Management of Delirium in the Context of Advanced or Life Threatening Illness
Massive Multi-Player Thumb-Wrestling!
Conflict of Interest Disclosure

- I do not have any financial interests or other relationships with any manufacturers of products or providers of services I might be discussing during the presentation.

- I will be discussing non-FDA approved uses for antipsychotics and benzodiazepines.
Objectives

1. Place delirium into appropriate medical context, accounting for goals of care, and choose a management strategy based on both of these.

2. Discuss delirium as reversible or irreversible based on context and goals of care.

3. Provide an overview of delirium with specific attention to the scientific data related to the impact delirium has on the patient, caregivers and healthcare staff.
Getting to Know You

- Disciplines?
- Experience with Palliative Care?
- Experience with delirium in this population?
- What are you hoping to get out of today?
Delirium: What is it?
Video – TM Describing Delirium
Delirium is sudden severe confusion and rapid changes in brain function that can occur with physical or mental illness.

4 hallmark features:
- Change in attention
- Change in level of consciousness
- Disorganized thinking
- Rapid onset with fluctuation

Associated features:
- Sleep cycle disturbances
- Hallucinations
- Mood lability
Delirium: the great pretender

- Also known as:
  - Confusion or acute confusional state
  - Encephalopathy
  - Terminal restlessness
  - ICU psychosis
  - Organic psychosis or organic brain syndrome
  - Acute brain failure
  - Sun-downing
  - Toxic metabolic state
  - Cerebral insufficiency

- Delirium is not depression or dementia
Delirium Subtypes

Hyperactive
Hypoactive
Mixed
Most prevalent?
Delirium is Highly Prevalent and has Serious Consequences...
Reported Prevalence

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalized elderly</td>
<td>14 – 56 %</td>
</tr>
<tr>
<td>ICU</td>
<td>70 – 87 %</td>
</tr>
<tr>
<td>Advanced cancer</td>
<td>25 – 85 %</td>
</tr>
<tr>
<td>and / or end-of-life</td>
<td></td>
</tr>
</tbody>
</table>

Consequences ...

6 month mortality ≈ 25%
Increased mortality 10 – 78%
Prolonged hospitalization 21 vs 9 days
Decreased likelihood of independent living 57 vs 92%
Increased dementia OR 6-9
Increased cost / resource utilization $4B Medicare (2011)

Cole and Primeau (1993) CMAJ 149: 41
Inouye SK. (1998) Acute Hospital Care 14: 745
...Consequences

101 cancer patients who recovered from delirium, 54% recalled experience

- Hypoactive delirium 43%
- Hyperactive delirium 66%

Distress (many reported severe)

- Patients 3.2 out of 4
- Spouses / caregivers 3.75
- Nurses 3.09

Caregiver Delirium Experience
Delirium has Many, Many Causes...

Many are Discoverable and Reversible...
Risk Factors for Delirium

- Vision impairment
- Medical illness
- **Cognitive impairment**
- Age >70
- Any iatrogenic event
- Physical restraints
- Malnutrition
- Add >3 meds
- Hypertension
- COPD

- ETOH abuse
- Smoking history
- Abnormal labs
- Foley
- Functional limitations
- Prior delirium
- Pre-op use of benzos or opioids
- Epidural
- Constipation
Most Common Causes...

- Fluid imbalance
- Infections
- Hepatic / renal failure
- Hypoxia
- Hematological disturbance

- Medications
  - Anticholinergics
  - Benzodiazepines
  - Opioids
  - Steroids
Many Causes are Treatable...

237 hospice inpatients with cancer

- 213 (90%) had 245 episodes of delirium
- Causes found in
  - 93 (61%) of 153 who had a workup
    - Multi-factorial in > 50%
  - Complete remission in 20%

...Many Causes are Treatable

104 inpatients with advanced cancer receiving palliative care

- 71 (68%) had 94 episodes of delirium
- Reversible in 50%
Delirium is Under-Recognized...
Often Under–Recognized...

2716 hospice patients
- Delirium recognized in only
  - 17.8 % of home care patients
  - 28.3 % of inpatients

299 home hospice patients
- RN estimated that 54% confused
- 1/3 severely disabled by the confusion

Irwin SA, et al. (2008) Palliative and Supportive Care 6: 159
228 end-stage cancer inpatients

- Delirium rate: 107 (46.9%)
  - Hypoactive: 68.2%

Recognition rate: 48 / 107 (44.9%)

- 20.5% in hypoactive cases

Why Under–Recognized?

- Complex presentation
- Inconsistent language
- Hypoactive sub-type
- Thought to be normal part of end-of-life
- Lack of access to psychiatric consultants
- Differential is complicated
How Do You Diagnose Delirium?
Assessment Includes

- Goals of care
- History
  - Context of the patient
  - Symptoms
- Mental status exam
- Physical exam
Goals of Care

- Initial patient & family goals
  - Goals can change
- Goals after diagnosis of delirium
  - Diagnostic work-up vs. palliate
- Goals after work-up
  - Reverse vs. palliate vs. irreversible
Context of the Patient (what’s going on now?)

- Underlying illness – how advanced?
- Functional status – how debilitated?
- Medications – changes over recent days to weeks to months?
- Allergies / adverse reactions/ alcohol & other substance use
Is Patient Actively Dying?

Signs of the Dying Process

- Altered level of consciousness
- Tachycardia
- Abnormal breathing patterns
- Loss of swallow / gag
- Oral / tracheal secretions
- Loss of sphincter control
- Oliguria / anuria
- Cyanosis
- Peripheral cooling
- Venous pooling / mottling
Assessment Can Include . . .

- Review medication history and evolution
- History & physical
  - Allergies/adverse reactions, ETOH, Benzos
  - Mental Status
- Chemistry workup
- Hematologic workup
- Infection workup
- Vitamin levels
- Basic assessment can ID >90% causes
Assessment Tools...

“Gold Standard”
- Experienced clinician
- DSM-IV criteria

Three types of standardized tools
- Screening
- Diagnosis
- Symptom severity
So is it Delirium?
## Assessment Tools

<table>
<thead>
<tr>
<th>Tool</th>
<th>Screening</th>
<th>Diagnosis</th>
<th>Severity</th>
<th>RN administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confusion Assessment Method (CAM)</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Delirium Rating Scale R-98 (DRS-R-98)</td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Memorial Delirium Assessment (MDAS)</td>
<td></td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Delirium Observation Screening Scale (DOSS)</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Single Question in Delirium (SQiD)</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Clock Drawing/mini-cog</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Mini Mental State Exam (MMSE)</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>
Delirium Observation Screening Scale

- Can be performed by a bedside nurse
- Purely observational
- Does not require cognitive tests
- Covers the main symptoms of delirium
- Takes minutes
<table>
<thead>
<tr>
<th>Observation of the patient (at any time did they…)</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dozes off during conversation or activities</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Is easily distracted by stimuli from the environment</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Maintains attention to conversation or action</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Does not finish question or answer</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Gives answers that do not fit the question</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Reacts slowly to instructions</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Thinks they are somewhere else</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Knows which part of the day it is</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Remembers recent events</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Is picking, disorderly, restless</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Pulls IV tubing, feeding tubes, catheters etc.</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Is easily or suddenly emotional</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Sees/hears things which are not there</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
DOSS Validity Results

Patient Population

- 54 medical in-patients
- 100 delirium assessments (using DRS)
- Mean age: 76.63 (SD 8.779)
- Sex: 40% Male; 60% Female
DOSS Validity Results

- **Delirium (DRS-R-98 >14)**
  - Sensitivity: **90%**
  - Specificity: **91%**
  - PPV: 53%
  - NPV: 99%
  - 8 false positives (7 identified sub-syndromal delirium)
  - 1 false negative out of 83

- **Sub-syndromal Delirium (DRS-R-98 8-14)**
  - Sensitivity: 53%
  - Specificity: 99%
  - PPV: 94%
  - NPV: 83%
Impact of DOSS study at UIHC

- Nurse and MD education
- Development of a delirium order set
- Development of a delirium family handout
- Current AHRQ grant
  - Develop a delirium prediction model
  - Embed model into EMR (only screen high risk patients)
  - Develop MD BPA
Delirium Prevention...
Pharm and non-pharm both effective
The higher the delirium incidence the more effective the intervention
- Studies with a delirium incidence >30% demonstrated the best efficacy

Pharmacological Delirium Prevention

- Studies have used anesthesia types, acetylcholinesterase inhibitors, antipsychotics, gabapentin

- Antipsychotics show the most promise
Antipsychotics for Delirium Prevention

430 elderly patients following hip surgery
- Haloperidol vs placebo
- No change in delirium rate but decreased LOS and cost

126 patients following cardiac surgery
- Risperidone vs placebo follow cardiac surgery
- Delirium decreased from 31.7 to 11.1% (p=0.009)

495 elderly patients prior to joint replacement
- Olanzapine vs placebo
- Delirium decreased from 40% to 14.3% (p=<0.0001)

852 patients age > 70 admitted to medicine service

<table>
<thead>
<tr>
<th>Target</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orientation</td>
<td>Introduce care team / daily schedule each shift, oriented 1 – 3x / day</td>
</tr>
<tr>
<td>Activity</td>
<td>Cognitive stimulation 3x / day</td>
</tr>
<tr>
<td>Mobility</td>
<td>Ambulate / range of motion 3x / day</td>
</tr>
<tr>
<td>Sleep</td>
<td>Non-pharmacological sleep protocol</td>
</tr>
<tr>
<td>Sensory aids</td>
<td>Glasses, hearing aids</td>
</tr>
<tr>
<td>Dehydration</td>
<td>Rehydrate as needed (oral)</td>
</tr>
</tbody>
</table>
In the treatment group

- Fewer episodes of delirium
  - 62 vs. 90 (9.9% vs. 15%, p = 0.03)
- Shorter duration
  - 105 vs. 161 days (p = 0.02)

422 patients followed up

- 87% partial or complete adherence
- 89% reduction of risk of delirium

Delirium Management...
General Principles

- Manage based on:
  - potential reversibility
  - goals of care

- Ensure safety

- Address environment

Potential Reversibility and Goals of Care
Potential Reversibility of Delirium

- Potentially Reversible

- Irreversible
  - Patient is actively dying
  - (terminal delirium)
  - Goals of care
  - Work-up / reversal unsuccessful
Goals of Care

- Initial patient & family goals
  - Goals can change
- Goals after diagnosis of delirium
  - Diagnostic work-up vs. palliate
- Goals after work-up
  - Reverse vs. palliate vs. irreversible
My Favorite Advance Directive Sites

- The Conversation Project
  http://theconversationproject.org/

- PREPARE
  https://www.prepareforyourcare.org/
Management Strategies...

- **Reverse**
  - Treat underlying causes

- **Relieve**
  - Non-pharmacological
  - Pharmacological
  - Consult psychiatry

- **Educate**
Always Use Non-pharmacological Treatments...
Non-Pharmacological Treatments Can Address

- Disordered thinking
- Disorientation
- Sleep disturbance
- Immobility
- Risk of falls / injury
- Sensory deprivation
- Dehydration
- Environmental factors
Great Resource for Non-Pharm

https://www.healthcare.uiowa.edu/IGEC/IAAdapt/
Non-pharm approach: Take 1
Non-pharm approach: Take 2
Use Pharmacological Treatments when Appropriate...
Pharmacological Management

- No medication is FDA approved for the treatment of delirium
- No published double-blind, randomized, placebo controlled trials
- Limited consensus among oncologists, geriatricians, psychiatrists, or palliative medicine specialists

Delirium Management Decision Tree

Context & Reasonable Goals of Care

Potentially Reversible
- Hyperactive
  - Medical Rx
  - Successful
  - Unsuccessful
- Hypoactive
  - Medical Rx
  - Successful
  - Unsuccessful

Irreversible
- Hyperactive
  - Medical Rx
- Hypoactive
  - Medical Rx
Potentially reversible, hyperactive

Context & Reasonable Goals of Care

Potentially Reversible

Hyperactive

Reverse Cause

Antipsychotics
## Antipsychotic Indications

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Anti-agitation</th>
<th>Sedation</th>
<th>Amnesia</th>
<th>Muscle relaxation</th>
<th>Anti-convulsant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>-</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>-</td>
</tr>
<tr>
<td>Risperidone</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>-</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td>-</td>
</tr>
</tbody>
</table>
1st Line Pharmacological Treatment

- Double-blind RCT of 30 AIDS patients
  - Haloperidol 0.4 - 3.6 mg daily, n = 11 vs
  - Chlorpromazine 10 - 80 mg daily, n = 13 vs
  - Lorazepam 0.5 - 10 mg daily, n = 6

- Haloperidol = chlorpromazine >> lorazepam

- Lorazepam stopped early due to adverse events
- Haloperidol & chlorpromazine minimal side effects

Pearls

- Use 1st generation antipsychotics

- Do **Not** Use Benzodiazepines
  - Not first-line treatment
  - Increase confusion, disinhibition, falls
  - Necessary for alcohol or sedative withdrawal

Cook IA. (2004)
Application of Pharmacological Principles Improves Management...
Antipsychotic Pharmacokinetic Guidelines

Plasma Concentration

- **Cmax** for SC / IM ≈ 30 min
- **Cmax** for PO / PR ≈ 60 min
- Half-life ($t_{1/2}$) ≈ 24 hrs

**Figure:**
- Graph showing changes in plasma concentration over time with peaks and half-life markers for different routes of administration.
Sample Orders... For Agitation

- **Haloperidol** - 1mg SQ q30min PRN
  - If 3 doses not effective call MD
  - Do not exceed 100mg in 24hrs
  - Schedule today’s PRN tomorrow
    - 1 or 2 x/day + same PRN

- **Chlorpromazine** – 50 mg SC q 30 min PRN
  - If 3 doses not effective, call MD
  - Do not exceed 2000 mg in 24 hr
  - Schedule today’s PRNs tomorrow
    - 1 or 2 x / day + same PRN
## Comparisons

<table>
<thead>
<tr>
<th>Names</th>
<th>Relative Potency</th>
<th>Available Formulations</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Haloperidol</strong></td>
<td>1</td>
<td>Tabs, liquid, IM/SQ</td>
<td>Gold standard&lt;br&gt;Also anti-nausea</td>
</tr>
<tr>
<td>(Haldol)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Chlorpromazine</strong></td>
<td>50</td>
<td>Tabs, liquid, IM/SQ, PR</td>
<td>May be more effective for highly agitated patient&lt;br&gt;More anticholinergic&lt;br&gt;Also helps with hiccups, SOB</td>
</tr>
<tr>
<td>(Thorazine)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Risperidone</strong></td>
<td>1.5</td>
<td>Tab, liquid, sublingual</td>
<td>Very similar to haldol</td>
</tr>
<tr>
<td>(Risperdal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Olanzapine</strong></td>
<td>2.5</td>
<td>Tab, IM, sublingual</td>
<td>More sedating, can worsen delirium</td>
</tr>
<tr>
<td>(Zyprexa)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Quetiapine</strong></td>
<td>50</td>
<td>Tabs</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; line in Parkinson’s</td>
</tr>
<tr>
<td>(Seroquel)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Pearls

- Treat agitation like a breakthrough symptom, e.g., pain
- Provide breakthrough (PRN) doses on the Time to maximum concentration (TCmax)
- If 3 doses not effective, call MD (time-limited trials)
- Provide routine doses once every Half-life ($t^{1/2}$)
## Common Adverse Events ...

<table>
<thead>
<tr>
<th>Drug</th>
<th>SE anti-cholinergic</th>
<th>sedation</th>
<th>orthostasis</th>
<th>QTc prolongation</th>
<th>EPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>haloperidol</td>
<td>×</td>
<td>✓</td>
<td>×</td>
<td>× (PO)</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ (IV)</td>
<td>✓</td>
</tr>
<tr>
<td>chlorpromazine</td>
<td>✓✓✓</td>
<td>✓✓✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>risperidone</td>
<td>×</td>
<td>✓</td>
<td>×</td>
<td>×</td>
<td>✓✓</td>
</tr>
<tr>
<td>olanzapine</td>
<td>✓</td>
<td>✓✓</td>
<td>×</td>
<td>×</td>
<td>✓</td>
</tr>
<tr>
<td>quetiapine</td>
<td>×</td>
<td>✓✓✓✓</td>
<td>✓</td>
<td>×</td>
<td>×</td>
</tr>
</tbody>
</table>
... Common Adverse Events

- Cochrane Review: TX of delirium in terminal illness
  - 1 study: chlorpromazine decreased cognitive performance
  - no significant increase in EPS

- Cochrane Review: efficacy and adverse effects of antipsychotics in delirium
  - 2 studies: no significant adverse effects
  - 1 study: Haldol increased incidence of dry mouth / EPS

Serious Adverse Events ...

- FDA Black Box Warning (2004): increased mortality in elderly with dementia-related psychosis
- Consistent across all antipsychotics
  - Relative Risk = 1.6 - 1.7
  - Absolute Risk = 3.5 vs 2.3% in placebo
- For every 9-25 persons helped, 1 death associated with use

Oregon Sudden Unexplained death Study
- 1,544 documented sudden cardiac deaths (SCD) and 774 matched controls
- multivariate logistic regression analysis adjusted for age, gender, and comorbidities
- patients on a 1st generation antipsychotic had a 3.76-fold increased risk of SCD ($P = .0002$)
- Patients on a 2nd generation antipsychotic had a 3.3-fold increased risk of SCD
... Serious Adverse Events

- Nested case-control; 62 cases

- Relationship between antipsychotic use and death:
  - Univariate \( \text{OR}=1.53 \ (95\% \text{ CI } = 0.83 - 2.80) \)
  - Multivariate \( \text{OR}=1.61 \ (95\% \text{ CI } = 0.83 - 2.80) \)

- Conclusion: antipsychotic use did not increase risk of dying in patients with delirium

Potentially Reversible Hypoactive

Context and Reasonable Goals of Care

Potentially Reversible

Hypoactive

Reverse Cause

?
Management of Hypoactive Delirium

- Few studies exist
- Limited data on the use of haloperidol or psychostimulants

Platt, M. 1994 Journal of Neuropsychiatry
Elie D. 2010 Can J Psychiatry
Irreversible Delirium

- Goals of care
- Work-up / reversal unsuccessful
- Patient is actively dying
  - (terminal delirium)
Two Roads to Death

USUAL ROAD
Hypoactive Delirium

Sick
Restless
Sleepy
Lethargic
Obtunded

Confused → Tremulous → Hallucinations

Semicomatose
Comatose

Seizures

MYOCOLLIC JERKS

DIFFICULT ROAD
Hyperactive Delirium

Dead

Mumbling

Sick

Hypoactive

Delirium
Terminal Delirium

Delirium during the active dying process
Prospetive, irreversible

- Altered level of consciousness
- Tachycardia
- Abnormal breathing patterns
- Loss of swallow / gag
- Oral / tracheal secretions
- Loss of sphincter control

- Oliguria / anuria
- Cyanosis
- Peripheral cooling
- Venous pooling / mottling
Irreversible Terminal, Hyperactive

- Signs of Active Dying
  - Irreversible
    - Hyperactive
      - Support
      - Benzodiazepines, Barbiturates, Propofol
## Benzodiazepine Indications

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Anti-agitation</th>
<th>Sedation</th>
<th>Amnesia</th>
<th>Muscle relaxation</th>
<th>Anti-convulsant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Midazolam</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td></td>
<td>✓</td>
<td>✓ / ✓</td>
<td>x</td>
<td>x</td>
<td>-</td>
</tr>
<tr>
<td>Opioids</td>
<td></td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>-</td>
</tr>
</tbody>
</table>
Sample Orders... For Agitation

- With signs of the dying process:
  - Lorazepam – 1 mg PO q 60 min PRN
    - If 3 doses not effective, call MD
    - Do not exceed 40 mg in 24 hr
    - Schedule today’s PRNs tomorrow
      - 3 x / day + same PRN schedule
Sample Orders... For Agitation

- With signs of the dying process:
  - Midazolam – 0.2 mg / kg SC load
    - then 0.1 mg / kg q 30 min x 2 PRN
    - Maintenance dose / hr = 25 % total dose to sedate
  - Consider alternative if need > 10 mg / hr

Benzodiazepines

Lethal Doses

- Lorazepam $LD_{50}$ = 5,000 mg
- Midazolam $LD_{50}$ = 10,000 mg

Not concerned about

- Amnesia, confusion, restlessness
- Hypotension
- Respiratory depression
When Benzodiazepines Fail

Propofol

Phenobarbital
Sample Orders... For Agitation

- With signs of the dying process:

  - Propofol – 1 mg / kg / hr IV
    - then 0.1 mg / kg q 30 min x 2 PRN
    - Increase by 0.5 mg / kg / hr q 15 - 30 min PRN
    - Do not exceed 6 mg / kg / hr

Sample Orders... For Agitation

- With signs of the dying process:
  - Phenobarbital – 10 mg / kg IV / SC load
    - May repeat q 1 hr x 2 PRN
    - Continuous infusion 10 – 20 mg / hr
    - Titrate PRN
    - Maintenance = 600 – 2400 / 24 hrs
**Pearls**

- Treat agitation like a breakthrough symptom, e.g., pain
- Provide breakthrough (PRN) doses on the time to maximum concentration (TCmax)
- If 3 doses not effective, call MD
- Time-limited trials
- Provide routine doses once every half-life ($t^{1/2}$)
It Takes a Team

- Cases can be complex
- Clinicians often unfamiliar with all possible treatments
- Complex cases stressful
- Mental health experts can help
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Questions?