Non-Pain Symptoms: Delirium, Depression, Anxiety at the EOL

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Disclosure Information

- I do not have any financial interests or other relationships with any manufacturers of products or providers of services I might be discussing in my presentation
- I will be discussing off-label uses of medications
Objectives:

- Discuss common mental illnesses at the end of life (anxiety, depression, delirium)
- Review prevalence, diagnosis and treatment of anxiety, depression and delirium at the end of life
- Brief review of dementia and agitation at the end of life
# Prevalence of Psychiatric Illness at EOL

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cancer</th>
<th>Community Elderly</th>
<th>NH residents</th>
<th>PC/hospice inpatient unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>6-8%</td>
<td>2-10%</td>
<td>10%</td>
<td>60-70%</td>
</tr>
<tr>
<td>Depression</td>
<td>14-31%</td>
<td>2% (47% post-CVA)</td>
<td>10-25%</td>
<td>14%</td>
</tr>
<tr>
<td>Delirium</td>
<td>10-42%</td>
<td>30-50%</td>
<td>14%</td>
<td>30-85%</td>
</tr>
<tr>
<td>Dementia</td>
<td>3-4%</td>
<td>50% (age &gt;85)</td>
<td>60-80%</td>
<td>40%</td>
</tr>
</tbody>
</table>
Impact of Psychiatric Symptoms at EOL

- Shortens life span (depression, delirium)
- Risk factor for suicide and PAS (depression)
- Bereavement outcomes worse
- Reduced QOL for both patients and caregivers (and healthcare providers)
Case of Mrs. B:

- 63 with severe COPD, oxygen dependent, short of breath with activity and uses a scooter when she is out of the house.
- She has been losing weight.
- She worries about “every little thing” and starts to panic when she can’t catch her breath.
- She insists on having at least 4 spare O2 tanks in her house and never goes out without at least 1 extra concentrator.
- She tells you that she is afraid that she will “suffocate” if she runs out of oxygen.
Anxiety Prevalence (DSM-IV Diagnosis)

- **Common:**
  - Advanced illness (6-8%)
  - Terminal illness (14%)
  - Caregivers (8%)

- GAD and panic disorder most common
- PTSD not uncommon (4% of caregivers)
Anxiety and Medications

- Medication that can cause anxiety
  - Caffeine
  - Steroids
  - Nicotine
  - Antidepressants, antipsychotics, stimulants
  - Sudafed
  - Synthroid over replacement
Anxiety Symptoms

- Symptoms are common and distressing (21-70%)
- Often presents with somatic symptoms
  - Tension or restlessness
  - Jitteriness or autonomic hyperactivity
  - Vigilance
  - Insomnia
  - Distractibility
  - Worry, apprehension, rumination
  - Shortness of breath
- Need to evaluate carefully for medical causes such as pain and dyspnea
- Often looks like GAD but can include panic attacks
Potential Sources of Anxiety Symptoms

- Actual underlying anxiety disorder
- Fear of death and the dying process
- Spiritual or existential concerns
- Chronic coping or personality style
- Medication side effects (akathesia from anti-emetics)
- Undertreated symptoms (pain, dyspnea, sepsis)
- Withdrawal states (sedatives, opioids)
- Delirium
- Anticipatory response to repeated aversive treatment (chemo)
Screening Tools

- Clinical Exam very effective
  - Do you feel nervous or jittery?
  - Have you felt fearful, distressed, or tense? Of anything in particular?
  - Do you avoid certain activities or people because of fear?
  - Are you afraid to close your eyes at night because of fear that you will die in your sleep?
- Hospital Anxiety and Depression Screen (HADS)
- Patient Health Questionnaire (PHQ-9)
GAD-7

**GAD-7 - Generalized Anxiety Disorder Scale**

Over the last two weeks, how often have you been bothered by the following problems?

<table>
<thead>
<tr>
<th>Problem</th>
<th>Not at all</th>
<th>Several days</th>
<th>Over half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feeling nervous, anxious, or on edge</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not being able to stop or control worrying</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Worrying too much about different things</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trouble relaxing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Being so restless that it’s hard to sit still</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Becoming easily annoyed or irritable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling afraid as if something awful might happen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

How difficult have those problems made it for you to do your work, take care of things at home, or get along with other people?

Score: 14

**Difficulty Level:** Somewhat difficult

**Severity Level:** Moderate Anxiety
Non-pharmacological Strategies: To Decrease Anxiety

- Explore fears/concerns in non-judgmental fashion
  - Listen, acknowledge, normalize, remain available
- Reassurance not usually effective
  - Can make highly anxious patients more anxious
- Supportive-expressive therapy
  - Aims to reduce symptoms and maintain coping, not cure
- Consider psychiatric referral
Pharmacological Anxiety Treatment

- Benzodiazepines are drugs of choice at EOL
  - Ativan (lorazepam) 0.5-1mg q4-6hrs prn
  - Xanax (alprazolam) 0.25-0.5 mg q4-6hrs prn
  - Can cause sedation, confusion, tolerance, disinhibition, gait instability, falls

- Antidepressants if life expectancy >8 weeks
  - Prefer: Sertraline (zoloft), citalopram (celexa), mirtazepine (remeron)
  - Avoid: paroxetine (anti-cholinergic), venlafaxine (withdrawal), bupropion (in the elderly, malnourished, seizure risk)
  - Start low and go slow to avoid increasing anxiety
Pharmacological Anxiety Treatment

- **Trazodone**
  - Sedating but can be given in low doses during the day (12.5-50mg q4hrs prn)

- **BuSpar**
  - Should be scheduled, takes 4-6 weeks to see an effect (7.5-10mg BID)

- **Consider sedating antipsychotics**
  - Chlorpromazine (thorazine), olanzepine (zyprexa), quetiapine (seroquel)
Anxiety Pearls

- Anxiety is very common
- Just ask!
- Benzodiazepines are the drug of choice in hospice patients (need caution since they can cause delirium)
- Can decrease by effectively managing other symptoms (pain/dyspnea)
Case of Mr. A:

- 82 y/o with lung cancer and pain from spinal mets
- PMH: anxiety and a conversion reaction: on Paxil
- Wife reports he is sleeping more and no longer wants to go out to restaurants or church with her. Patient says these activities are too painful.
What diagnosis is most likely for Mr. A?

1. Return of his anxiety disorder
2. New onset depression
3. Expected changes at EOL
4. Poorly controlled pain
5. A grief reaction
What piece of information would be the most helpful for clarifying his diagnosis?

1. Mr. A feels sad at times
2. Mr. A no longer enjoys anything
3. Mr. A occasionally wishes he were dead
4. Mr. A has low energy and a poor appetite
5. Mr. A worries about who will care for his wife after he dies
Although depression is common at the end of life it is not a normative response to a terminal diagnosis.
- Little empirical research
- Common (15-60%) in cancer pts
- No screening tools have been validated in end-of-life patients
- Associated with excessive functional morbidity and mortality
- Is it really delirium? Anxiety?
Depression

- Bi-directional relationship with co-morbid medical conditions
  - medical illness correlates with presence of depression and predicts functional outcome and mortality
  - Cancer patients with pain are twice as likely to develop psychiatric complications as are patients without pain

- Medications that can cause depression
  - Steroids, Interferon, Interleukin-2, Tyrosine Kinase inhibitors (imatinib), Zidovudine, Vinblastine
Risk Factors for Late-Onset Depression in Women (female-male ratio 2.5:1)

Medical illness
Hypothyroidism (50%)
Myocardial infarction (45%)
Macular degeneration (33%)
Diabetes (8% to 28%)
Cancer (24%)
Coronary artery disease (20%)

Central nervous system disease
Parkinson's disease (25% to 70%)
Alzheimer's disease (15% to 57%)
Multiple sclerosis (27% to 54%)
Stroke (26% to 54%)
Huntington's disease (9% to 44%)
Brain microvascular ischemic disease (20%)
Mini-Mental State Examination score <24

Medications
Beta-blockers
Interferon alfa
Many anticancer drugs
Signs of Major Depression

- Somatic symptoms less useful in advanced disease
  - fatigue, appetite changes, decreased libido, sleep disturbances may all be related to the underlying disease
- Focus on neurovegetative symptoms
  - Dysphoria – sad, flat affect, distraught
  - Anhedonia – lack of anything pleasurable
  - Feelings of worthlessness, hopelessness, helplessness, guilt and despair
- Have a high index of suspicion if:
  - Pain not responding as expected
  - Requests to end life early
Suicide

- Women attempt 2x as often, men 4x more likely to succeed
- White men over 85 are at highest risk to complete
- Always assess in patients with depressive symptoms
- Talking about it decreases risk (does not increase risk)
- Red flags:
  - Socially isolated
  - Has concrete plan
  - History of serious attempt
  - Knows someone who successfully suicided
- If risk high – DON’T leave patient alone, immediately consult a psychiatrist – may need in-patient care or involvement of authorities
Screening Tools for Depression

- 2 questions (97% sensitive, 67% specific)
  - “During the past month, have you been bothered by feeling down, depressed or hopeless?”
  - “During the past month, have you been bothered by little interest or pleasure in doing things?”
  - At EOL Sensitivity of 55%, specificity of 75%

- Hospital Anxiety and Depression Scale
- Patient Health Questionnaire (PHQ)
- Geriatric Depression Screen
**PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)**

Over the last 2 weeks, how often have you been bothered by any of the following problems? (Use ✔ to indicate your answer)

<table>
<thead>
<tr>
<th>Item</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
Grief is common, major depression is not
Grief comes and goes in waves
Grief can worsen with disease progression but hope is maintained
Sleep disorders, somatic distress, concentration and social withdrawal common to both
Both can have a passive death wish

The Post-Bereavement Phenomenology Inventory (PBPI)
I am filled with despair nearly all the time, and I almost always feel hopeless about the future.  

I feel sadness a lot of the time, but I believe that eventually, things will get better.

I will probably never get back to feeling like my "old self" again.  

Things are really tough now, but I'm hopeful that, with time, I will feel more like my "old self."

When friends or family call or visit, and try to cheer me up, I don’t feel anything, or I may feel even worse.  

When friends or family call or visit, and try to cheer me up, I usually “perk-up” for a while and enjoy the social contact.
### Grief Compared with Depression in Terminally Ill Patients

<table>
<thead>
<tr>
<th>Characteristics of Grief</th>
<th>Characteristics of Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients experience feelings, emotions, and behaviors that result from a particular loss</td>
<td>Patients experience feelings, emotions, and behaviors that fulfill criteria for a major psychiatric disorder, distress is usually generalized to all facets of life</td>
</tr>
<tr>
<td>Almost all terminally ill patients experience grief, but only a minority develop full-blown affective disorders requiring treatment</td>
<td>Major depression occurs in 1-53% of terminally ill patients</td>
</tr>
<tr>
<td>Patients usually cope with distress on their own</td>
<td>Medical or psychiatric intervention is usually necessary</td>
</tr>
<tr>
<td>Patients experience somatic distress, loss of usual patterns of behavior, agitation, sleep and appetite disturbances, decreased concentration, social withdrawal</td>
<td>Patients experience similar symptoms plus hopelessness, helplessness, worthlessness, guilt and suicidal ideation</td>
</tr>
<tr>
<td>Grief is associated with disease progression</td>
<td>Depression has an increased prevalence (up to 77%) in patients with advanced cancer; pain is a major risk factor</td>
</tr>
<tr>
<td>Patients retain the capacity for pleasure</td>
<td>Patients enjoy nothing</td>
</tr>
<tr>
<td>Grief comes in waves</td>
<td>Depression is constant and unremitting</td>
</tr>
<tr>
<td>Patients express passive wishes for death to come quickly</td>
<td>Patients express intense and persistent suicidal ideation</td>
</tr>
<tr>
<td>Patients are able to look forward to the future</td>
<td>Patients have no sense of a positive future</td>
</tr>
</tbody>
</table>
Treatment of Depression

- Aggressively treat other physical symptoms
- Consider psychotherapy (CBT)
- Encourage exercise
- Antidepressants (SSRIs) for a life expectancy over two months
- Psychostimulants
SSRIs
- Good for co-morbid anxiety and irritability
- partial response at 1 month increase dose to try to get full response
- If no response at one month change agents
- If fail 2 SSRIs change class

SNRI
- Can decrease pain but runs risk of withdrawal syndrome

Other
- Mirtazapine (remeron) can increase appetite and improve sleep
- Buproprion (wellbutrin) can reduce fatigue but also lowers the seizure threshold and may worsen anxiety
- TCA’s (tri-cyclic antidepressants) can increase appetite, decrease pain but are anti-cholinergic (can cause delirium)
Depression Treatment

- Pick a few antidepressants that you feel comfortable prescribing and know those drugs.

- Recommended (due to low drug/drug interactions):
  - **Sertraline** – Start 25mg po daily (increase 50-100mg/day)
  - **Citalopram** – Start 5mg po daily (increase to 10-20mg/day)
  - **Venlafaxine** – Start 37.5mg po BID (increase to XR 225mg/day)

Benefits of Psychostimulants

- Response often seen within 2 days
  - 73% response in cancer patients (non-controlled)
  - Discontinuation from side effects <10%
- Augment opioid analgesia
- Diminish opioid sedation
- May increase appetite
- Can be used in conjunction with SSRIs
- Start with 5 mg Qam, qnoon
  - double if no effect in 2 days
  - stop if no improvement in a week
Methylphenidate Review

- 1950-2008 (included case studies, focus on medically ill elderly)
- Mechanism of action:
  - Blocks dopamine reuptake (striatum)
  - Blocks norepinephrine and serotonin (weak)
  - “mixed results”
  - overall beneficial with mood and fatigue
  - +/- apathy, cognition, motivation
  - may help with “hard to wean” vent patients
- Side effects uncommon
  - agitation/restless, tachycardia, confusion, insomnia
  - Resolve with dose decrease or discontinuation
- Monitoring: consider EKG with cardiac history, check warfarin levels, use caution with TCAs
Other Treatments

- ECT - effective and safe but rarely utilized
  - Would consider in a patient with a vegetative depression that doesn’t respond to stimulants
- Ketamine
  - Has been given both orally and IV
  - Early trials are promising
  - Not enough data to recommend
Depression Pearls

- Depression is not a normal part of the dying process
- Need to screen
- Treatment is effective
- Consider a psychostimulant trial early
Case of Ruby Resident:

- 87 y/o MWF with dementia and ovarian cancer. Needs assistance with iADLs.
- Was awake most of the night talking about the “kids who kept coming into her room”
- Very sleepy in the morning but oriented
- Later in the day couldn’t remember how to drink out of a straw
Delirium

• Also called: acute confusional state, brain failure, encephalopathy, organic brain syndrome, terminal restlessness, terminal agitation, intensive care unit psychosis

• Very common
  • 25-40% in cancer patients
  • >50% home hospice patients
  • up to 85% in the terminal stages

• Often mistaken for depression or anxiety
  • Emotional alterations are common
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
A. Disturbance in attention and awareness (reduced ability to focus, sustain or shift attention, reduced orientation)

B. The disturbance develops over a short period of time (usually hours to days), represents a change from baseline, and tends to fluctuate over the course of the day

C. Disturbance in cognition (memory, orientation, language, perception)

D. Criteria A and C not better explained by another neurocognitive disorder (dementia) or coma

E. There is evidence that the disturbance is caused by the direct physiological consequences of a medical condition, intoxication or withdrawal
Delirium Types

- Hypoactive
- Hyperactive
- Mixed
- Reversible
- Irreversible
Delirium and Depression

- Often co-morbid and symptoms commonly overlap
- 100 pts admitted to inpt hospice (Leonard 2009)
  - 34% dx of delirium, 30% subsyndromal delirium, 37% with MDD
  - 54% patients with delirium had core features of MDD (38% of subsyndromal)

- Is the depression real or just a delirium sub-type?
- Need to rule out delirium before we diagnose depression
Delirium and Dementia

- Age and cognitive impairment are the strongest risk factors for developing delirium
- Can be difficult to separate out
- Delirium may be a precursor to a dementia and may cause long lasting cognitive changes
# Differential Diagnosis of Dementia, Depression and Delirium

<table>
<thead>
<tr>
<th>Clinical Feature</th>
<th>Dementia</th>
<th>Depression</th>
<th>Delirium</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>Insidious (months to years)</td>
<td>Acute or insidious (weeks to months)</td>
<td>Acute (hours to days)</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>Months to years</td>
<td>Months to years</td>
<td>Hours to weeks</td>
</tr>
<tr>
<td><strong>Course</strong></td>
<td>Chronic and progressive</td>
<td>May be chronic</td>
<td>Fluctuating</td>
</tr>
<tr>
<td><strong>Progression</strong></td>
<td>Irreversible</td>
<td>Usually reversible</td>
<td>Usually reversible</td>
</tr>
<tr>
<td><strong>Level of Consciousness</strong></td>
<td>Usually clear</td>
<td>Clear</td>
<td>Altered</td>
</tr>
<tr>
<td><strong>Orientation</strong></td>
<td>Disoriented</td>
<td>Oriented</td>
<td>Variable</td>
</tr>
<tr>
<td><strong>Attention</strong></td>
<td>Intact except in late stage</td>
<td>May be decreased</td>
<td>Impaired</td>
</tr>
<tr>
<td><strong>Concentration</strong></td>
<td>Intact except in late stage</td>
<td>May be decreased</td>
<td>Impaired</td>
</tr>
<tr>
<td><strong>Speech</strong></td>
<td>Coherent until late stage</td>
<td>Coherent (may be latent in severe)</td>
<td>May be incoherent or latent</td>
</tr>
<tr>
<td><strong>Thought Process</strong></td>
<td>Limited</td>
<td>Organized</td>
<td>Disorganized</td>
</tr>
<tr>
<td><strong>Perception</strong></td>
<td>May have hallucinations (paranoia more common)</td>
<td>Mood congruent hallucinations in severe cases</td>
<td>Hallucinations are common (often visual)</td>
</tr>
<tr>
<td><strong>Psychomotor activity</strong></td>
<td>Variable</td>
<td>May be slowed in severe cases</td>
<td>Variable</td>
</tr>
<tr>
<td><strong>Sleep pattern</strong></td>
<td>Variable</td>
<td>Often increased but may have early AM awakenings</td>
<td>Variable, days and nights commonly confused</td>
</tr>
</tbody>
</table>
Why Identify? Why Treat?

- Common
- Shortens life expectancy
  - 6 mo mortality up to 25%
- 50% of hospitalized patients with delirium are discharged before delirium resolves
  - 20% patients discharged home placed within 1 year
- Increases chance of nursing home placement from hospitalization (73% vs 30%)
- Distressing to patient and family
- Robs patients of time and decreases opportunities to make final plans and decisions
- Increases hospital LOS and cost
Which is not a risk factor for delirium?

1. Age
2. Cognitive impairment
3. Pain
4. Opioid use
5. Constipation
6. Gender
Delirium Risk Factors

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

- ETOH abuse
- h/o smoking
- Abnl labs
- Foley
- Functional limitations
- Prior delirium
- Medications (benzos, opioids, anticholinergic)
- Epidural
- Constipation
Medications Which Can Cause Delirium

- Anti-cholinergics (i.e., diphenhydramine, atropine, scopolamine)
- TCA’s
- Anti-inflammatoris (i.e., NSAIDS, steroids)
- Benzodiazepines (i.e., valium, zolpidem)
- Cardiovascular (i.e., digoxin, antihypertensives)
- Diuretics (furosemide)
- GI (ranitidine)
- Lithium
- Opioids
Why Consider Screening for Delirium?

- Majority of delirium is missed or not diagnosed
  - PC team missed 54% of hypoactive delirium and 80% of hypoactive delirium in terminal cancer inpts
- Delirium has short and long term impact for everyone (patient, family, healthcare providers)
- Delirium can be reversed in over 50% of the cases
- Treatment of delirium improves long term outcomes
Delirium Screening Instruments

- Multiple instruments
- Good review articles
- CAM-ICU great for ICU patients
  - Not effective out of the ICU
- CAM- sensitivity/specificity depends on training
- Most screening tests require some sort of cognitive testing
  - A few such as DOSS and ICDSC-9 are observation based

- Delirium is a clinical, bedside diagnosis
The ideal tool is sensitive and specific and easy to perform

- Common tools
  - CAM
  - CAM-ICU
  - SQiD
  - DOS
CAM: Confusion Assessment Method

- Built into many EMRs
- Bedside assessment tool
- Challenging to operationalize
  - Requires cognitive assessment and substantial (ongoing) interviewer training
- All forms require a cognitive assessment
Feature 1: Acute onset and fluctuating course
Is there evidence of an acute change in mental status from the patient’s baseline? Did the (abnormal) behaviour fluctuate during the day, that is, tend to come and go, or increase or decrease in severity?

Feature 2: Inattention
Did the patient have difficulty focusing attention, for example being easily distractible or having difficulty keeping track of what was being said?

Feature 3: Disorganised thinking
‘Was the patient’s thinking disorganised or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?’

Feature 4: Altered level of consciousness
Overall, would you rate this patient’s level of consciousness anything other than normal (alert)?
3D-CAM

- http://www.hospitalelderlifeprogram.org
- CAM operationalized with embedded cognitive testing
- Designed to be completed in 3 minutes
- Validated in 201 inpatients age >74 years
  - Compared to clinical interview
  - 95% sensitive, 94% specific

Marcantonio, Ann Intern Med, 2014
### 3D-CAM ASSESSMENT

**Coding Instructions:** Incorrect also includes “I don’t know,” and No response/verbal response. For any “Incorrect” or “Yes” responses, check the box in the final column designating which feature is present.

**Observer Ratings:** To be completed after asking the patient questions 1-10 above.

<table>
<thead>
<tr>
<th>Feature</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Can you tell me the year we are in right now?</td>
<td>Correct</td>
<td>Incorrect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Can you tell me the day of the week?</td>
<td>Correct</td>
<td>Incorrect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Can you tell me what type of place is this? (hospital)</td>
<td>Correct</td>
<td>Incorrect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. I am going to read some numbers. I want you to repeat them in backwards order from the way I read them to you. For instance, if I say “6-5-3”, you would say “3-5-6”. OK? The first one is “7-5-4” (1-5-7).</td>
<td>Correct</td>
<td>Incorrect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. The second is “8-2-4-3” (9-4-2-8).</td>
<td>Correct</td>
<td>Incorrect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Can you tell me the days of the week backwards, starting with Saturday? (S,F,T,W,T,M,S) may prompt with “What is day before …” for up to 3 prompts.</td>
<td>Correct</td>
<td>Incorrect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Can you tell me the months of the year backwards, starting with December? (D,N,O,S,A,J,J,M,A,F) may prompt with “What is month before …” for up to 2 prompts</td>
<td>Correct</td>
<td>Incorrect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. During the past day have you felt confused?</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. During the past day did you think that you were not really in the hospital?</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. During the past day did you see things that were not really there?</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Feature</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. Was the patient sleepy, stuporous, or comatose during the interview?</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Did the patient show excessive aboersion with ordinary objects in the environment (hypervigilant)?</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Was the patient’s flow of ideas unclear or illogical, for example tell a story unrelated to the interview (tangential)?</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. Was the patient’s conversation rambling, for example did he/she give inappropriate or off target responses?</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Was the patient’s speech unusually limited or sparse? (e.g. yes/no answers)</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16. Did the patient have trouble keeping track of what was being said during the interview?</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17. Did the patient appear inappropriately distracted by environmental stimuli?</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18. Did the patient’s level of consciousness fluctuate during the interview, for example, start to respond appropriately and then drift off?</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. Did the patient’s level of attention fluctuate during the interview, e.g., did patient focus on the interview or performance on the attention tasks vary significantly?</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Did the patient’s speech/verbalizing fluctuate during the interview, e.g., patient sound home or intent vs. lost?</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Optional Questions:** Complete only if Feature 1 is NOT checked and Feature 2 is checked and either Feature 3 or 4 is also checked.

<table>
<thead>
<tr>
<th>Feature</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>21. Contact a family member, friend, or health care provider who knows the patient well and ask: “Is there evidence of an acute change in mental status (memory or thinking) from the patient’s baseline?”</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22. IF SECOND OR HOSPITALIZATION OR LATER AND PREVIOUS 3D-CAM RATING ARE AVAILABLE: Review previous 3D-CAM assessments and determine if there has been an acute change in performance, based on ANY new “positive” items</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**CAM Summary:** Check if Feature Present in column above.

<table>
<thead>
<tr>
<th>Feature</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camium Requires Feature 1 and 2 and Either 3 or 4: Present Not Present</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

**3D-CAM**
CAM-ICU

- Quick (<2 min) delirium assessment in ICU patients
- Can effectively train staff to perform it in 20 minutes
- Sensitive and Specific (even with dementia)
- Used with the RASS (Richmond Agitation and Sedation Scale)
- Translated and validated in 10 languages
- Sensitivity 93-100% and specificity 98-100% (very strong inter-rater reliability)

- Best for use in the ICU
# CAM-ICU Worksheet

## Feature 1: Acute Onset or Fluctuating Course

<table>
<thead>
<tr>
<th>Score</th>
<th>Check here if Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the patient different than his/her baseline mental status? OR Has the patient had any fluctuation in mental status in the past 24 hours as evidenced by fluctuation on a sedation/level of consciousness scale (i.e., RASS/SAS), GCS, or previous delirium assessment?</td>
<td>Either question Yes ( \rightarrow )</td>
</tr>
</tbody>
</table>

## Feature 2: Inattention

**Letters Attention Test** (See training manual for alternate Pictures)

**Directions:** Say to the patient, "I am going to read you a series of 10 letters. Whenever you hear the letter ‘A’, indicate by squeezing my hand." Read letters from the following letter list in a normal tone 3 seconds apart.

SAVEAHAART or CASABLANCE or ABAADADAAY

Errors are counted when patient fails to squeeze on the letter "A" and when the patient squeezes on any letter other than "A."

| Number of Errors >2 | ☐ |

## Feature 3: Altered Level of Consciousness

Present if the Actual RASS score is anything other than alert and calm (zero)

| RASS anything other than zero | ☐ |

## Feature 4: Disorganized Thinking

**Yes/No Questions** (See training manual for alternate set of questions)

1. Will a stone float on water?
2. Are there fish in the sea?
3. Does one pound weigh more than two pounds?
4. Can you use a hammer to pound a nail?

Errors are counted when the patient incorrectly answers a question.

| Combined number of errors >1 | ☐ |

**Command**

Say to patient: "Hold up this many fingers" (Hold 2 fingers in front of patient) "Now do the same thing with the other hand" (Do not repeat number of fingers) "If the patient is unable to move both arms, for 2nd part of command ask patient to "Add one more finger"

An error is counted if patient is unable to complete the entire command.

## Overall CAM-ICU

Feature 1 plus 2 and either 3 or 4 present = CAM-ICU positive

| Criteria Met | ☐ |

CAM-ICU Positive (Delirium Present)

| Criteria Not Met | ☐ |

CAM-ICU Negative (No Delirium)

---

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CAM-ICU Video
DOS:
Delirium Observation Screening Scale

- Can be performed at bedside
- Purely observation
- Does not require cognitive tests
- Covers the main symptoms of delirium
- Take less than 5 mins
<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>

<3 = not delirious
≥3 = probably delirious
100 general medical inpatients, age > 64 years
- Sensitivity: 90% (CI 0.54-0.99)
  - 8 false positives (all identified sub-syndromal delirium)
- Specificity: 91% (CI 0.83-0.96)
  - 1 false negative out of 83

- 50 assessments in home hospice patients
  - Sensitivity: 97% (CI 0.81-1.00)
    - 5 false positives (3 met criteria for sub-syndromal delirium)
  - Specificity: 89% (CI 0.75-0.96)
    - 1 false negative
Screening Recommendations

- **SQiD (single question in delirium)**
  - “Do you think [insert pt name] has been more confused lately?”
  - 80% sensitive and 71% specific in inpt oncology patients
- **Basic cognitive tests**
  - Verbal trails (alternate alphabet and numbers to 10)
  - Days of week or months of year backwards
  - Clock-draw
  - Count backwards from 20 to 1 (good for dementia pts)
Delirium Management

1. Make diagnosis
2. Support/educate patient and family
3. Non-pharmacologic interventions
4. Establish goals (need prognosis)
5. Consider work-up/treatment of potentially correctible etiologies
6. Aggressively treat distressing symptoms
50% of delirium can be reversed even when patients are in the final days of life
## Delirium Basic Evaluation

- Good history and physical
  - Pain assessment
  - Constipation
  - Medication review
  - Dehydration
- Tests
  - (if indicated or desired)

<table>
<thead>
<tr>
<th>Initial investigation</th>
<th>More specific tests</th>
<th>Reasons to order specific tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood count</td>
<td>Electrocardiogram</td>
<td>Existing cardiac disease</td>
</tr>
<tr>
<td>Blood urea and nitrogen levels</td>
<td>C reactive protein (CRP) and erythrocyte sedimentation rate (ESR)</td>
<td>Suspected inflammatory disease</td>
</tr>
<tr>
<td>Electrolytes</td>
<td>Urinalysis, urine and blood cultures, Chest X-ray</td>
<td>Suspected infection</td>
</tr>
<tr>
<td>Blood sugar</td>
<td>Urine toxicology screen</td>
<td>Suspected drug use</td>
</tr>
<tr>
<td>Liver function</td>
<td>Vitamin B12, folate</td>
<td>Malnutrition</td>
</tr>
<tr>
<td>Thyroid function</td>
<td>EEG</td>
<td>Suspected seizures</td>
</tr>
<tr>
<td>Arterial blood gases</td>
<td>Computed tomography (CT) scan or magnetic resonance imaging (MRI) scan of the brain</td>
<td>Suspected cerebral cause (stroke or brain metastasis)</td>
</tr>
<tr>
<td></td>
<td>Lumbar Puncture (LP)</td>
<td>Suspected meningitis</td>
</tr>
</tbody>
</table>
Delirium Type

Reversible vs irreversible: A more useful construct?
Delirium Management

- Educate Family and Staff
- Treat underlying cause
- Ensure safety
- Manage symptoms
  - Disease symptoms (pain, dyspnea, nausea etc)
  - Delirium symptoms (psychosis, agitation etc)

Free Delirium Family Handout: http://www.healthcare.uiowa.edu/igec/publications/collaborative-publications/
Delirium Management Decision Tree

Support/Education of Family & Patient

Non-pharmacological, Interventions

Context

Potentially Reversible

Goals of Care Consistent with Reversal

Goals of Care Not Consistent with Reversal

Palliate Symptoms (e.g., Agitation, Breathlessness, Pain)

Time-limited Trial to Find / Reverse Causes

Hyperactive

Hypoactive

First Generation Antipsychotics

Little Evidence to Guide

Successful

Unsuccessful

Taper Interventions as Appropriate

Irreversible Work-up / Reversal Failure / Actively Dying

Palliate Symptoms (e.g., Agitation, Breathlessness, Pain)

Hyperactive

Irreversible due to: Active Dying

First Generation Antipsychotics, Benzodiazepines, Phenobarbital, Propofol

Hypoactive

Irreversible due to: Goal of Care Choice or Work-up / Reversal Failure

First Generation Antipsychotics, Benzodiazepines, Phenobarbital, Propofol

Little Evidence to Guide

Taper Interventions as Appropriate

Taper Interventions as Appropriate
Non-pharmacologic Interventions

- **Cognitive**
  - Orientation (calendar, caregiver names)
  - Activities (cognitively stimulating)

- **Sleep**
  - Regular routine
  - Sleep aids (relaxing music, massage)
  - Environmental (eliminate noise, night-time meds)

- **Mobility** (range of motion, limit IV’s, etc)

- **Visual Aids** (glasses, large dial phones, etc)

- **Hearing Aids** (check ear wax)

- **Volume repletion for dehydration**
  - beverage of choice available and offered frequently
Other Delirium Interventions

- Opioid rotate (methadone and fentanyl preferred)
- PCA for pain control
- Methylphenidate for hypoactive delirium
- Rehydration (oral, hypodermoclysis, IVF)
- Music reduced post-op delirium in elderly
Pharmacologic Treatment

- No medication is FDA approved for the treatment of delirium
- No published double-blind, randomized, placebo controlled trials
  - Few controlled trials
  - Small numbers
  - Various patient populations
    - post-op, ICU, cancer, AIDS, hip fractures
Haldol v. Lorazepam

- Double-blind RCT
- 244 AIDS patients consented
- 30 (12%) patients developed delirium
- Haloperidol (n = 11)
- Chlorpromazine (n = 13)
- Lorazepam (n = 6)
- Haloperidol = chlorpromazine > lorazepam
Delirium Treatment

- Anti-psychotics are the treatment of choice
  - Shown to both prevent as well as resolve delirium
- All antipsychotics have suspected efficacy
- Typicals (haloperidol, chlorpromazine)
  - Greatest evidence base
  - Cheaper
  - Multiple routes of administration
Delirium Prevention

- Higher the incidence the more effective prevention
- Good data for non-medication prevention
  - HELP program
- Emerging data for medication prevention
  - Specifically antipsychotics but data mixed

- Melatonin mixed efficacy (may be dose dependant)
  - ? Ramelteon (rozirem)

Antipsychotic Adverse Effects

- Sedation
- Postural hypotension
- Falls
- Extrapyramidal
  - Parkinsonism
- Cerebrovascular
  - OR 2.1, ARI ~1%
- Mortality
  - Infection and cardiac
- Metabolic side effects (weight gain, etc.)
Antipsychotics and Mortality

In Dementia
- Black Box Warning Issued in 2004
- Consistent across all antipsychotics
- Relative risk = 1.6-1.7
  - Absolute risk = 3.5% vs. 2.3% with placebo
- Number Needed to Harm = 83
  - Number need to treat = 5-14
  - For every 9-25 persons helped, 1 death associated with use

In Delirium
- No evidence that mortality is increased

Elie, 2009
Jeste, 2008
# Antipsychotic Side Effects

<table>
<thead>
<tr>
<th>Drug (daily dose range)</th>
<th>Aripiprazole (2-10 mg)</th>
<th>Haloperidol (0.25-2 mg)</th>
<th>Olanzapine (2.5-7.5 mg)</th>
<th>Quetiapine (12.5-150 mg)</th>
<th>Risperidone (0.25-2 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand Name</td>
<td>Abilify</td>
<td>Haldol</td>
<td>Zyprexa</td>
<td>Seroquel</td>
<td>Risperdal</td>
</tr>
</tbody>
</table>

### Movement Side Effects

<table>
<thead>
<tr>
<th>Movement Side Effects</th>
<th>Aripiprazole</th>
<th>Haloperidol</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>□□</td>
<td>□□□</td>
<td>□□</td>
<td>□</td>
<td>□□</td>
</tr>
</tbody>
</table>

### Central Nervous System

<table>
<thead>
<tr>
<th>Sedation</th>
<th>Aripiprazole</th>
<th>Haloperidol</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>□□</td>
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<td>□□□□□</td>
<td>□□</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Confusion, delirium, other cognitive worsening</th>
<th>Aripiprazole</th>
<th>Haloperidol</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>□</td>
<td>0</td>
<td>□□</td>
<td>□</td>
<td>□□</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Worsening psychotic symptoms</th>
<th>Aripiprazole</th>
<th>Haloperidol</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>□</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

### Cardiovascular / Metabolic

<table>
<thead>
<tr>
<th>Orthostatic hypotension</th>
<th>Aripiprazole</th>
<th>Haloperidol</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>□?</td>
<td>□□</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Edema</th>
<th>Aripiprazole</th>
<th>Haloperidol</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>□?</td>
<td>0</td>
<td>□</td>
<td>0</td>
<td>□□</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight gain/glucose ↑</th>
<th>Aripiprazole</th>
<th>Haloperidol</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>□?</td>
<td>□□□</td>
<td>□</td>
<td>□□</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Triglyceride ↑</th>
<th>Aripiprazole</th>
<th>Haloperidol</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>□□□□□</td>
<td>□□□□□</td>
<td>□□</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Urinary incontinence/UTI</th>
<th>Aripiprazole</th>
<th>Haloperidol</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>□□□□</td>
<td>□□</td>
<td>□□</td>
<td>□□</td>
<td>□□</td>
</tr>
</tbody>
</table>
Common Antipsychotics

Typical
- Chlorpromazine (Thorazine)
- Thioridazine (Mellaril)
- Prochlorperazine (Compazine)
- Haloperidol (Haldol)
- Fluphenazine (Prolixin)
- Perphenazine (Trilafon)

Atypical
- Risperidone (Risperdal)
- Ziprasidone (Geodon)
- Olanzapine (Zyprexa)
- Quetiapine (Seroquel)
- Clozapine (Clozaril)
- Aripiprazole (Abilify)
# Typical Formulations

<table>
<thead>
<tr>
<th>Generic names</th>
<th>Relative Potency</th>
<th>Available Formulations</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td>100</td>
<td>tabs, liquid, IM/SQ, suppository</td>
<td>May be more effective for highly agitated patient. More anticholinergic. Can help with hiccups.</td>
</tr>
<tr>
<td>Fluphenazine</td>
<td>2</td>
<td>tabs, liquid, Long acting IM/SQ</td>
<td>Very similar to haloperidol.</td>
</tr>
<tr>
<td>Perphenazine</td>
<td>8</td>
<td>Tabs, liquid, IM</td>
<td>Often not recognized by family/care centers</td>
</tr>
<tr>
<td>Thioridazine</td>
<td>95</td>
<td>tabs, liquid</td>
<td>More cardiac concerns.</td>
</tr>
</tbody>
</table>
## Atypical Formulations

<table>
<thead>
<tr>
<th>Generic names</th>
<th>Relative Potency</th>
<th>Available Formulations</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>7.5</td>
<td>Tab, liquid, IM, disk melt (SL)</td>
<td>Little data for delirium</td>
</tr>
<tr>
<td>Abilify</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clozapine</td>
<td>100</td>
<td>Tabs</td>
<td>Needs intensive monitoring, 2nd line in Parkinson’s</td>
</tr>
<tr>
<td>Clozaril</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olanzapine</td>
<td>5</td>
<td>Tab, IM, rapid dissolving (SL)</td>
<td>More sedating, can worsen delirium</td>
</tr>
<tr>
<td>Zyprexa</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quetiapine</td>
<td>100</td>
<td>Tabs</td>
<td>1st line in Parkinson’s</td>
</tr>
<tr>
<td>Seroquel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td>2</td>
<td>Tab, liquid, rapid dissolving (SL)</td>
<td>Very similar to haloperidol</td>
</tr>
<tr>
<td>Risperdal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>60</td>
<td>Caps, IM</td>
<td>Little data for delirium</td>
</tr>
<tr>
<td>Geodon</td>
<td></td>
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</table>
Common Medication Doses

Antipsychotics
- Haloperidol 0.5-1mg Q30min
  - PO has ½ life of 24 hr
  - IV has ½ life of 12 hrs
- Chlorpromazine 25-50 mg PO/PR TID QID
- Olanzapine 2-5 mg PO/SL QD
- Risperidone 0.5 mg PO/SL BID
- Quetiapine 50-100 mg PO BID

Sedatives
- Lorazepam 0.5-1mg PO/IV/SQ q4hr
- Diprivan (Propofol) 10mg IV bolus (then 10mg/hr)
- Midazolam 1-2mg IV q1hr
Terminal Delirium

- Is it just part of normal dying?
  - Accumulation of toxic metabolites
  - Electrolyte disturbances
  - Organ failure
- Diagnosis usually made retrospectively
  - Significant restlessness/agitation in final days of life
- Most common reason for palliative sedation
Terminal (or Irreversible) Delirium

- Treatment recommendations (IV or SQ)
  - Antipsychotic (higher doses)
  - If antipsychotic is ineffective or sedation is desired
    - Sedative agent (lorazepam, midazolam, propofol)

- Case Study
  - 83 year old, end stage lung cancer, previously independent, in care center for failing ADLs
  - Restless, agitated, pacing, striking out
  - Started SQ chlorpromazine 20mg/hr with 20mg q30min bolus-increased to 100mg/hr with 50mg q30min bolus
  - Was comfortable, confused, conversant, not pacing or striking out in last 2 days before death
When you talk to the nurse she says that Ruby has been more confused and she thinks Ruby has delirium. What should you do?

2. Nothing, delirium is expected and no big deal.
3. Review her medication list.
4. Schedule lorazepam qhs.
5. Stop all opioids.
Delirium Pearls

- Common and distressing - maintain a high index of suspicion
- Can often be reversed by simple measures even in dying patients
- Treat symptoms aggressively to improve long-term outcome
- First generation anti-psychotics are treatments of choice for distressing symptoms
Dementia

- Dementia is a terminal diagnosis
- At some point the patient stops living with dementia and begins dying from dementia
- Common progression
  - Food refusal
  - Dysphasia and choking
  - Weight loss
  - Secondary infections (aspiration pneumonia, UTIs)
Behavioral Disturbances in Dementia

- Disruptive physical behaviors
  - Wandering, pacing
  - Physical threats or violence
- Disruptive verbal behaviors
  - Verbal outbursts/aggressiveness
  - Disruptive vocalizations
What to do: Behavioral Disturbances

- Try to remove things that aggravate
- Consider pain, medical conditions, hunger, thirst
- Remember not to TEACH
- Try to distract to something else
What to do for Psychosis?

- Don’t argue or “point out the truth”
  - Reassure, distract to something pleasant
    - E.g., don’t repeatedly remind of spouse/parent’s death, etc
- Identify the symptoms
- Consider medications (i.e., Sinemet) or illness which may be contributing
What to do in General?

- Deal with fluctuations
  - Don’t blame
    - What works one day doesn’t always work the next

- Consider scheduled pain medications

- Expectations
  - Symptom reduction or stabilization may = success
  - Focus on quality of life, daily function, autonomy
Drug Treatment for Agitation

- Antipsychotics most commonly used
- Treat agitation like another breakthrough symptom
- Start with prn dosing and dose on the Cmax
- Calculate scheduled dose based on needed prn amount in previous 24 hrs
Antipsychotic Pharmacokinetics

- **SC / IM**: ≈ 30 min
- **PO / PR**: ≈ 60 min
- **Cmax**: for all ≈ 24 hrs

Adapted with permission from S. Irwin San Diego Hospice
Moderate Agitation

- **Haloperidol 1-2 mg SQ/PO**
  - Increase dose by 1mg q Cmax until controlled

- **Alternatives**
  - **Chlorpromazine 50-100 mg SQ up to 2g/d**
    - Increase dose by 50 mg q Cmax until controlled
    - SQ can burn, infusing 1 mg dexamethasone q24hr can help
    - Oral bio-availability variable, more sedating
  - **Risperidone 0.25-1 mg PO q1hr up to 6 mg/d**
  - **Olanzapine 5-10 mg PO q1hr up to 30 mg/d**
  - **Quetiapine 25-100 mg PO q1hr up to 1200 mg/d**
Severe Agitation

- Imminent risk of harm to self or others due to agitation
  - Haloperidol 2-5 mg x 1
  - Add diphenhydramine* 50-100 mg
    - Protects against EPS and adds sedation
  - ± lorazepam* 1-2 mg
    - Can also consider midazolam

* Mix very slowly in order in same syringe:
  - Lorazepam ➤ Haloperidol ➤ Diphenhydramine
Severe Agitation

- Alternatives
  - Chlorpromazine 50-100 mg SQ up to 2g/d
    - Increase dose by 50 mg q Cmax until controlled
    - Likely don’t need diphenhydramine
    - Use ± lorazepam
  - Olanzapine 5-10 mg IM up to 30 mg/d
    - MR x 1 in 2hrs, MR x 1 again 4 hours after that
    - Expensive
  - Ziprasidone 10-20 mg IM up to 40 mg/d
    - MR 10 mg q2 hrs
    - MR 20 mg q4 hrs
    - Expensive
Dementia Related Agitation

- Antipsychotics may no longer be first line
- Consider behavioral/non-pharm techniques first
- Some evidence for:
  - Beta-blockers
    - propranolol 10 mg qd to 160 mg tid (start 20-40 mg bid)
  - Gabapentin
    - 100 – 300 mg q1hr up to 3600 mg/d
  - Trazodone
    - 25 – 50 mg q1hr up to 300 mg/d
  - Acetylcholinesterase inhibitors
  - High dose SSRIs
Agitation Pearls

- Treat agitation like you treat pain
- Dose break-through on Cmax
- Dose scheduled on ½ life
- Use time limited trials

References for agitation management in dementia and delirium (pocket cards, video vignette training and more)

http://www.healthcare.uiowa.edu/igec/IAADAPT
Questions?