | Tongue/ cheek lacerations | GTCS |
| 10. THYROID | Enlarged | Hyperthyroidism |
| 11. HEART | Cardiomegaly | • Heart failure<br>• Hypertensive disease |
| | Arrythmia | Inadequate CO<br>Embolism |
| 12. LUNGS | Congestion | • Primary pulmonary failure<br>• Pulmonary edema |
| 13. BREATH | Alcohol | |
| | Ketones | Diabetes |
| 14. LIVER | Enlargement | Cirrhosis |

| PARAMETER | FINDING | CLINICAL IMPLICATIONS |
|---|---|---|
| 15. NERVOUS SYSTEM | | |
| ➢ Reflexes- muscle stretch | Asymmetry with Babinski's sign | • Mass lesion<br>• Cerebrovascular disease<br>• Prexisting dementia |
| ➢ Abducent nerve | Lateral gaze weakness | • ICT |
| ➢ Limb Strength | Asymmetrical | • Mass lesion<br>• Cerebrovascular disease |
| ➢ Autonomic | Hyperactivity | • Anxiety<br>• Delirium |

# LABORATORY WORK-UP

- **STANDARD STUDIES**

1. Blood chemistries ( electrolytes, renal, hepatic, glucose
2. Complete blood count and diffrential count
3. Thyroid function tests
4. Syphilis serology
5. HIV antibody
6. Urinanalysis
7. Electrocardiogram
8. Electroencephalogram
9. Chest radiograph
10. Blood and urine drug screens

- **ADDITIONAL TESTS WHEN INDICATED**

1. Blood, urine, CSF culture study
2. B12, folic acid concentration
3. CT or MRI brain

# DIFFERENTIAL DIAGNOSIS

- Dementia
- Schizophrenia
  - Hallucinations and delusions more prominent
  - No change in level of consciousness or orientation
- Depressive Disorder
  - EEG
- Brief psychotic disorder
- Dissociative disorder
- Factitious disorder

# Delirium vs Dementia

| FEATURE | DEMENTIA | DELIRIUM |
|---|---|---|
| Onset | Slow | Rapid |
| Duration | Months to years | Hours to weeks |
| Attention | Preserved | Fluctuates |
| Memory | Impaired remote memory | Impaired recent and immediate memory |
| Speech | Word-finding difficulty | Incoherence (slow or rapid) |
| Sleep-wake cycle | Fragmented sleep | Disruption, reversal |
| Thoughts | Impoverished | Disorganized |
| Awareness | Unchanged | Reduced |
| Alertness | Usually normal | Hypervigilant or reduced vigilance |

# MANAGEMENT

- Delirium is increasingly being recognized as a sign of serious underlying illness.
- Recent estimates of in-hospital mortality rates among delirious patients have ranged from 25 to 33%, a rate similar to that of patients with sepsis.

# MANAGEMENT

SYMPTOMATIC MANGEMENT

- Two symptoms- psychosis and insomnia

| Pharmacological Agent | Dosage | Side Effects | Comments |
|---|---|---|---|
| **Typical Antipsychotics** | | | |
| Haloperidol (Haldol) | 0.5–1 mg p.o. twice a day (may be given every 4–6 hr as needed, too) | Extrapyramidal side (EPS) effects<br>Prolonged QTc | Most commonly used<br>Can be given intramuscularly |
| **Atypical Antipsychotics** | | All can prolong QTc duration | |
| Risperidone (Risperdal) | 0.5–1 mg a day | EPS concerns | Limited data in delirium |
| Olanzapine (Zyprexa) | 5–10 mg a day | Metabolic syndrome | Higher mortality in dementia patients |
| Quetiapine (Seroquel) | 25–150 mg a day | More sedating | |
| Benzodiazepine | | | |
| Lorazepam (Ativan) | 0.5–3 mg a day and as needed every 4 hr | Respiratory depression, paradoxical agitation | Best use in delirium secondary to alcohol or benzodiazepine withdrawal<br>Can worsen delirium |

# MANAGEMENT

SYMPTOMATIC MANGEMENT

- ECT- last resort in severe agitation not responding to pharmacotherapy.
- Zolpidem and Trazodone- to reset sleep-wake cycle

# MANAGEMENT

TREATMENT OF UNDERLYING CAUSE

1. Anticholinergic medication
   - Physiostigmine- repeated dosing
   - Cardiac monitoring
   - Donepezil, Rivastigmine, Galantamine- not well-studied
2. Wernicke's encephalopathy
   - i.v. or i.m. Thiamine immediately

# MANAGEMENT

TREATMENT OF UNDERLYING CAUSE

3. Substance Intoxication

- BZDs, Alcohol, Hepatic encephalopathy- Flumazenil
- Opiates- Naloxene, Naltrexene
  - Cardiac and respiratory monitoring

4. Substance Withdrawal

- BZD- first line for alcohol withdrawal delirium

# MANAGEMENT

TREATMENT OF UNDERLYING CAUSE

5. Parkinsonism Patients-
   - Stop or attenuate anti-parkinsonian medications weighing the pros and cons of worsening motor symptoms.
   - Give Clozapine if delirium persists. If not tolerated Quetiapine can be considered.
6. Systemic infections- appropriate antibiotics.
7. Correction of metabolic derangements
8. Correction of underlying nutritional, endocrinal or systemic dysfunction

# MANAGEMENT

SUPPORTIVE TREATMENT

- Reorientation by the nursing staff and family combined with visible clocks, calendars, and outside-facing windows
- Prevent sensory isolation or sensory overload
- Maintaining proper nutrition and volume status as well as managing incontinence and skin breakdown.
- Physical activity initiation
- Minimal interruptions and maintain sleep pattern through cues.

# MANAGEMENT

- Access to home bedding, clothing, and nightstand objects makes the hospital environment less foreign
- Psychosocial support by both staff and family or friends.

# MANAGEMENT

PREVENTION

- **The Yale Delirium Prevention Trial** demonstrated the effectiveness of intervention protocols targeted toward six risk factors:

1. Orientation and therapeutic activities for cognitive impairment,
2. Early mobilization to avert immobilization. Non-pharmacologic approaches to minimize the use of psychoactive drugs
3. Communication methods and adaptive equipment for vision and hearing.
4. Interventions to prevent sleep deprivation.
5. Early intervention for volume depletion.

# PRINCIPLES OF MANAGEMENT

1) Determine the cause and treat it
2) Avoid exacerbation
3) Provide supportive care
4) Manage the behaviour by pharmacological and non-pharmacological methods
5) Restoration of cognitive and self care functions
6) Psycho-education of the family members

# PROGNOSIS

- Symptoms of delirium usually last about 7 days in most patients, but there is much variability, contributing to persistent symptoms of delirium at 6 to 8 weeks for severely ill patients.
- The increased mortality risk associated with delirium was maintained at 12, 24, and 36 months, with a risk ratio of at least 2 at all time points. The increased risk of cognitive and functional impairment remained.
- The prognosis of delirium is almost certainly not, therefore, one of early full recovery. Rather, delirium is a condition with a slow recovery and one which often fails to resolve completely.

# BURDEN OF DELIRIUM

- Increased nursing care
- Increased length of stay
- Increased risk of cognitive decline
- Increased risk of functional decline
- Increased mortality
- Delay in postoperative mobilization
- Prevention of early rehabilitation
- Increased rate of nursing home placement
- Increased need for home care services
- Increased distress to caregivers
- Barrier to psychosocial closure in terminally ill patient

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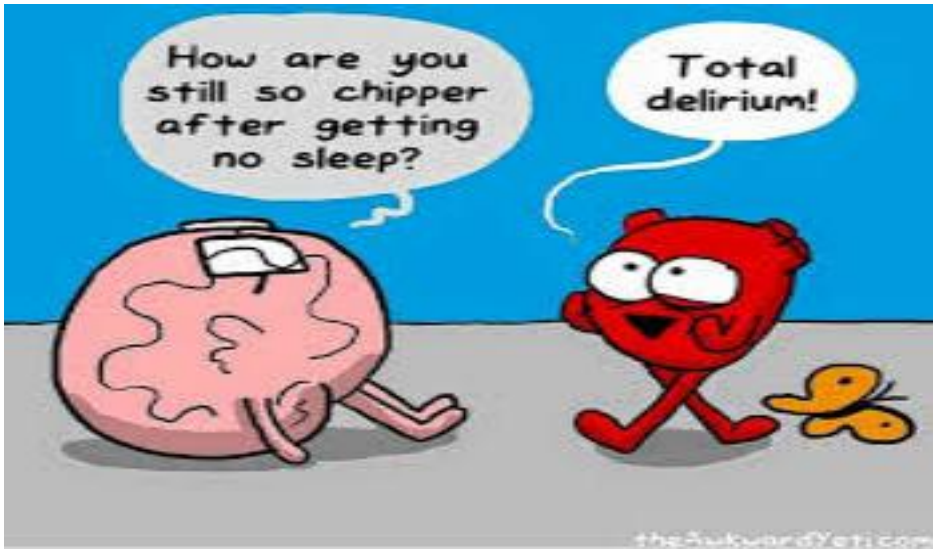
How are you still so chipper after getting no sleep?
Total delirium!

# THANK YOU