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Assessment and Management of Delirium

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Disclosure Slide

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Delirium

- Definition
- Prevalence
- Pathophysiology
- Etiology
- Diagnostic criteria (DSM-5)
- Clinical features
- Evaluation instruments
- Management

Definition

Transient organic brain syndrome characterized by the acute onset of disordered attention (arousal) and cognition, accompanied by disturbances of psychomotor behavior and perception

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Definition

- Syndrome composed of disturbances:
  - consciousness
  - attention (i.e., arousal)
  - cognition
- Abrupt onset and fluctuating course
- Types: Hypoactive, Hyperactive, Mixed

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Subsyndromal Delirium (SSD)

- Presence of any core delirium symptoms without presence of all diagnostic criteria
- Severity of scores on rating scales are below the diagnostic threshold
- Intermediate between full syndrome (FDS) and no delirium

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Definition

- Very distressing for patients, family members, and staff
- Often misdiagnosed or unrecognized, poorly treated
- Predictor of:
  - increased morbidity/distress/mortality in patients, family, staff; (21 vs. 39 days survival) in cancer patients
  - increased risk of self-harm, harm to staff
  - longer hospitalization
- Interferes with symptom assessment and control

LeGrand, Susan B. Delirium in Palliative Medicine: A review. *Journal of Pain and Symptom Management* October 2012;44(4)

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Prevalence

- All hospitalized patients 10%
- Hospitalized cancer patients 8 to 40%
- Terminally ill cancer patients 80%
- Elderly patients with medical illnesses, incidence is ranging from 25% to 41%
- Common neuropsychiatric complication of hospitalized AIDS patients (Tross)

Hosie A, Davidson PM, Agar M, Sanderson CR, Phillips J. Delirium prevalence, incidence, and implications for screening in specialist palliative care in patient settings: a systematic review. *Palliative Med* 2013;27:486-498

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Etiology

- Discovered in fewer than 50% terminal patients
- **Malignant causes:**
  - cancer related
    - brain tumor
    - metastases
  - cancer-treatment related
    - radiation therapy
    - chemotharapy
  - paraneoplastic syndromes

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Etiology

- **Nonmalignant causes:**
  - metabolic abnormalities (dehydration, electrolyte imbalance)
  - organ failure (liver, renal)
  - medications side effects (benzo, cortico, opioids)
  - infection/sepsis
  - nutritional deficiencies
  - hypoxia

Pathophysiology

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- Numerous theories with support
- Different abnormalities of neurotransmitters of various areas of brain:
  - Decreased oxidation metabolism
  - Direct effect on neurotransmitters (acetyl choline, dopamine)
  - Age-related neurotransmitter changes
  - Increased inflammatory cytokines
  - Stress reaction
  - Changes in intraneural signals
    - Leading theory:
      - Decreased cholinergic activity
      - Increased dopaminergic activity

LeGrand, Susan B. Delirium in Palliative Medicine: A review. *Journal of Pain and Symptom Management* October 2012;44(4)

Clinical Features

- Recent onset
- fluctuation of signs, symptoms
- clinical variants:
  - hypoalert/hypoactive
  - hyperalert/hyperactive
  - mixed
- Essential elements:
  - impaired cognition
    - memory impairment
    - confusion
  - impaired emotions
    - dysphoria
    - hypomania
  - impaired perception
    - illusions
    - hallucinations
  - impaired arousal
    - increased, decreased
    - less responsive, distractible

Delirium: DSM-5

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Diagnostic Criteria

A. A disturbance in attention (i.e., reduced ability to direct, 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 a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.

C. An additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception).

D. The disturbances in Criteria A and C are not better explained by another preexisting, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.

E. There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e., due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies.

Neurocognitive Disorders. In: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Washington, DC: American Psychiatric Association, 2013

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Behavioral Symptomatology

- Early symptoms
  - Change in sleep patterns; restlessness and transient periods of disorientation
  - Increased irritability
  - Withdrawal; refusal to talk to staff or relatives
  - Forgetfulness that was not previously present

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Behavioral Symptomatology

- Late symptoms
  - Refusal to cooperate with reasonable requests
  - Anger, swearing, shouting, and abusive or physical outbursts
  - Demanding to go home; pacing the corridor
  - Illusions: misidentifying staff; visual and sensory clues
  - Delusions: misinterpreting events, usually paranoid in nature; fears of being harmed or poisoned by chemotherapy
  - Hallucinations: visual or auditory

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Hypoactive Delirium

- Also called hypoalert, hypoaroused
- Psychomotor retardation, lethargy, sedation, reduced awareness of surroundings
- Different from depression, sedation due to opioids, obtundation in last days of life
- Most common in palliative care setting
- Occurs most commonly with hypoxia, metabolic disturbances, and anticholinergic medications
- Higher mortality

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Hyperactive Delirium

- Restlessness, agitation, hypervigilance, hallucinations and delusions
- 13% to 46% in palliative care setting
- Correlated with alcohol and drug withdrawal, drug intoxication, medication adverse effects

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Assessment Instruments

- Diagnostic classification systems
  - DSM-5
  - ICD-9, ICD-10
- Diagnostic interview instruments
  - Delirium symptom interview (DS)
  - Confusion Assessment Method (CAM) - ICU & Peds versions

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Assessment Instruments

- Delirium rating scales
  - Delirium Rating Scale (DRS)
  - Confusion Rating Scale (CRS)
  - Memorial Delirium Assessment Scale (MDAS)
- Cognitive impairment screening scales
  - Mini-Mental State Exam (MMSE)
  - Short Portable Mental Status Questionnaire (SPMSQ)
  - Cognitive Capacity Screening Examination Test (BOMC)

Delirium and **Dementia** (clinical features)

Feature	Delirium	Dementia
Impaired memory	+++	+++
Impaired thinking	+++	+++
Impaired judgment	+++	+++
Clouding of consciousness	+++	--------
Major attention deficits	+++	+
Fluctuation over course of day	+++	+
Disorientation	+++	++

+++=always present; ++=usually present; +=present sometimes; ----- =usually absent

Breitbart W, et al. Psychiatric Aspects of Symptom Management in Cancer Patients. American Psychiatric Press. Washington, 1993, p.40

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Delirium and **Dementia** (clinical features)

Feature	Delirium	Dementia
Vivid perceptual disturbances	++	+
Incoherent speech	++	+
Disrupted sleep-wake cycle	++	+
Nocturnal exacerbation	++	+
Insight	++	+
Acute or subacute onset	++	-------

+++=always present; ++=usually present; +=present sometimes; ----- =usually absent

Breitbart W, et al. Psychiatric Aspects of Symptom Management in Cancer Patients. American Psychiatric Press. Washington, 1993, p.40

Depression and Hypoactive Delirium

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Features	Hypoactive Delirium	Depression
Arousal	hypoaroused	normal
Cognitive Changes	Memory, dysnomia, +++	Mild deficits, subjective
Temporal Onset	Abrupt	Slow
Perceptual Disturb	Up to 75% of patients	Rarely
Thought Content	Paranoid delusions	Guilt, hopelessness…
Mood Symtoms	Labile, disinhibition	Sad, depressed
Psychomotor Activity	Quiet, slowed	Slowed, quiet,
Family History	N/A	common
Neurological Exam	Asterixis, frontal release	Usually normal
Past Psychiatric History	May be present	Not uncommon

Breitbart W, Alici Y. Agitation and delirium at the end of life: "We couldn't manage him." *JAMA* 2008;300(24):2898-2910, E1

Delirium Management: Treatment of Underlying Cause(s)

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- Evaluation is dependent on goals of care
- Reversibility:
  - reversible in 50%:
    - medications
    - hypercalcemia
    - metabolic abnormalities
    - infection
    - dehydration
  - irreversible:
    - metabolic derangements (renal, liver)
    - hypoxic encephalopathy

Delirium Management: Nonpharmacological Measures

- Reassuring: presence of person at bedside
- Orienting
- Massage
- Limit number of people in room
- Oxygen delivery
- Well-lit room
- Environment: calm, familiar objects
- Support to patient and family

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Delirium Management: Pharmacological Measures

- Limited trials to evaluate the management of delirium
- Fewer trials to compare regimens in controlled fashion
- Treatment controversial

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Delirium Management: Pharmacological Measures

- neuroleptics
- benzodiazepines

Drugs

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	Approximate daily dosage range (mg)	Route
Neuroleptics		
Haloperidol (Haldol)	0.5-5mg q2-12h	PO, IV, SC, IM
Quetiapine (Seroquel)	25-150mg q12	PO
Chlorpromazine (Thorazine)	12.5-50mg q4-12h	PO, IV, IM
Droperidol (Inapsine)	0.5-5mg q12h	IM, IV
Olanzepine (Zyprexa)	5-10mg bid	PO
Risperidone (Risperdal)	1-3mg bid	PO
Benzodiazepines		
Lorazepam	0.5-2.0mg q1-4h	PO, IV, IM
Midazolam	30-100mg per 24h	IV,SC

- PO= orally, IV= intravenously, SC= subcutaneously, IM= intramuscularly
- Benzodiazepines can cause or increase delirium. Use short acting if sedation is needed and with caution

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Pharmacological Management

- **Typical antipsychotics:**
  - **Haloperidol** →first line / practice standard
    - (few anticholinergic effects, minimal cardiovascular adverse effect, lack of active metabolites, different routes of administration)
    - 1-2 mg po every 4 hours. Not to exceed 20 mg in 24 hours
    - QTc prolongation and torsades de pointes
    - Add lorazepam for severe agitation (help sedate, minimize extrapyramidal effects)

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Pharmacological Management

- **Atypical antipsychotics** (risperidone, olanzepine, quietapine, ziprasidone, aripiprazole):
  - No statistically significant difference than Haldol
  - No difference in toxicity (except in high dose of Haldol (6.5mg))
  - Efficacy is equivalent to Haldol, suggestion of fewer EPS

Lonergan E, Britton AM, Luxenberg J, Wyller T. Antipsychotics for delirium. *Cochrane Database Syst Rev* 2007;(2) CD005594

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Pharmacological Management

- **Sedative agents: Benzodiazepines**
  - 30% of patients do not have symptoms controlled by antipsychotics
  - Role unclear
  - Not first line (unless benzo withdrawal)
  - Use in combination with antipsychotics
  - Can cause and increase delirium (caution)
  - Use of lorazepam, midazolam (shorter acting)

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Pharmacological Management

- **Psychostimulants**
  - For hypoactive delirium
  - Only case reports and one open-label study

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"Terminal" Delirium / Sedation

- Most common symptoms requiring sedation
- Rates of sedation 10%-52%
- Controversial topic
- Indication: intractable delirium
- Drugs of choice: midazolam, lorazepam

Bush SH and al. End-of-Life delirium: Issues regarding recognition, optimal management, and the role of sedation in the dying phase. *J Pain Symptom Management* 2014;48(2);215-230

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Pharmacological Prevention of Delirium

- Prophylactic use of pharmacologic agents in the prevention of delirium have had mixed results at best

- Prophylactic neuroleptics do not prevent delirium in palliative care settings

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Conclusion

- Delirium is a frequent, devastating complication of advanced disease
- Pathophysiology is related to neurotransmitters: decrease in cholinergic activity, increase in dopaminergic activity
- Work-up and treatment should be in accord with GOC
- Treatment with neuroleptics is the treatment of choice
- Haldol is the best and most practical drug
- Benzos need to be used with caution; they can increase delirium

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Assessment and Management of Delirium

Q/A

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