Delirium in the Medical Hospital

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Delirium

- Definition
- Epidemiology
- Risk Factors & Etiology
- Neuropathogenesis
- Financial Impact & Length of Stay
- Morbidity & Mortality
- Relationship to Dementia
- Work-up & Treatment
- Recovery
Delirium

- Also known as:
  - Altered Mental Status
  - **Acute Brain Failure**
  - Encephalopathy
  - Acute Confusional State
  - ICU Psychosis
  - Hepatic/Hypoxic/Uremic/etc. Encephalopathy
  - Toxic Psychosis
  - Posttraumatic Confusion
Delirium in the DSM V

A. Disturbance in **Attention** (reduced ability to direct, focus, sustain and shift attention) **AND** Disturbance in **Awareness** (reduced orientation to environment)

B. Develops over hours to days, change from baseline and **fluctuates** during the day.

C. Additional disturbance in **cognition** (memory, disorientation, language, visuo-spatial ability or perception)
Delirium Definition

• ‘A serious disturbance in mental abilities that results in confused thinking and reduced awareness of your environment’. (Mayo Clinic)

• ‘An acute mental disturbance characterized by confused thinking and disrupted attention usually accompanied by disordered speech and hallucinations’. (Webster)

• Acute & fluctuating disorder of Consciousness (attention, awareness of self/environment and wakefulness), resulting in neuropsychiatric symptoms. (Psychosomatic Medicine Textbook)
Delirium

- Acute decline or change in mental status
Disorders of Consciousness

Coma

Vegetative State

Minimally Conscious State

Delirium

Normal

- Aroused - Conscious - Sleep/Wake

+ Aroused - Aware - Sleep/Wake

+ Aroused
+ Inconsistently Follows/Tracks
+ Sleep/Wake
- Intent

+ Aroused
+ Higher Level Deficits
+ Disrupted Sleep/wake
+ Intent
Findings in Delirium
Findings in Delirium

• **Diffuse Cognitive Deficits**
  – Inattention
  – Disorientation (time, place, person)
  – Impaired memory (short & long term, verbal & visual)
  – Visuo-constructional impairment
  – Executive function
  – Ability to abstract
Findings in Delirium

• **Temporal Course**
  – Acute or abrupt onset
  – Fluctuating severity over 24 hours
  – Usually reversible
  – Subclinical syndrome (precedes or follows)
  – Possible Prodrome?
Findings in Delirium

• Psychosis
  – Perceptual disturbance (illusions, AVTOG hallucinations)
  – Delusions (paranoid and poorly formed)
  – Thought disorder (tangential, circumstantial, LOA)
Findings in Delirium

• **Sleep-Wake Disturbance**
  – Fragmented throughout 24 hours
  – Reversal of normal cycle
  – Sleeplessness
Findings in Delirium

• **Motor Behavior** (often used to describe phenotype)
  – Hyperactive (30%)
  – Hypoactive  (24%)
  – Mixed       (46%)
Findings in Delirium

• **Language Impairment**
  – Word-finding difficulty/paraphasia
  – Comprehension deficits
  – Altered semantic content
  – When severe, can mimic expressive/receptive aphasia
Findings in Delirium

• **Altered or Labile Affect**
  – Any mood can occur (commonly incongruent)
  – Anger or irritability
  – Hypoactive delirium ‘labeled as depression’
  – Lability (rapid shifts)
  – Unrelated to mood preceding delirium
  – Fear
  – Anxiety
  – Perplexity
‘The Clinical Picture’

- Disturbance of Cognition
- Disturbance of Consciousness & Attention
- Disturbance of Circadian Rhythm
- Disturbance of Psychomotor Activity
- Disturbance of Emotion

Delirium
Delirium

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• Recovery
Epidemiology

- General Adults: 10-24%
- General Surgery: 37-46%
- Post-Op: 10-60%
- Stroke: 13-48%
- HIV/AIDS: 20-40%
- ‘Frail-Elderly’: 60%*
- Medical ICU: 60-80%
- Advanced Cancer: 85%*
- CABG: 25-32%
- Cardiotomy: 50-67%
- B/L Knee Replacement: 41%*
- Femoral Neck Fx Repair: 65%* (*Denotes ‘up to’)
Epidemiology

- Emergency Room - 8-17%
- Nursing Home - 20-56%
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Risk Factors & Etiology

- Age >75 years old
- Baseline cognitive dysfunction
- Male gender
- Sensory impairment
- Use of IV lines, catheters, restraints
- Sleep deprivation
- Over-sedation
- Poorly controlled pain
Risk Factors & Etiology

- Infections (UTI and Pneumonia common)
- Hip fracture
- Hyper/Hypo- thermia
- Hypotension/Hypo-perfusion
- Hypertension (‘encephalopathy’)
- Hypoxia
- Malnutrition & nutrition deficiency
  (Wernicke/B12, folate)
Risk Factors & Etiology

• Metabolic ‘Encephalopathy’ (cardiac, hepatic, renal, MI, PE)
• Endocrinopathy (thyroid)
• Electrolyte/water imbalance & dehydration
• Hyper/Hypo-glycemia, -natremia, -kalemia
• Dehydration
• Elevated cortisol
• Low Albumin
Risk Factors & Etiology

- CNS pathology (CVA, ICH, NPH)
- Trauma (physical or surgery)(burns)
- Medication (polypharmacy, psychoactive, serotonergic, anticholinergic, OTC)
- Substance abuse/withdrawal
- Heavy metals
- Toxins
- Cancer
Probability Of Delirium vs Age

![Graph showing the probability of transitioning to delirium against age, with a p-value of 0.004.](image)
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Neuropathogenesis
Neuropathogenesis

- Impaired neurotransmitters and neural circuitry leads to a final pathway which results in a common clinical expression; delirium.
- The final neural network involves regions and circuits that support consciousness and higher level thinking.
- Dysfunction can occur in cortical and subcortical regions.
- EEG findings are generally seen (‘diffuse slowing’).
Neuropathogenesis

• **Acetylcholine**
  – Reduced cholinergic activity is the best established mechanism for delirium (Benadryl)
  – **Cholinergic system** is involved in:
    • Cortical activation
    • REM sleep induction
    • EEG fast-wave activity
    • Motor components of behavior
    • Attention, learning, memory, mood, etc.
Neuropathogenesis

- Dopamine
  - increased in delirium

- GABA
  - Increased or decreased in delirium

- Cytokines, false neurotransmitters, quinolinic acid, interleukin, C reactive protein, etc.
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Financial Impact of Delirium

• Costs Medicare $164 billion per year. (2011)
• Costs hospital >$11 billion per year.
• Post-hospital costs are $153 billion per year
• Increased Re-hospitalization
• Increased ER visits
• Increased Institutionalization
• Increased Rehabilitation
• Increased Home care services
• Increased Caregiver burden
Financial Impact of Delirium

• Milbrandt et al. (2004) compared costs in mechanically ventilated MICU patients.
• Controlled for age, comorbidity of illness, degree of organ dysfunction, nosocomial infection, hospital mortality.
• Median ICU cost >$13k for non-delirious patient and >$22k for delirious patient.
• Total hospital cost >$27k for non-delirious patient and >$41k for delirious patient.
Length of Stay in Delirium

- Emond (2018)- Increased LOS by >4 days.
- Francis (1990)- Increased LOS by 5-10 days.
- McCusker (2003)- Increased LOS by >7 days.
- Han (2011)- Patients who were delirious in the ER stayed twice as long in the hospital when compared to non-delirious patients.
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Morbidity & Mortality of Delirium

- Functional & cognitive decline
- Increased rates of dementia
- Institutionalization
- Post-traumatic stress disorder
- Caregiver burden
- Poor participation PT & OT
- Pull tubes, IVs, catheters
Morbidity & Mortality of Delirium

- Self-harm from delusions and hallucinations
- Disruptive behavior
- Poor PO intake & failure to thrive
- Falls (head trauma & fractures)
- Decubitus ulcers
- Urinary incontinence & UTI
- Poor performance in ADL’s
- Medication refusal
Morbidity & Mortality of Delirium

• Increased risk of death (4-65%)
• Increased risk of death (4-65%)
• Increased risk of death (4-65%)

• Francis (1990) notes 8% vs 1% rate of mortality in the elderly in the acute medical setting when delirium is present.
• Curyto (2001) 3 year mortality 75% vs 51%.
Recognition of Delirium

• 1 out of every 3 physicians recognizes delirium

• 1 out of every 3 nurses recognizes delirium

• In literature recognition of delirium is associated with less mortality and shorter length of stay (opposite is true as well)
Delirium Rating Scales

- RASS
- IQCODE
- NEECHAM Confusion Scale
- Nursing Delirium Screening Scale
- Delirium Observation Screening Scale/Delirium Observation Scale
- Intensive care delirium screening checklist
- Pediatric Anesthesia Emergence Delirium scale
- Global Attentiveness Rating
- Delirium Symptom Interview
- Saskatoon Delirium
- Checklist
- Delirium Rating Scale-revised version
- Memorial Delirium Assessment Scale
- Confusion Assessment Method
- CAM-ICU
- Pediatric CAM-ICU
- Clinical Assessment of Confusion - A and B
- Delirium Rating Scale
- Delirium Rating Scale-Revised-98
- Confusion Assessment Method
- Clock Drawing test
- Delirium
- Cognitive Test for Delirium
- Digit Span Test
- Vigilance “A” Test
- Mental state
- Questionnaire
- Care Unit assessment tool
- Short Portable Mental Status Questionnaire
- Delirium-O-Meter
- Delirium Index
- Memorial Delirium Assessment Scale
- Confusional State Evaluation Scale
- Delirium Assessment Scale
- Delirium Severity Scale
- Mini Mental Status Examination
- Delirium Motor Checklist, Delirium
- Motor Symptom Scale
- Richmond Agitation and Sedation Scale
- Motoric items of Delirium Rating Scale, Delirium Rating Scale-Revised-98, Memorial Delirium Assessment Scale
- Delirium Etiology Checklist
- Pediatric Anesthesia Emergence Delirium scale
- Delirium Experience Questionnaire
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What is the Cognitive Baseline?
Figuring Out Baseline

• How long is your DAD having difficulty with memory? (*Duration/Trajectory*)
• When is the last time MOM was like you and I in terms of orientation, memory, interaction, etc.? (ask about *consistency of cognitive strengths*)
• When did you notice Grandpa get worse? (*acute worsening*)
• Did Grandma develop psychosis, mood, agitation, suicidality or homicidality? (*or is it old*)
• Find the impairment and track its course through history (*counting, spelling, bills, groceries, etc.*)
## What is New & What is Old?

<table>
<thead>
<tr>
<th></th>
<th>Delirium</th>
<th>Dementia</th>
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<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>Acute/Subacute</td>
<td>Insidious</td>
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<tr>
<td><strong>Course</strong></td>
<td>Fluctuating</td>
<td>Progressive</td>
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<td><strong>Reversibility</strong></td>
<td>High</td>
<td>Low</td>
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<tr>
<td><strong>Consciousness</strong></td>
<td>Impaired</td>
<td>Clear until late stage</td>
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<tr>
<td><strong>Attention/Memory</strong></td>
<td>Inattention &amp; Impaired short/long-term retrieval</td>
<td>Attentive &amp; Impaired short term retrieval (long-term in late stages)</td>
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<td><strong>Hallucinations</strong></td>
<td>Commonly visual (or any other)</td>
<td>Visual or auditory</td>
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<tr>
<td><strong>Delusions</strong></td>
<td>Fleeting, fragmented, persecutory</td>
<td>Fixed and paranoid</td>
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</table>
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Work-up & Differential Diagnosis

• Discovering the etiology is key.
• Treating the underlying etiology is the 1st step in treatment.
## Work-up & Differential Diagnosis

### Laboratory Tests
- Medication Evaluation
- CBC/BMP
- LFT
- TFT
- UA/Urine Culture
- Blood Culture
- Urine Toxicology/Blood Alcohol
- Thiamine/B12/Folate
- ESR
- NH3
- Glucose
- PTH
- Calcium
- EKG
- CK
- PO4
- HCG
- ALB
- HIV/RPR

### Imaging Tests
- Chest X-ray
- Abdominal X-ray
- CT Head
- CT Abdomen/Pelvis
- MRI Head/A/P
- EEG
- LP
- MRV
- D-Dimer
- ANA/DS-DNA
- ACE Level
- Lyme
- Quantiferon
- Lead/Mercury/Other
- Antibody Spectrum
- PET scan
Non-Pharmacologic Treatment

• Correct malnutrition, electrolytes, dehydration.
• Remove immobilizing lines, tubes, catheters and restraints.
• Correct sensory deficits (glasses, hearing aids).
• Promote normal circadian rhythm (lights, curtains, noise).
• Environmental stimulation (orientation, TV, newspaper)
• Minimize isolation.
Pharmacologic Strategy

- Avoid anticholinergic medication.
- Avoid GABA-ergic drugs (BZD!!!!!!).
- Adequately treat pain.
- Avoid opioids for behavior.

On to symptom-targeted treatment with medication...
# Neurochemical Pathways

<table>
<thead>
<tr>
<th>Delirium Source</th>
<th>ACH</th>
<th>DA</th>
<th>GLU</th>
<th>GABA</th>
<th>5HT</th>
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<th>His</th>
<th>Cytok</th>
<th>HPA axis</th>
<th>NMDA activity</th>
<th>Changes in RBF</th>
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<td>Hepatic Failure (encephalopathy)</td>
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Symptom-targeted Treatment

- **General Treatment Options:**
  - Melatonin (PO)
  - Precedex (IV)
  - Clonidine (PO, Patch or Epidural)
  - Zofran (PO/IM/IV)
  - Rivastigmine (PO or Patch)
  - Namenda/Donepezil/Amantadine (PO)
  - Tylenol (PO/IV)
Symptom-targeted Treatment

• Hyperactive/Agitation Phenotype:
  – Antipsychotics
    • Haloperidol/Haldol (PO/IM/IV)
    • Olanzapine/Zyprexa (PO/IM)
    • Risperidone/Risperdal (PO)
    • Quetiapine/Seroquel (PO)
    • Ziprasidone/Geodon (PO/IM)
  – AED/Mood Stabilizer
    • Valproic Acid/Depakote (PO/IV)
    • Oxcarbazepine/Trileptal (PO)
    • Carbamazepine/Tegretol (PO/IV)
    • Gabapentin/Neurontin (PO)
Symptom-targeted Treatment

• Hypoactive (‘Depressed’) Phenotype
  – Antipsychotics
    • Haloperidol/Haldol (PO/IM/IV)
    • Risperidone/Risperdal (PO)
    • Aripiprazole/Abilify (PO & IM unavailable)
  – Stimulants
    – Modafinil/Provigil
  – Amantadine
  – Bromocriptine
  – Memantine/Namenda
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Recovery

• Delirium by definition is reversible.
• Requires treatment of underlying cause and ‘weeks to months’ of time to formally ‘recover’.
• Many follow-up studies showing poor cognitive performance months after acute delirium.
Recovery

Cognitive Functioning vs Time
Additional Considerations

• **Metoclopramide/Reglan** is a D2 antagonist, often given to children, pregnant women and elderly for nausea.

• **Prochlorperazine/Compazine** is a D2 antagonist given for nausea.

• **Promethazine/Phenergan** is a DA blocker and used for nausea. Created in 1940s.

• **Droperidol** is a D2 antagonist used for nausea and migraines.
Additional Considerations

• **Black Box Warning with Antipsychotics for Dementia with Psychosis**
  – Increased risk of death over 10 weeks (mode).
    • 2.6% in placebo group.
    • 4.5% in the treatment group.
  – Death due to cardiovascular causes.
    • *Ex: Heart failure & sudden death*
  – Death due to infectious causes.
    • *Ex: Pneumonia*
  – 1.6-1.7 times the risk of death in placebo patients
Additional Considerations

• Extra-pyramidal Symptoms
• Metabolic Syndrome
• EKG abnormalities
• Blood Dyscrasia
• Pancreatitis
• ......
A Final Thought…

• Is there a safer way to address **acute agitation** and/or **psychosis** in the elderly with delirium & dementia? **Appetite? Sleep? Sadness?**

• Please consider the route when answering this question; PO/IM/IV.
References

- Emond et al. Incidence of delirium in the Canadian emergency department and its consequences on hospital length of stay: a prospective observational multicentre cohort study. BMJ Open 2018
- HELP Website http://www.hospitalelderlifeprogram.org
- Pandharipande et al. Lorazepam is an independent risk factor for transitioning to delirium in the intensive care unit patients. Anesthesiology 2006.
Thank You

Questions