Management of Delirium, Agitation, and Terminal Restlessness

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Objectives

- Define delirium and its subtypes
- Describe the clinical significance and prevalence of delirium and its impact on patients, caregivers, and the healthcare system
- Apply appropriate delirium screening tools to guide the diagnosis of delirium
- Identify both pharmacological and non pharmacological management strategies for treating patients with delirium

What is Delirium?

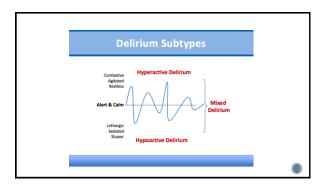
- Delirium is a state of confusion that comes on very suddenly and lasts hours to days.
- It means the patient cannot think very clearly, can't pay attention and is not really aware of their environment.
- Sometimes people will call it other things such as a change in mental status, "sundowning", "terminal agitation", or "ICU psychosis", but it is all delirium.



Subtypes of Delirium

- Hypoactive
 Least recognized
 Apathy Lethargy Sedation

- Hyperactive
 Most recognized
 Restlessness Agitation Combativeness
- Mixed Type
 Fluctuating periods of both



Risk Factors for Delirium

- DemographicGender: MaleAge: >65 years

- Cognitive Status
 Dementia, Depression, Previous Delirium
- Functional Status
 Immobility, Dependence for ADLs, Falls hx
- Sensory ImpairmentHearing or Vision
- Nutritional Status
 Malnutrition or Dehydration
- Medications
- Polypharmacy, Psychoactive Meds, ETOH
- Medical History
 Stroke, Neurological Dz, Metabolic Dz, Hepatic or Renal Failure, severity of illness, fracture or trauma

Differential Diagnoses

- E: Electrolytes (Na, Ca, BUN, Glucose)
- L: Lack of Drugs (pain, ETOH, Rx)
- I: Infection
- R: Reduced Sensory Input
- I: Intracranial (stroke, seizure, meds....rare)
- U: Urinary retention, fecal impaction, meds
- M: Myocardial (PE, MI, CHF)

Delirium v. Dementia

Feature	Delirium	Dementia
Onset	Acute	Insidious
Course	Fluctuating	Constant
Attention	Disordered	Generally Preserved
Consciousness Hallucinations	Disorded/Often Present	Generally Preserved Generally Absent
Involvement	Often Present	Generally Absent

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- Underlying principle diagnosis
- Comorbidities
 Functional Status
- Prognosis
 Goals of Care (GOC)
- Irreversible:
- Time limited diagnostic and therapeutic trial:
 - Failed
- Inconsistent with GOC
 Underlying physiological processes are unclear or irreversible.
 Prognosis (hours to days)

Incidence/Prevalence

- Approximately 1/3 of patients 70 years and older admitted to a general medical service are delirious.
- 50% have symptoms upon admission and the other 50% develop them in-house.
- 67% of delirium cases are missed.
- In general, 30-80% of patients admitted to the ICU will experience delirium
- In the geriatric population, however, the incidence is as high as 70-87%
- The most common risk factor for elderly patients to develop delirium is underlying dementia which is present in 66% of all cases of delirium.
- It is estimated that 30-40% of cases of delirium are preventable, therefore utilization of prevention strategies is essential

Delirium in hospice and palliative care settings

- Delirium is common across clinical settings but is particularly common in palliative care, where its prevalence has been found to be up to 12% at initial community assessment and 68% in the final weeks of life.
- Delirium indicates a poor prognosis in palliative care patients, precipitating increased hospital admissions, morbidity and mortality, as well as communication loss and patient and family distress.
- Management of delirium encompasses treating potentially reversible causes and using non-pharmacological and pharmacological interventions. Up to half of all delirium cases in terminally ill patients are reversible if the underlying causes are identified and treated.
- Many terminally ill people prefer to be cared for at home. Detirium management can be provided in patients' homes but delirium may still contribute to unplanned admissions if the patient or caregivers become distressed

 (Haris et al., 2020)



Consequences

- Institutionalization
 PTSD
- Caregiver burden
- Long-term cognitive deficits
 Increased rates of dementia
- Hospital costs > \$11 billion/per (USD)
- Post-hospital costs >\$153 billion/year (USD)
- ED visits
- Institutionalization
 Rehabilitation
- · Formal home care services

Delirium and Mortality

- Analysis of data from Project Recovery, a controlled clinical trial of a delirium prevention intervention from 1995 to 1998 with follow-up through 2000.
- Patients > 70 years old without delirium and were at immediate to high risk and were receiving usual care (n = 469)
- 70 developed incident delirium (15%)
- Patients with delirium were more likely to: be restrained (37%), develop a hospital acquired condition (37%), develop other noxious insults (63%), 90 day mortality (24%).
- Restraining devices, HACs, and additional noxious insults were more frequent among patients with definium, increased mortality in a graded manner, and were responsible for a significant percentage of the association of delirium with death
- Dharmarajan et al. (2017). Pathway from Delirium to Death: Potential In-Hospital Mediators of Excess Mortality. JAGS, 65(5): 1026-1033.

The Patient Experience

• PTSD in one-in-three ICU survivors

"But she wasn't prepared for the flashbacks. She was drowning, poisoned by nurses, crawling on the floor of a walk-in freezer full of amputated limbs. The images came to her unbidden, memories of events she had never experienced."



The Patient Experience



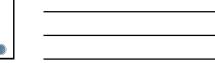


Caregiver Burden

- Several papers report that moderate to severe levels of distress are experienced by the majority of caregivers of patients with delirium
- \bullet Distress was found to be greater in caregivers compared with patients experiencing delirium
- Patient correlates of caregiver distress include poor physical performance status, the presence of hyperactive delirium, hallucinations, agitation, cognitive decline and incoherent speech

Effect on caregivers at end-of-life

- $\, \cdot \,$ If symptoms are severe, the patient may need to be moved to an inpatient setting, thus preventing the goal of dying at home
- \bullet Delirious patients may behave in ways that are surprising and disturbing to those who know them
- $\,$ $\,$ Delirium may impair communication between the dying loved one and the caregiver, thus limiting quality time spent together
- Lack of understanding of terminal delirium can cause uncertainty among family members and can negatively impact grieving



Screening	
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Confusion Assessment Method (CAM)	
*Assesses the presence, severity, and fluctuation of 9 delirium features: acute onset, inattention, disorganized	
thinking, altered level of consciousness, disorientation, memory impairment, perceptual disturbances, psychomotor	
agitation or retardation, and altered sleep wake cycle Grover S, Kate N. Assessment scales for delirium: A review. World J Psychatr 2012: 2(4): 58-70	
]
Confusion Assessment Method (CAM)	
Acute onset and fluctuating course: Is there evidence of an acute change in mental status from the patient's baseline? Does the behavior fluctuate during the day, tend to come and 90, or increase/decrease in severity?	

Altered level of consciousness:

What is the patient's level of consciousness: alert (normal), vigilant (hyper-alert), lethargic (draws, easily aroused), stupor (difficult to arouse), or coma (unarousable)

If features 1 and 2 and either 3 or 4 are present, a diagnosis of delirium is suggested

Nursi	ing Del	lirium	Scree	ning
Scale	(NuDl	ESC)		

• Five item scale that combines items from the Confusion Rating Scale (CRS) which looks at disorientation, inappropriate behavior, inappropriate communication, and illusions/hallucinations plus a fifth item rating unusual psychomotor retardation

Nursing Delirium Screening Scale (NuDESC)

Disorientation

Disoriented to person, place, and time, 1 = disoriented but easily oriented, 2 = disoriented x 2 or x 3 and not easily oriented

Beginning time to the disorient of the disorien

| Inappropriate Communication: | 0 - appropriate, 1 - unclear thinking or rambling speech, 2 = incoherence, nonsensical or unintelligible speech

<u>Illusions/hallucinations:</u>
 0 = none, 1 = paranoia, fears, 2 = hallucinations, distortions of visual objects

Pyvchomotor Retardation:
 0 = none, 1 = delayed or slow responsiveness, 2 = excessive sleeping, somnolent, lethargic

 ${\ \ ^{\circ}}$ Score of > or = to 2 indicates the patient is screening positive for delirium

Ivan

- 87 year old Russian speaking gentleman, PMH significant for Vascular Dementia, hx of CVA 3 year's ago with residual R hemiparesis and dysphagia on ground diet, crushed meds and thin diquids. He is a long-term care resident and was frought into the hospital d/t AME (lethary), reduced PD intake and found to have asyrration PMA and dehydration with AME. Pertinent Iabs on admission: Who CS 17, Na 15-8, BUT 5, Cred 17 i (1) at baseline, AME 2, To Trotein hypoxic with pulssor of 89-91% on RA, requiring Z I via NC. He is not 02 dependent at baseline.
- This admission, SLP evaluated and made recommendations for strict NPO. A dobhoff tube was placed to provide nutrition and ensure ability to administer medications. He self-removed x 1 and it was replaced, and he was placed in restraints.
- You find him very agitated, picking at the sheets, yelling out in Russian, he does not make eye contact and cannot be redirected. He is restrained and needs 1:1 supervision. Staff reports that he has periods of agitation fluctuating with periods of unresponsiveness.
- His wife states that although he has been confused in the past, he has never been this
 agitated, this is a marked change in his status

Non	Pharma	ıcolog	ical	
Inte	rvention	is for	Deli	rium

- Prevention
- Early Detection
- •Elimination or correction of underlying causal factors
- •General symptomatic and supportive measures and interventions

Treatment

Interventions should be chosen based on goals of care as well as where the patient is in their illness trajectory!!

Early Recognition and Training

- •Train staff on how to screen at risk patients with a standard screening tool (CAM, etc)
- Educate staff on the essential aspects of delirium: risk factors, prevention, screening, interventions

Assess and Intervene

- Polypharmacy
 Review all medication at least every 24 hours
 Keep sedatives to a minimum
 Check drug interactions
 Don't forget about drug withdrawal

- Asses and medicate for pain appropriately
 Use non opioid analgesia if possible
 Consider rotating agent
- HypoxemiaO2 appropriate?

- If appropriate, check for metabolic and electrolyte disturbances
- Treat infections if appropriate and in line with goals of care
 Hydration/nutrition

- If tolerated, encourage oral hydration
 Consider short term IV hydration if appropriate
 Assist with feeding
- Sleep

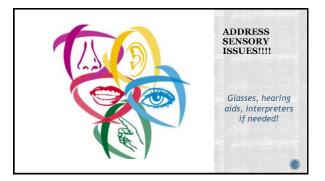
Assess and Intervene

- Assess bowels
 When was the last BM?
- Assess urinary status
 ? urinary retention
 ? d/c urinary catheters
- Don't forget about drug and alcohol withdrawal: both rx and recreational
- Mobility
 Minimize 'attachments'
 Ambulate if safe
 ROM
 Get them OOB

- Orientation board with names of care team and date
- Family or familiar objects, during Covid this is often impossible due to restrictions

 Avoid moving people unless necessary

- Communication
 Orienting communication
 Slow, simple repetitive
 Address the patient by name



The T-A-DA method of management: Tolerate, Anticipate, and Don't Agitate



T-A-DA

- <u>Tolerate</u>: Allow patients to respond naturally to their situation while under close observation
- <u>Anticipate</u>: Anticipate behaviors:
- Ex: patients with delirium will pull on anything not normally present - minimize 'attachments'
- <u>Don't Agitate</u>: Decrease environmental agitators: lights, noise, visitors, television, music, etc. If reorientation helps, use it, if not: don't keep doing it

Pharmacological Management

- No medications have been approved by the US Food and Drug Administration (FDA) for treatment of delirium
- In addition, there are few controlled studies of pharmacologic management in delirium
- **However, most advocate for a trial of pharmacologic management of symptoms (after non pharmacological management strategies have been applied) if the patient is in significant distress, they pose a safety risk to themselves or others, or their behaviors are impeding essential aspects of his or her medical care

What the is rationale for using antipsychotics??

- It is thought that delirium is due in part to an imbalance of neurotransmitters with reduced cholinergic activity and/or and excess of dopamine
- Antipsychotics are dopamine receptor antagonists, goal is to decrease dopamine and increase cholingergic activity

Use is controversial!

- FDA black box warning of increased risk of death when antipsychotics are used to treat elderly patients with dementia related psychosis
- SNF's dont like them!!
- 2017 CMS issued a rule revising the requirements for LTC facilities surrounding antipsychotics
- No one wants to impact their STARS rating
- ${\ensuremath{\,^\circ}}$ FDA has issued a warning against risk of QTc prolongation and torsades de pointes with IV haldol
- The Agar et al Study

The Agar et al Study

- Double blind, parallel-arm, dose titrated randomized trial conducted at 11 Australian inpatient hospice or hospital palliative care sites from 8/08-8/14 with patients identified as experiencing delirium
- The aim of the study was to determine if risperione or haldol, given in addition to managing the precipitants of delirium and providing supportive nursing care, provided additional benefit in symptom reduction compared with placebo
- Study duration was 72 hours
- Study sample of 247 patients (82 received risperidone, 81 received haldol, 84 received placebo)
 - Agar, et al. Eficacy of Oral Risperidone, Haloperidol, or Placebo for Symptoms of Delirium Among Patients in Palliative Care. JAMA Intern Med. 2017; 177(1):34-42.

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- Behavioral, communication, and perceptual symptoms of delirium associated with distress in patients receiving palliative care were greater in those treated with antipsychotic drugs than in those receiving placebo
- The outcomes and direction of findings were similar for both the risperidone and haldol arms, suggesting that this may be an antipsychotic class effect
- Poorer overall survival was noted in the haldol group (73% more likely to die than placebo) as well as the risperidone group (29% more likely to die)
- Compared with placebo, participants in both groups had more extrapyramidal side effects

The Details

- Participants in the risperidone arm had delirium symptom scores that were significantly higher than those in the placebo arm (on average 0.48 units higher)
- Participants in the haldol arm had delirium scores that were higher than in the placebo arm (on average 0.24 units higher)
- In addition midazolam use was significantly lower among those in the placebo arm compared with the risperidone and haldol arms combined

Their conclusion...

"Antipsychotic drugs should not be added to manage specific symptoms of delirium that are known to be associated with distress in patients receiving palliative care who have mild to moderately severe delirium. Rather, management relies on ensuring systematic screening..., reversing the precipitants of delirium, and providing supportive interventions"

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- Up to Date (literature review through December 2020):

 "A cautious trial of psychotropic medication should be reserved for treatment of severe agitation or psychosis"
- They suggest a short term trial of haldol 0.5-1mg
- Cochrane review January 2020:
- Cochrane review January 2020:

 "We found no high quality evidence to support or refute use of drug therapy for delirium symptoms in terminally ill adults. We found low-quality evidence that risperidone or haldoperidol may slightly worsen delirium symptoms of mild to moderate severity for terminally ill people compared to placebo. We found moderate to low-quality evidence that haldoperidol and risperdone may slightly increase extrapyramidal adverse events for people with mild to moderate severity delirium. Given the small number of studies and participants on which current evidence is based, further research is essential"

Antipsychotic drugs

	Dose	Route of administration	Level of sedation
Haldol	-Starting dose: 0.5-1mg -Can be given ig 1 hour pm -Micc dose 10mg/dose	PO, IM, SC, IV	Less sedating
Atypicals: Olanzapine	-Starting dose 2.5-5mg -Max dose 30mg/day	PO, ODT, IM, SC	More sedating
Risperidone	-Starting dose: 2.5-5mg - Max dose 30mg/day	PO, ODT, IM, SC	Less sedating
Quetiapine	-Starting dose 12.5-50mg -Max dose 600-900mg/day	PO only	Very sedating
Chlorpromazine	-Starting dose 25-50mg -Max dose 200- 800mg/day	PO,IV,IM,SC,PR	Very sedating

What about benzodiazepines????

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- Objective was to compare the effect of lorazepam vs placebo as an adjuvant to haloperidol for persistent agitation for patients with delirium in the setting of advanced cancer
- Double blind, parallel group, placebo controlled, randomized clinical trial in which patients with hyperactive or mixed delirium received either lorazepam + haloperidol or placebo + haloperidol
- · Conducted at the MD Anderson Cancer Center
- $\,^{\circ}$ Protocol was all received 2mg of IV haloperidol every 4 hours with another 2mg every hour prn, those in the lorazepam arm got a single dose of 3 mg of IV lorazepam, placebo arm got identically appearing IV NS

Results

- Those who received lorazepam + haloperidol had a greater reduction of RASS score than those who received placebo + haloperidol and were perceived as being more comfortable by both blinded caregivers and nurses
- Those who crecived forazepam + haloperidol required significantly lower doses of rescue neuroleptics
- There was no significant between group differences found in delirium related distress and survival

Conclusion was that in this preliminary trial of hospitalized patients with agitated delirium in the setting of advanced cancer, the addition of lorazepam to haloperidol as compared with haloperidol alone resulted in significantly greater reduction in agitation

Ivan

- 87 year old Russian speaking gentleman, PMH significant for Vascular Dementia, hx of CVA 3 years ago with residual R hemiparesis and dysphagia on ground diet, crushed meds and thin liquids. He is a long-term care resident and was brought into the hospital d/t AMS (lethargy), reduced PO intake and found to have aspiration PNA and dehydration with AKI. Pertinent labs on admission: VMSC 17, Na 154, BUN 54, Creat 1.9 (1.0 at baseline), Alb 2.9, Tot Protein 5.4. He remains hemodynamically stable and was admitted to the medical floor. He is hypoxic with pulsox of 89-91% on RA, requiring ZL via NC. He is not 02 dependent at baseline.
- You speak to staff and find out that a live Russian interpreter has not been available, they have been trying to use the language line with little success. His wife has not been able to visit frequently due to Covid restrictions
- $\, \bullet \,$ Wife's goal is for comfort, she is devastated seeing him in this agitated state

Palliative Sedation

- Sometimes patients experience distressing symptoms at end of life that are refractory to intensive palliative care interventions
- The intention of palliative sedation is to deliberately induce a temporary or permanent light to deep sleep, not hastening death, but with the goal of relief of symptoms
- The goal is to relieve unendurable physical, spiritual, or psychological distress in patients close to death, it requires that comfort is the priority goal of care

Hospice and Palliative Nurses Association (HPNA) Position Statement on Palliative Sedation

- Palliative sedation can be used for imminently dying patients to manage refractory symptoms unrelieved by optimal palliative care
- Hospice and palliative nurses must possess sufficient knowledge about the use of palliative sedation (including the ethical and legal justification of use) in order to inform patients, families and other health care providers in making decisions around its use
- Interventions and/or sedative doses should be used to relieve suffering without the intention of hastening death

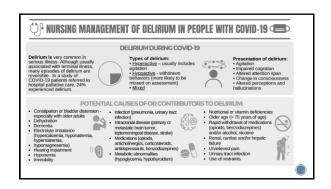
- A nurse can object to the use of palliative sedation and has the right to transfer care. However, those nurses who choose not to participate in palliative sedation are directed to continue to provide care until responsibility for care is transferred to an equally competent colleague to avoid abandonment
- Informed consent must be used (either the patient or the surrogate decision maker)
- It requires interdisciplinary assessment of the patient to determine the refractory nature of their symptoms

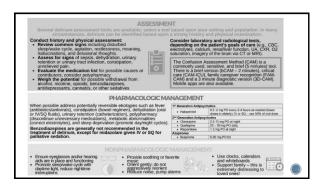
 The full position statement from HPNA can be viewed here: https://advancingexpertcare.org/position-statements/ 	
NH Board of Nursing Position Statement The NH BON endorses the Position Statement on Palliative Sedation from the Hospice and Palliative Nurses Association The administration of sedation requires continuous monitoring of the patient and ability to respond immediately and appropriately to any adverse reaction or complication	
Hospice and Palliative Care Federation of Massachusetts *The justification for use is based on the ethical principles of beneficence, non-maleficence, autonomy and fidelity *The intent is the relief of suffering and not to end the patient's life *The decision to initiate sedation must be preceded by a comprehensive interdisciplinary assessment of the patient and a discussion of treatment expectations and options *Informed consent is required	

- The patient's primary physician will be involved in the decision to initiate palliative sedation. The patient's physician and and the hospice medical director must agree on the decision
- Palliative sedation may be implemented in an inpatient setting or at home. For patients who remain at home, a continuous care nurse must be provided for at least 24 hours
- Once the patient is sedated, mediations are not increased unless there is evidence of renewed distress

Drug	Starting dose	Titration	Maintenance dose	Considerations
Midazolam (versed)	Loading dose of 1- 5mg IV or 8Q, followed by an infusion of 0.5- 1.5mg/hr	May strate q 1-2 hour pm based on the number of pm doses	1-20mghr, may give pm bolus dosing of 2.5-5mg every 30-60 min if needed	It has a short half life so it is easily reversible
Lorazepam	Loading dose of 1- 5mg IV or SQ followed by infusion of 0.5-1.5mg/tr	Titrate in increments of 0.5-1mg every 15 minutes x 3, then hourly so needed	4-40mg/day	May cause paradoxical agitation
Phenobarbital	May be given rectally 60-200mg about every 8 hours 1-3mg/kg IV or SQ loading dose followed by infusion of 0.5mg/kg/hr	PR may increase in increments of 30mg IV/SQ increase in increments of 1mg/kg/hr every hour as needed	Approx 50mg/hr (weight based)	It has a long half life and reversal is difficult









A note on compounded medications in hospice

- Despite a lack of evidence of benefit, the compounded product ABH gel (lorazepam, diphenhydramine, and haloperidol) continues to be prescribed for individuals in hospice and palliative care settings for the treatment of nausea and vomiting and terminal deltrium.
- More effective and reliable pharmacological and nonpharmacological strategies exist for the treatment of these conditions in the palliative care and hospice settings.
- The continued use of ABH gel makes for a pricey placebo and delays the treatment of end-of-life symptoms with modalities that work.
 - (Taggart Blaszczyk et al., 2021)

Conclusions

- •Screen patients at risk for delirium
- Try to find the etiology of the problem and 'fix it' if it is in line with goals of care
- Always use non pharmacological interventions
- Reserve medication for patients in severe distress, and use the lowest dose for the shortest time

Ivan

- 87 year old Russian speaking gentleman, PMH significant for Vascular Dementia, hx of CVA 3 years ago with residual R hemiparesis and dysphaga on ground diet, crusted meds and thin logids. He is a long-term care resident and was supported to the control of the control of
- This admission, SP evaluated and made recommendations for strict NPO. A dobboff tube was placed to provide nutrition and ensure ability to administer medications. He self-removed x 1 and it was replaced, and he was placed in restraints.
- He is full code.
- Palliative care was consulted to assist in clarification of goals of care and to assist in symptom management.
- Upon initial consultation:
- You find this patient:
- Restrained, Yelling out , On 1:1 supervision
- His wife (also Russian speaking) is at the bedside, distraught and her primary concern is his inability to eat or drink.



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• David is a 64 yo gentleman with prostate cancer with mets to the bone and liver. He was recently admitted to hospice after a hospitalization for pneumonia and is receiving care at home. Upon admission to hospice he was alert and oriented. He has intense back pain radiating to his right leg which started increasing 5 days ago. Due to his increasing pain, his team has ramped up his pain medication quickly. His MS contin was increased to 90mg bid and he has been receiving 15-30mg of MSIR about every 2 hours for the last 3 days. Gabapentin was added as well and his current dose is 600mg tid. He was started on dexamethasone 4mg bid 2 days ago. Over the last few days, his po intake has been poor. He became restless, and his team added lorazepam 0.5mg q 6 hours prn 2 days ago, average use about 3 times a day. This morning his wife called stating that he is 'not himself'. Upon exam, he is restless, climbing out of bed and picking at his pajamas. He is mumbling incoherently and does not make eye contact. She states at times he yells out and appears afraid, this fluctuates with periods of unresponsiveness.

David

- His last BM was 3 days ago. He has been urinating regularly, but his wife states that in the last 24 hours, his urine has become 'very dark in color and has an odor'. Upon exam, his mucous membranes are dry. He has a congested cough with bilateral rhonchi. His BP is 90/52, pulse is 102, respiration rate is 28 and his O2 sat is 87% on room air
- His wife is distraught, their daughter and her family are flying in from California in a few days and they were hoping he could spend some quality time with him. She is visibly exhausted from having been up with him all night.

Louise

- 85 year old woman with PMH of cognitive impairment, atrial fib on warfarin, prior CVA, CAD, hyperlipidemia, hypothyroidism, vit b12 deficiency. ALF resident, recently returned to her apartment after hospitalization for CVA and STR stay, HCP invoked during her STR stay. She returned to the ALF with hospice services. She is now experiencing paranoid persecutory delusions, poor PO intake, incontinence and ataxia. Urinalysis negative, Vit b12 is 800, TSH 38
- Widowed, adult step-children. Masters degree in Education. Prior to this CVA was driving and managing finances with assistance from her POA. HCP is a friend and former colleague.
- Meds: Levothyroxine, Atenolol, Losartan, Zoloft, Vit B 12 injection monthly, Warfarin, Melatonin, Zyprexa PRN

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• Edith is an 82 yo woman with widely metastatic pancreatic cancer on hospice services. She had been cared for at home by her daughter but unfortunately they both tested positive for Covid. Her daughter became symptomatic and Edith was moved to the hospice house for respite care. Because of her Covid status, she was placed on the designated Covid precaution suite at the house and was somewhat isolated. Shortly after she was admitted, she became increasingly agitated and was transitioned to GIP care. She started spitting out oral medications. she was given Haldol but this seemed to make her agitation worse.

Management of Agitation Video

https://youtu.be/GrJypBgHUxk

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