Delirium
The Acute Syndrome of Brain Insufficiency

David P. Kasick, M.D.
Assistant Professor of Clinical Psychiatry
and
Nathan O’Dorisio, M.D.
Assistant Professor of Internal Medicine
Ohio State University Medical Center

Delirium by Other Names
- Encephalopathy
- Metabolic Encephalopathy
- Hepatic Encephalopathy
- Acute Mental Status Change
- ICU Psychosis/ICU Syndrome
- Acute Organic Brain Syndrome
- Toxic Psychosis
- Febrile Insanity
- Acute Confusional State

History
- Etymology: Latin, from delirare
  ✓ “Out of the furrow” (in plowing)
- Physicians have long recognized states of altered behavior associated with:
  ✓ Fever, poisons, or other medical and neurological diseases
- Hippocrates provided the first written description of the syndrome

DSM-IV-TR Criteria
Delirium due to a General Medical Condition
- Disturbance of consciousness
  ✓ Reduced ability to focus, sustain or shift attention
- Impairment of lucidity or other cognitive function or development of a perceptual disturbance
  ✓ Not better accounted for by a dementia
- Distinctive clinical course
  ✓ Develops over a short period of time and tends to fluctuate during the course of the day
- Evidence that the disturbance is caused by the direct physiologic effects of a general medical condition, substance use, or substance withdrawal
### “Consciousness”

- “Paying attention” or “awareness”
- Ability to mentally respond to sensory experiences, including:
  - Awareness of immediate environment and circumstances
  - Ability to focus and sustain attention
  - Ability to shift attention
- Delirium always includes impairment of consciousness

### “Lucidity”

- “Clarity of thought”
- Effective use of cognitive functions for interacting with the immediate environment:
  - Memory registration, storage, and retrieval
  - Recognition, comprehension
  - Concentration
  - Reasoning and judgment
  - Language skills, ability to communicate

### The Continuum of Consciousness

<table>
<thead>
<tr>
<th>Stuporous</th>
<th>Somnolent</th>
<th>Relaxed</th>
<th>Alert</th>
<th>Attentive</th>
<th>Vigilant</th>
<th>Hyperaroused</th>
<th>Distractable</th>
<th>Hypervigilant</th>
<th>Coma</th>
</tr>
</thead>
</table>

### “Lucidity”

- Impairment of consciousness can impair lucidity
- Impairment of lucidity does not necessarily imply impairment of consciousness, nor vice versa
The Continuum of Lucidity

- IMPAIRED LUCIDITY
- NORMAL LUCIDITY
- DISORIENTED TO PLACE
- CONFUSED
- ACCURATELY AWARE
- COHERENT
- FLUENT
- ORGANIZED
- DISORIENTED TO SELF
- DISORIENTED TO TIME

Delirium is frequently misdiagnosed

- Hypoactive symptoms:
  - “Dementia”
  - “Acute Onset Dementia”
  - “Acute Onset Depression”
- Hyperactive symptoms:
  - “Acute Onset Psychosis”
  - “Acute Schizophrenic Break”
- 23-42% of patients referred to C/L psychiatrists for depression were diagnosed with delirium

Subtypes of Delirium

- Hyperactive (~25%)
  - Sympathetic nervous system hyperactivity
  - Psychomotor agitation
  - Verbal or physical aggression
  - Motor perseveration
  - Wandering
  - Increased alertness to stimuli
  - Mood lability, anger, euphoria
  - Mixed (~35%)
    - Signs and symptoms of both types

- Hypoactive (~25%)
  - Lethargy and somnolence
  - Withdrawn, apathetic
  - Decreased response to stimuli
  - Psychomotor retardation
  - Clouded consciousness, inattention
  - Slow speech

Delirium vs. Dementia

<table>
<thead>
<tr>
<th></th>
<th>DELIRIUM (acute onset)</th>
<th>DEMENTIA (gradual onset)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONSCIOUSNESS</td>
<td>Impaired, Fluctuating</td>
<td>Normal</td>
</tr>
<tr>
<td>LUCIDITY</td>
<td>Impaired, Fluctuating</td>
<td>Impaired</td>
</tr>
<tr>
<td>COGNITIVE FUNCTIONING</td>
<td>Impaired, Fluctuating</td>
<td>Impaired</td>
</tr>
<tr>
<td>SYMPTOMS</td>
<td>Any are possible</td>
<td>Typically restricted</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(cognitive)</td>
</tr>
</tbody>
</table>
## Clinical Features Suggesting Delirium in a Psychotic Patient

- Altered level of consciousness
- Rapid onset of symptoms
- Recent onset of impairment of memory and other cognitive functions
- Disorientation for time and place (not caused by delusional thinking)
- Impaired awareness of the environment

## Why is recognizing and treating delirium so important?

- Morbidity and mortality of any serious disease are doubled with delirium
  - 3 month mortality rate is ~28%
  - 1 year mortality rate is ~50%
- Harbinger of death or worsening medical illness
- 10% of hospitalized patients have delirium at any point in time
  - 20% with severe burns
  - 30% hospitalized with AIDS
  - 40% of elderly at some point during general hospital stay

## Clinical Features Suggesting Delirium in a Psychotic Patient

- Predominance of hallucinations in modalities other than auditory
- Presence of a general medical condition capable of altering metabolic support of brain function
- Evidence of use of a psychoactive substance capable of causing delirium during intoxication or withdrawal
- Onset of first psychotic episode after age 45
- No history of mental illness or premorbid symptoms

## Prevalence of Delirium in Specific Populations

<table>
<thead>
<tr>
<th>Population</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency Department</td>
<td>10-14%</td>
</tr>
<tr>
<td>Hospitalized medically ill patients</td>
<td>10-30%</td>
</tr>
<tr>
<td>Hospitalized elderly patients</td>
<td>10-40%</td>
</tr>
<tr>
<td>Cancer Patients</td>
<td>25%</td>
</tr>
<tr>
<td>Intensive Care Unit</td>
<td>30%</td>
</tr>
<tr>
<td>Post-CABG</td>
<td>30%</td>
</tr>
<tr>
<td>Postoperative Patients</td>
<td>10-51%</td>
</tr>
<tr>
<td>Patient with AIDS</td>
<td>30-40%</td>
</tr>
<tr>
<td>Cardiac Surgery patients</td>
<td>&lt; 74%</td>
</tr>
<tr>
<td>Terminally ill patients</td>
<td>&lt; 80%</td>
</tr>
<tr>
<td>Coexistent brain disease</td>
<td>&lt; 81%</td>
</tr>
</tbody>
</table>
Increased Risk for Delirium in Patients with:

- CNS disorders
  - HIV, Parkinson’s, CVA, etc.
- Postoperative states
- Very young or old age
- Dependence on alcohol or sedative hypnotics
- Underlying dementia
- Mental retardation
- Severe burns
- Sensory deprivation
- Undertreated pain
- Polypharmacy

Some Characteristics of Delirium

- Acute onset and fluctuating course are strongly suggestive
  - “Waxing and waning”
  - Change from baseline
  - Often obtained from nursing staff or family
- Altered consciousness
- Inattention, difficulty with focus, easily distractible
  - Problems keeping track of what is being said
- Impairment of lucidity or other cognitive function

Impact of Delirium

- Utilization of greater amounts of hospital resources
- Increased rates of ECF placement and length of hospital stays
- More frequent major postoperative complications
- Experience poor functional recovery

Some Characteristics of Delirium

- Delirium may include any psychiatric symptom:
  - Psychotic symptoms
    - Delusions, hallucinations, thought disorder, paranoia, fearfulness
    - Disorganized speech and thinking
      - Rambling or irrelevant conversation
      - Unclear or illogical flow of ideas
      - Unpredictable switching from subject to subject
### Some Characteristics of Delirium

- Mood symptoms
  - Emotional lability
  - Depression to Euphoria
  - Irritability, agitation
- Anxiety

### Some Characteristics of Delirium

- Psychomotor increase or decrease
- Nonspecific, nonlocalizing neurological abnormalities
  - Tremor, asterixis, myoclonus, change in muscle tone

### Some Characteristics of Delirium

- Memory deficits
- Disorientation
- Visual-constructional impairment
- Language disturbance
- Sleep-wake cycle disturbance

### Clinical Course of Delirium

- **Onset:**
  - Typically acute (hours to days)
  - Occasionally subacute (days to weeks)
  - May be abrupt
- **Diurnal variation:**
  - FLUCTUATION is characteristic and highly suggestive
  - Lucidity is typically best in morning
  - Confusion is typically greatest at night
- **Environmental interaction:**
  - Worsened by excessive sensory stimulation or marked sensory deprivation
**Clinical Course of Delirium**

- **Duration:**
  - Typically hours to days
  - Sometimes weeks to months

- **Outcome:**
  - Many have full recovery
    - Often not by the time of discharge
  - Persistent cognitive deficits are common
    - Dementia, amnestic syndromes
    - New, lower cognitive baseline
  - Progression to other injuries and death

**Pathophysiology**

- Causes are often multiple and additive
  - Each cause alone may or may not be able to cause delirium by itself
    - 56% of elderly patients with delirium had a single cause
    - Remaining 44% had an average of 2.8 etiologies
  - Beware: “Their basic labs look normal”

**Pathophysiology / Etiology**

- Current understanding is limited
- Results from disturbances of metabolic function of the brain
- A large number of different abnormalities may alter brain metabolism
  - Hence the large list of potential etiologies

- The entire neuronal population of the brain is affected
- Several theories exist:
  - Dysfunction of the Reticular Activating System (RAS)
    - Arousal and motivation centers in brainstem
  - Dysfunction of neurochemical systems
    - Noradrenergic, GABAergic, dopamine, and serotonin systems
  - Hypofunction of cholinergic system
    - Classic model of anticholinergic drug toxicity
      - "Hot as a Hare, Dry as a Bone, Red as a Beet, Mad as a Hatter, Blind as a Bat"
Delirium: Identifying the Underlying Problem

- The primary treatment of delirium:
  - Diagnose and correct the underlying medical cause(s)

Delirium: Emergent Differential ("WHHHHIMP")

- Wernicke’s or Withdrawal
- Hypoxia
- Hypoglycemia
- Hypoperfusion
- Hypertension
- Infection or Intracranial bleed
- Meningitis
- Poisons or Medications

Delirium: Differential ("I WATCH DEATH")

- Infection
  - Sepsis, encephalitis, meningitis, syphilis, HIV, etc.
- Withdrawal
  - Alcohol, benzodiazepines, barbiturates

Delirium: Differential ("I WATCH DEATH")

- Acute Metabolic
  - Electrolyte disturbance (especially Na+)
  - Renal Failure
  - Hepatic Failure
  - Acidosis or alkalosis
- Trauma
  - Closed head injury, postoperative states, heat stroke, severe burns
Delirium: Differential ("I WATCH DEATH")

- **CNS Pathology**
  - Abscess, hemorrhage, hydrocephalus, subdural hematoma, seizures, CVA, tumors, metastases, vasculitis, sleep deprivation
- **Hypoxia**
  - Anemia, carbon monoxide poisoning, hypotension, pulmonary failure, cardiac failure
- **Deficiencies**
  - Vitamin B₁₂, folate, thiamine, niacin

Substances Associated with Delirium

- Anticholinergics
- Anticonvulsants
- Cimetidine
- Ranitidine
- Inhalants
- Cardiac glycosides
- Tricyclic antidepressants
- Nifedipine
- Solvents
- Cocaine
- Opiates
- Antihypertensives
- Clonidine
- Antiparkinsonians
- Amphetamines
- Theophylline
- Captoril
- Antivirals
- Organophosphates
- Benzodiazepines
- Alcohol
- Steroids
- Lithium
- Antibiotics
- Furosemide
- Muscle Relaxants
- Hallucinogens
- And many more.....

Drugs whose anticholinergic effects may increase the risk of delirium...

<table>
<thead>
<tr>
<th>Drug</th>
<th>Anticholinergic Level*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cimetidine</td>
<td>0.86</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>0.55</td>
</tr>
<tr>
<td>Theophylline</td>
<td>0.44</td>
</tr>
<tr>
<td>Digoxin</td>
<td>0.25</td>
</tr>
<tr>
<td>Lanoxine</td>
<td>0.25</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>0.22</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>0.22</td>
</tr>
<tr>
<td>Furosemide</td>
<td>0.22</td>
</tr>
<tr>
<td>Isosorbide</td>
<td>0.15</td>
</tr>
<tr>
<td>Warfarin</td>
<td>0.12</td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>0.11</td>
</tr>
<tr>
<td>Codeine</td>
<td>0.11</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>0.11</td>
</tr>
</tbody>
</table>

* ng/ml in atropine equivalents
Assessment of the Patient with Delirium

Basic Laboratory Tests

- Chem 10
- LFT's
- CBC
- EKG
- CXR
- ABG or pulse ox
- Urine Tox Screen
- Blood/Urine cx

- Measurement of serum drug levels
- B12, folate
- TSH
- UA

Management of Delirium

#1: Provide Medical Care

Goal: Find (and correct) the medical reason(s) for the delirium

- Interview patient and family
- History, physical and neurologic exam
- Establish baseline

Assessment of the Patient with Delirium

Additional Tests

- Order as indicated by clinical history
- EEG
  - Generalized slowing (unless withdrawal)
- Brain CT or MRI
- LP
- Ammonia
- ESR

- Heavy metal screen
- Urine porphyrin levels
- ANA
- HIV
- RPR/VDRL

Management of Delirium

- Review and discontinue nonessential medications
- Review and monitor vitals
- Determine if patient is in significant pain
- Avoid interruptions in sleep, whenever possible
- Cognitive Testing, if needed
  - Delirium Rating Scale
  - Confusion Assessment Method
  - Mini Mental Status Exam
Management of Delirium

• #2: Prevent and manage disruptive and dangerous behaviors
  ✓ Place the patient in a room near the nursing station/natural light
  ✓ Order a sitter for any dangerous behavior
  ✓ Medical hold order
    • You cannot “pink slip” a patient to a general hospital bed

• #3: Use medications as needed
  ✓ Antipsychotics for agitation
    • Haldol, Risperdal, Seroquel, others
  ✓ Avoid benzodiazepines unless in alcohol or sedative-hypnotic withdrawal delirium
  ✓ Avoid narcotics unless the patient has significant pain
    • Do not use meperidine (seizures, delirium, serotonin syndrome)
  ✓ Avoid anticholinergic medications
    • Effects are additive

Management of Delirium

✓ Low bed position
✓ Use restraints only if necessary
  • Emergencies or if medications fail
  • May try Posey vest/bed belt first
✓ Avoid placing in a room with another delirious patient
✓ Avoid a room cluttered with equipment or furniture

• #4: Facilitate reality
  ✓ Encourage presence of family members
  ✓ Provide familiar cues
    • Analog clock, calendar
  ✓ Provide adequate day and night lighting
    • Sunny side rooms
    • Use a night light
  ✓ Minimize transfers
### Management of Delirium

- Maximize staff continuity
- Reduce excessive environmental stimuli (noise)
- Orient patient to staff, surroundings, and situations repetitively
  - Especially before procedures
- Repeatedly reassure the patient
- Ensure use of hearing aids, glasses, dentures
- Encourage the use of personal belongings

### Typical (aka First Generation) Antipsychotics

- Haloperidol
  - Oral, IM, IV
  - Efficacy well established
  - No optimum dose established but scheduled low doses are preferable to large doses administered PRN
  - Dosage: 1-2 mg every 2-4 hrs
    - (0.5-1 mg every 6-12 hrs in elderly)
- Lower risk of EPS with IV forms
- May lengthen QTc: risk for torsades de pointes (significant risk in patients with alcoholic cardiomyopathy)
- May lower seizure threshold
- To convert IV to oral dosage, double the IV dose

### QTc Prolongation with Antipsychotics

- Prolongation greater than 450 msec or 25% over previous EKG is concern
- Telemetry, cardiac evaluation, and dosage reduction
- Monitor serum magnesium and potassium in critically ill patients
### Atypical (aka Second Generation) Antipsychotics

- **Risperdal** (risperidone)
- **Zyprexa** (olanzapine)
- **Seroquel** (quetiapine)
- **Geodon** (ziprasidone)

- Reasonable clinical evidence for use of all atypical antipsychotics
- Questionable increased risk of CVA in elderly (short term use less risky, ~3 days)

### Additional Treatments for Delirium

- **Cholinergics**
  - Traditionally used for anticholinergic toxicity
  - Data exists to potentially support use in other types
  - Rivastigmine, donepezil, physostigmine

- **Melatonin**
  - Case reports of efficacy in postoperative delirium

- **Depakote**

### Benzodiazepines

- Use only for alcohol or benzodiazepine withdrawal state or seizure activity
- Benzo monotherapy alone found ineffective in general delirium
- Combined use with antipsychotics
  - Some increase in symptom reduction - but -
  - May worsen mental status or cause disinhibition
- Avoid in hepatic encephalopathy, severe respiratory depression
- Prefer benzos that are glucuronidated (LOT)
  - Lorazepam, Oxazepam, Temazepam

### Additional Treatments for Delirium

- Paralytics/sedation/ventilation support
  - Extreme cases in which agitated delirium presents serious risk of harm
  - Hyperdynamic heart failure, ARDS, thyroid storm, self-injurious behavior, withdrawal states

- **ECT**
  - Not of value in general delirium
  - Potential treatment for NMS

- Better screening and rapid treatment intervention programs have more value than attempts to predict who will become delirious
Competence vs. Capacity

- The presence of delirium does not always automatically mean that a patient is “incompetent” or lacks capacity to give informed consent
  - Competency is a legal term, determined by a judge
  - Decision making capacity can be assessed by physicians
- Assessment of patient’s understanding and appreciation must be done about proposed intervention
  - For a specific decision at a specific point in time
- If deemed “incapable” (lacking capacity) it is typically a transient incapacity not requiring formal guardianship papers, hearing, etc.
- Consent can be obtained from surrogate decision maker/legal next of kin

Summary

- Correct treatment of delirium can be lifesaving
- Failure to manage delirium results in increased morbidity, mortality, and costs to the healthcare system

Summary

- Delirium is a common clinical syndrome
- Diagnosis of delirium is frequently missed or misdiagnosed
  - Psychiatric consultation may help clarify that symptoms are not consistent with serious mental illness (depression, schizophrenia, bipolar mania, etc.)
  - Misattribution of behavioral symptoms/mental status changes to a primary psychiatric condition is a common but critical conceptual error
- Think of the symptoms of delirium as a harbinger of worsening underlying medical illness
  - Find and treat the underlying medical cause
- Much can be done behaviorally, environmentally, and pharmacologically to improve clinical outcomes
- Treating delirium will test your observation and communication skills
  - Remember the increasing importance of “customer satisfaction scores”
Delirium Algorithm

Case #1

1. As a consulting psychiatrist, you are asked to evaluate a 77 year old male for “new onset schizophrenia.” He was brought to the hospital by ambulance after his wife called 911 when he had an acute onset upon waking early this morning of confusion, disorientation for time and place, inattention, clouded consciousness, auditory hallucinations, paranoia, and screaming “Fire in the hole!” and “Take cover!”

2. His wife of 54 years is present at the bedside and provides a seemingly reliable history. She says that he has multiple medical problems including hypertension, hypothyroidism, diabetes, and high cholesterol. He has been feeling ill recently and was treated for a “chest infection” by the family doctor. He takes 12 different medications on a daily basis, including several with anticholinergic properties. He has no personal or family history of mental illness and no history of substance abuse. He retired from a career as an insurance salesman at age 65. They have 3 children and eight grandchildren.

3. You correctly diagnose delirium and recommend a full medical workup to find the underlying medical cause and other delirium treatment options to his medical team.
Case #1

Which of the following factors is most helpful in distinguishing delirium from schizophrenia in the above vignette?

a. clouded consciousness  
b. the patient behaving unpredictably  
c. the patient’s wife is frightened  
d. the patient’s paranoia  
e. auditory hallucinations

Correct answer: A

References


Case #1

Which of the following suggest delirium rather than schizophrenia?

a. social or occupational dysfunction  
b. the presence of delusions  
c. rapid onset of altered level of consciousness  
d. the presence of psychosis  
e. disorganized behavior

Correct answer: C