Delirium: Recognizing, Assessing and Managing Terminal Restlessness

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Overview: Delirium

Q1:
Which symptom is characteristic of delirium?

a) impairment of only short term memory
b) impairment of attention
c) agitation or restlessness
d) delusions or hallucinations

Delirium
Delirare: to be crazy
De lira: to leave the furrows

Early Descriptions
“they move the face, hunt in empty air, pluck nap from the bedclothes...all these signs are bad, in fact deadly”
Hippocrates:400 BCE

“Sick people...lose their judgment and talk incoherently...when the violence of the fit is abated, the judgment presently returns...”
Celsus: 1st Century BCE

What is it?
**Delirium**

- Synonyms: acute confusional state, organic brain syndrome, encephalopathy, terminal agitation, terminal restlessness
- Often mistaken for depression, anxiety, or dementia

**Terminal Agitation:**
A symptom or sign: thrashing, agitation that may occur in the last days or hours of life.
May be caused by:
- pain
- anxiety
- dyspnea
- delirium

**Clinical Subtypes: Delirium**

- Hyperactive
- Mixed
- Hypoactive

**DSM-IV Criteria: Delirium**

- Disturbance of consciousness affecting attention
- Change in cognition
- Develops over a short period of time, and may fluctuate
- Caused by physiologic consequence of a general medical condition

**Delirium vs. Dementia vs. Depression**

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

**Dying with Dementia**

- Agitation • 87%
- Confusion • 83%

*J. Geriatric Psychiatry 1997*

**Why bother identify and treat?**
### Q2:
Delirium is experienced in up to what percentage of terminally ill cancer patients?

- a) 10%
- b) 18%
- c) 40%
- d) 85%

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**Delirium is common WHY TALK ABOUT IT?**

Up to 85% people experience it at end of life
25-40% of hospitalized cancer patients

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**Delirium is harmful WHY TALK ABOUT IT?**

Interferes with meaningful communication and interaction

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**Delirium hurts relationships WHY TALK ABOUT IT?**

Creates sense of fear and helplessness

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**Delirium conflicts with patient goals WHY TALK ABOUT DELIRIUM?**

JAMA 2000; 284: 2476-2482 • NEJM 2002; 346: 1061-1090

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**Delirium causes caregiver distress WHY TALK ABOUT IT?**

Am J Geriatr Psychiatry 2003; 11: 309 - 319

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>70% seriously ill patients want cognitive awareness

89% patients refuse treatments that impair cognition
Delirium is common
Delirium is harmful
Delirium hurts relationships
Delirium conflicts with patient goals
Delirium causes caregiver distress

WHY TALK ABOUT IT?

WHAT CAUSES IT?

Q3:
Which is not a risk factor for delirium?

a) Age
b) Cognitive impairment
c) Gender
d) Opioid use
e) Constipation

Case: Paul
• Paul is 72 years old, with Alzheimer’s disease and lung cancer.
• Retired dentist, active and “in charge”
• Now agitated, combative, trying to get out of bed

What patients are at risk?

Drugs, drugs, drugs, dehydration
DMotion, encephalopathy, environmental change
Low oxygen, low hearing/seeing
Infection, intracerebral event or metastasis
Retention (urine or stool)
Intake changes (malnutrition, dehydration), Immobility
Remia, under treated pain
Metabolic disease

WHAT CAUSES IT?
Q4: Which of the following medications can cause delirium?

- a) Lorazepam
- b) Hyoscymine
- c) Dexamethasone
- d) All of the above
- e) None of the above

Diagnosis of exclusion
Delirium during the dying process
Signs of the dying process
Multiple causes, often irreversible

TERMINAL DELIRIUM
CAN IMPENDING DEATH CAUSE IT?

Case: Paul – is he at risk for delirium?

<table>
<thead>
<tr>
<th>Predisposing factors</th>
<th>Possible precipitating factors</th>
</tr>
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<tbody>
<tr>
<td>Dementia</td>
<td>Drug side effects?</td>
</tr>
<tr>
<td>Age</td>
<td>Hypoxemia?</td>
</tr>
<tr>
<td>Metastatic lung cancer</td>
<td>Infection?</td>
</tr>
<tr>
<td>Immobility</td>
<td>Constipation?</td>
</tr>
<tr>
<td>Poor oral intake</td>
<td>Urinary retention?</td>
</tr>
<tr>
<td>Polypharmacy</td>
<td>Metabolic disorder?</td>
</tr>
<tr>
<td></td>
<td>Brain metastases?</td>
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<tr>
<td></td>
<td>Emotional distress?</td>
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</table>

General Assessment: Delirium

- Hospice diagnosis, co-morbidities
- Onset of mental status change
- Oral intake, urine output, bowel movements
- Recent medication history
- Review of systems: fever, N/V, pain, dyspnea, cough, edema, decubiti
- Alcohol or illicit drug use
- Falls, safety
- Emotional, spiritual distress

Assessment: Paul

- Metastatic non-small cell lung cancer
- Severe Alzheimer’s disease
- More restless, combative in last 3 days
- Hand-fed small, pureed meals & thickened liquids but minimal in 3 days
- Small amount dark urine, no BM in 1 week
**Assessment Tools: Delirium**

- Confusion Assessment Method (CAM)
  - 94-100% sensitive, 90-95% specific
  - 10-15 minutes by trained interviewer
- SQiD (single question in delirium)
  - “Do you think Paul has been more confused lately?”
  - 80% sensitive and 71% specific in oncology patient

**Confusion Assessment Method**

<table>
<thead>
<tr>
<th>Feature 1: Acute Onset and Fluctuating Course</th>
</tr>
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<tbody>
<tr>
<td>Obtained from a family member or nurse:</td>
</tr>
<tr>
<td>- Is there evidence of an acute change in mental status from the patient’s baseline?</td>
</tr>
<tr>
<td>- Did the (abnormal) behavior fluctuate during the day, that is, tend to come and go, or increase and decrease in severity?</td>
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</table>

<table>
<thead>
<tr>
<th>Feature 2: Inattention</th>
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<tbody>
<tr>
<td>Did the patient have difficulty focusing attention, for example, being easily distractible, or having difficulty keeping track of what was being said?</td>
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</table>

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<thead>
<tr>
<th>Feature 3: Disorganized thinking</th>
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<tbody>
<tr>
<td>Was the patient’s thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Feature 4: Altered Level of consciousness</th>
</tr>
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<tbody>
<tr>
<td>Overall, how would you rate this patient’s level of consciousness?</td>
</tr>
<tr>
<td>- Alert (normal), vigilant (hyperalert), lethargic (drowsy, easily aroused), stupor (difficult to arouse), or coma (unarousable)</td>
</tr>
</tbody>
</table>

The diagnosis of delirium by CAM requires the presence of features 1 and 2 and either 3 or 4.

**Diagnostic Approach to Delirium**

- Delirium is a clinical, bedside diagnosis
- Careful, gentle approach to patient
- Appearance, vital signs
- Focused exam based on history
- Consider rectal exam, catheter

**Paul’s assessment: Delirium**

- Lethargic, frail, elderly man lying in hospital bed; fidgeting of arms, legs; slow but persistent attempts to sit up or slide between siderails; quiet but anxious expression
- CAM: all features present
- Afebrile, BP 105/62, HR 95, RR 24
- Positive findings:
  - MM dry;
  - Foley catheter w/cloudy, dark urine;
  - abd distended but soft;
  - quiet BS; rectal +stool;
  - decubitus stable w/o infection

**Next steps: managing delirium weighing benefits & burdens**

- Lab tests
- Treating underlying cause(s)
- Treating agitation
### Paul’s follow up

**Goals of care:** Peaceful death at home • DNH • no needlesicks

<table>
<thead>
<tr>
<th>Treated the treatable</th>
<th>Treated the delirium</th>
</tr>
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<tbody>
<tr>
<td>• Disempaction, daily bowel regimen</td>
<td></td>
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<tr>
<td>• Treated UTI w/ liquid antibiotics</td>
<td></td>
</tr>
<tr>
<td>• Weaned lorazepam</td>
<td></td>
</tr>
<tr>
<td>• Haloperidol 0.5-1mg SL qHS and q8hrs prn</td>
<td></td>
</tr>
<tr>
<td>• Calmer environment</td>
<td></td>
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<tr>
<td>• Improved communication</td>
<td></td>
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<tr>
<td>• Encouraged safe movement</td>
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</table>

In 2-3 days, Paul was back to baseline

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### Delirium MANAGEMENT

**Prevention Protocol: Delirium**

- Orient
- Stimulate
- Mobilize
- Sleep (non-pharmacologic)
- Create restful night-time environment
- See
- Hear
- Eat/drink (based on goals of care)


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### Hospice approach to prevention

**Know the risk factors**

- Communicate
- Engage healthy relationships

**Develop a prevention/intervention plan of care**

- Address faith
- Legacy
- Relationships

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### Once it’s happened

**First step in the management of delirium**

**RECOGNIZING AND NAMING**
**Q5:** Delirium is reversible in what percentage of cases?

a) ~ 50%
b) ~ 25%
c) ~ 10%
d) ~ 1%

50% Delirium can be reversed


**Paul: follow up**

- His goals of care: to stay at home, avoid needlesticks
- Disimpacted stool, daily laxative regimen started
- UTI diagnosed and treated
- Weaned down lorazepam from 2mg to 0.25mg with good effect
- Started haloperidol 0.5-1mg SL aHS and q6 hours prn
- Created calmer environment, started legacy work

Back to baseline in 2-3 days

**Q6:** Which of the following are appropriate interventions for delirium?

a) Music during turns/personal care 
b) Minimize ambient sound (alarms, bells, voice) 
c) Aromatherapy such as Lavender or Melissa with bed bath 
d) Spiritual interventions such as prayer, ritual, meditation 
e) Cognitive behavioral therapy for PTSD 
f) Engaging family or familiar people in care 
g) All of the above
Assessing severity of agitation

1. Irritability
2. Hostile
3. Hostility
4. Lability
5. Intense stare
6. Motor restlessness
7. Uncooperative

Hierarchy of interventions for agitated delirium

1. Emergency medicine
2. Seclusion and/or restraint
3. Verbal intervention
4. Check for needs, non-pharmacologic

Step 1: Treat underlying causes
Step 2: Non-pharmacological
Step 3: Pharmacological
Address family, caregivers and other psychosocial impacts of delirium

Case 2: Rosie’s distress

- 88 yo great-grandmother with end-stage pulmonary fibrosis, renal insufficiency.
- “CMO” and morphine drip was started to treat her dyspnea – then sent home with hospice.

Please help! She is moaning, agitated, in pain even when we touch her lightly. Other times, we can’t wake her up.

Delirium Management

**STEP 1: TREAT UNDERLYING CAUSE**

Drugs, drugs, drugs, dehydration
Emotion, encephalopathy, environmental change
Low oxygen, low hearing/seeing
Infection, intracerebral event or metastasis
Retention (urine or stool)
Intake changes (malnutrition, dehydration), Immobility
Uremia, under treated pain
Metabolic disease

**STEP 1: TREAT CAUSE**

Dopamine, neurotoxicity:
- Morphine metabolized in the liver to
  - Morphine 6-glucuronide
  - Morphine 3-glucuronide
- Builds up disproportionately in renal failure
- Neuroagitation:
  - Increased RR, agitation, myoclonus, and sometimes seizures

Opioid neurotoxicity: important cause

Anti-psychotics may worsen opioid neurotoxicity: benzodiazepines and phenobarbital are treatments of choice
Rosie’s distress: treat underlying cause

Attempt to reverse morphine neurotoxicity
- Stop morphine
- Start lorazepam or phenobarbitol
- Consider IV/SQ fluids depending on goals of care

PRN SL oxycodone or IV fentanyl if needed for pain or dyspnea or schedule methadone
Oxygen for hypoxemia-induced delirium

**STEP 1: TREAT CAUSE**

Treat the pain
Address sleep-wake cycle
Create familiar environment
Facilitate range of motion & exercise

**AGITATION WITH DEMENTIA**

Sleep-wake cycle: normalize
Melatonin 3-7mg in the evening, with sunset.

**Delirium Management**

**STEP 2: NON-PHARMACOLOGIC APPROACH**

Physical environment & body

- **Sight**
  - Light/dark cycles, visual cues, familiar faces
- **Sound**
  - Reduce ambient noise, music therapy, familiar voices
- **Smell**
  - Cleanliness, aromatherapy, home cooking
- **Touch**
  - Massage, physical therapy, movement
- **Taste**
  - Drink if thirsty – but hydrating drinks. Eat if hungry – and assure good bowels.

**NON-PHARMACOLOGIC APPROACH**

- Engage chaplaincy
- Acknowledge faith, legacy, regret

- Engage social work & psychology
- Consider past troubles, history

- Engage aide, housekeeping, family
- Consider the 5 senses

- Nurses, aides, and doctors
- Exquisite care of the body

- Emotional
- Existential
- Environment
- Physical
Case 3: Mr. U

65 year old retired engineer with metastatic lung cancer to bone.

HPI: Severe pain, principally in area of leg requiring complex pain management. Now he is experiencing increased confusion, agitation, restlessness at night.

Past Medical History: Generally healthy until diagnosis.

Social History: Married to a non-catholic woman. Has 2 grown daughters. Raised Catholic but has not been to church much since his marriage.

Case 3: Mr. U’s agitation

- Physical: under treated pain
- Emotional: sadness at losing his family
- Existential:
  - Fear of afterlife
  - Unresolved conflicts
  - Never married in the Church

Existential Causes of DELIRIUM

Johann Rudolf Schnellberg after Fuseli’s “Head of a damned Soul from Dante’s Inferno” (1775)

Delirium Management

STEP 3: PHARMACOLOGIC APPROACH

Hypoactive delirium

- Day-night cycle can be critical
- Methylphenidate 5mg qam and qnoon
  - Watch for anxiety, symptomatic palpitations

STEP3: PHARMACOLOGIC Delirium Management
If all else fails, use **antipsychotics**

**MANAGING DELIRIUM**

**Antipsychotics** are the **mainstay** of pharmacologic treatment.

**FDA Black Box Warning!**
But they increase death!
Increased risk by 1.6 – 1.7 RR
absolute increase from 2.3% to 3.5% during intervention
Risk / benefit and goals of care

**STEP3: PHARMACOLOGIC Delirium Management**

**Pharmacology of Anti-psychotics**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cmax</th>
<th>T ½</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td>25mg SQ/IV/PR q3 hours prn up to 2g/day</td>
<td>1-4 hours 16-30 hours</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>25-100mg PO q1 hour prn up to 1200 mg/day</td>
<td>1-2 hours 6-7 hours</td>
</tr>
<tr>
<td>Risperidone</td>
<td>0.25-1mg PO q1 hour up to 6mg/d</td>
<td>1-1.5 hours 3-24 hours</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>5-10mg PO q4 hours prn up to 30mg/day</td>
<td>4-6 hours 20-70 hours</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>0.5 – 2 mg q1 hr prn</td>
<td>30 min – 1 hour 4-6 hours</td>
</tr>
</tbody>
</table>

**Profiles of antipsychotics**

- **Chlorpromazine**
- **Quetiapine**
- **Risperidone**
- **Olanzapine**
- **Haloperidol**

Adapted from www.PalliativeDrugs.com

**Chlorpromazine vs. Haloperidol**

<table>
<thead>
<tr>
<th>Antipsychotic Agent</th>
<th>Chlorpromazine</th>
<th>Haloperidol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedation</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>EPS</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Orthostatic</td>
<td>+++</td>
<td>+</td>
</tr>
</tbody>
</table>

**** = very high incidence, +++ = high incidence, ++ = moderate incidence, + = low incidence

Drug Facts and Comparisons (Oct 2003)
More on Anti-psychotics

<table>
<thead>
<tr>
<th>Length of use</th>
<th>↓ Sed</th>
<th>↑ Sed</th>
<th>- EPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-7 Days</td>
<td>Haloperidol 0.5-2 mg q1 hour prn IM, IV, SC PO (tab/sol) SC</td>
<td>Chlorpromazine 12.5-25 mg q 3 hours prn up to 3 grams/day IM, IV, PR SCIP PO</td>
<td>erratic</td>
</tr>
<tr>
<td>&gt;7 Days</td>
<td>Risperidone (Risperdal) PO: tab, sol, odt IM: long acting</td>
<td>Olanzapine (Zyprexa) PO: tab, odt IM: intermittent</td>
<td>Quetiapine (Seroquel) PO: tab, odt IM: intermittent</td>
</tr>
</tbody>
</table>

Choose based on level of behavior
If more hyperactive, consider atypical antipsychotics
If more hypoactive, consider haloperidol
Titrate medication if initial dose is not effective.
Consider switching medication if:
- Lengthy treatment anticipated
- Lack of response despite increase dose.

Inadequate or no response:
Reassess cause again, depending on goals of care.
Consider sedation if needed.
benzodiazepines, barbiturates or propofol
This is palliative sedation!

Agitated delirium - severe
For imminent risk of harm to self or others due to agitation, mix in following order:
- Lorazepam 1-2mg
- Haloperidol 2-5mg
- Diphenhydramine 50-100mg

Agitated delirium – severe
(alternatives)
- Chlorpromazine 50-100mg SQ/PR up to 2g/day
  - Increase dose by 25-50mg q1-4 hours until controlled
  - Likely to not need diphenhydramine
  - Consider lorazepam along side
- Olanzapine 5-10mg IM q4 hours up to 30mg/day
- Phenobarbital 20-40mg starting dose q3 hours
  - especially useful for brain mets.

Hierarchy of interventions for agitated delirium
- Emergency medicine
- Seclusion and/or restraint
- Verbal intervention
- Check for needs, non-pharmacologic
- Voluntary medication

Step 1: Treat underlying causes
Step 2: Non-pharmacological
Step 3: Pharmacological
Address family, caregivers and other psychosocial impacts of delirium

Adapted from Scott Irwin, San Diego Hospice
Case 4: Philip’s struggle
63 yo retired photographer with end-stage CHF, in the context of drug abuse history. He was an active duty veteran. He was estranged from his family and no longer active in his Jewish faith. Severe dyspnea. Now over 2 weeks becoming increasingly confused multiple times each day. Sometimes confusion is agitated, sometimes somnolent.

Philip’s struggle
“Philip has terminal agitation, and I think he needs more ...?”
– Is it terminal agitation, or something else?
– How can you find out?

Based on what we’ve talked about this far: What would your next step be?

Addressing Philip’s DELIRIUM
Step 1: reverse the reversible
- Opioids rotated
- Benzodiazepines weaned
- Assessment for UTI – negative
- Poor hydration/nutrition – not reversed due to goals of care
- Oxygen increased

Step 2: Non-pharmalogic
- Social worker addressed PTSD
- Chaplain was involved

Step 3: Psychopharm
- Hyperactive periods less intense BUT mental status continued to wax and wane
- Haloperidol was started

Tending to delirium takes a community

Philip’s struggle
Despite aggressive interventions, he awoke with more alertness for a brief period of time. Now he showed signs of active dying: Mottling of hands and feet Irregular breathing patterns Chlorpromazine suppositories were given. He died peacefully 7 days later.
Agitation is a sign not a diagnosis

RECOGNIZING DELIRIUM

Know the difference delirium vs dementia vs anxiety

RECOGNIZING DELIRIUM

Terminal delirium
diagnosis of exclusion
Should not be presumed

RECOGNIZING DELIRIUM

Prevent it • know the risks
Recognize it • assess often
Reverse it • reverse the reversible
Treat it • non-pharmacologic • antipsychotic • sedatives

CONFRONTING DELIRIUM

THANK YOU