Delirium Order Set

UConn Health

Kaitlyn Elliott

Objectives

- Define delirium, hyperactive delirium, hypoactive delirium, and mixed delirium
- Explain the prevalence, outcomes, risk factors, pathogenesis, and etiologies associated with delirium
- Explain how medications can contribute to delirium
- Understand pharmacy delirium consults and the role of a pharmacist
- Describe the treatment for delirium
- Understand the new order sets for delirium

Definitions

- Delirium (DSM-V)
  A. Disturbance in attention (i.e. reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment)
  B. Develops over a short period of time, represents an acute change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day
  C. An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability, or perception)
  D. Disturbances in A and C are not better explained by a pre-existing, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal such as coma
  E. There is evidence from the history, physical exam or lab findings that the disturbance is direct physiological consequence of another medical condition, substance intoxication, or withdrawal (i.e. due to a drug abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies.

European Delirium Association/American Delirium Society, 2014

Definitions

- Hyperactive delirium
  - Restless or agitated patient
- Hypoactive delirium
  - Lethargic and apathetic
  - Often missed
  - Associated with poorer prognosis
- Mixed hyperactivity and hypoactivity

Prevalence

- Can occur in approximately 56% of hospitalized patients
  - Older patients: 20-79%
  - Non-ventilated ICU: 20-50%
  - Ventilated ICU: 60-80%
- Post operative delirium
  - 48% of patients experience delirium

Fosnight; Rosenthal, 2015

Outcomes

- Predisposes patients for :
  - Cognitive deterioration
    - 32-96% will leave the hospital without complete resolution of symptoms
  - Higher mortality
    - Morality rate for non-delirious patients- 2%
    - Mortality rate for delirious patients- 11%
  - Hospitalization
    - Longer hospital stays
      - Average 5-10 additional days
    - Each day spent in delirium in the ICU is associated with 20% increased risk of prolonged hospitalization and a 10% increased risk of death
  - Institutionalization
    - More likely to be discharged to nursing facility than to home

Fosnight, Rosenthal, 2015

Risk Factors

Predisposing

- Age greater than 85 years
- >1 activity of daily living impairment
- Vision impairment
- Dementia or baseline cognitive impairment
- Mini-Mental Status Exam <24
- Greater severity of illness
- BUN:Creatinine Ratio >18, elevated creatinine or BUN
- Hypocalemia
- Hyponatremia
- Hypoalbuminemia
- Elevated hepatic enzymes
- Hyperamylasemia
- Hyperbilirubinemia
- Low arterial pH or metabolic acidosis
- <20 kg/m2 body mass index

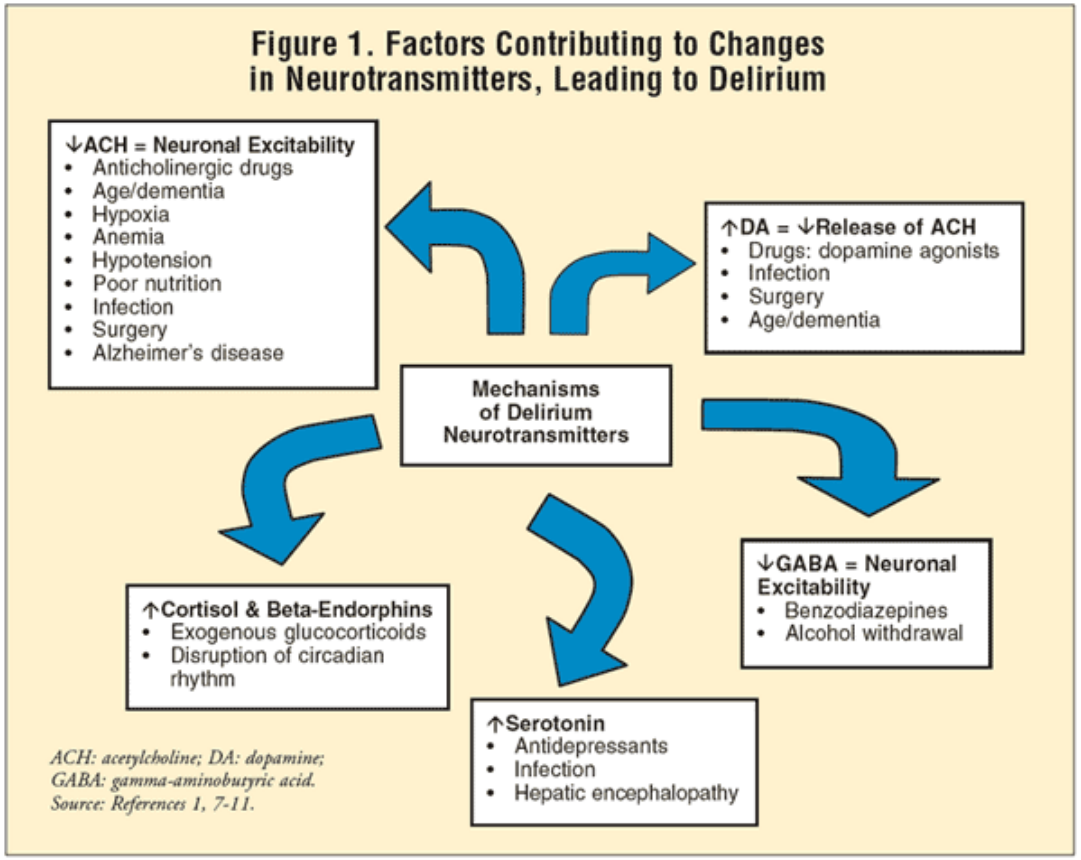
Precipitating

- Physical restraints
- Bladder catheter
- Out of bed <1 time/day
- Medications: Anticonvulsants, Antiemetics, Midazolam
- Benzodiazepine before admission to ICU
- >2 psychoactive agents
- >3 drugs added
- In emergency department for >12 hours
- Malnutrition
- Respiratory insufficiency
- Infection
- Sepsis
- Fever
- Hypotension
- Anemia

Fosnight

Pathogenesis

- Poorly understood but thought to be related to:
- Acute illness
- Neurotransmitter disturbance
  - GABA
  - Glutamate
  - **Acetylcholine**
  - Serotonin
  - Norepinephrine
  - **Dopamine**
  - Tryptophan
- Decrease in oxygenation of the brain
- Increase in cytokines that affect neurotransmitters
- Disturbances in cellular signaling
- Extensive cerebral hypoperfusion
- Disturbances in tryptophan metabolism
- Dementia



Mergenhagen, 2008; Fosnight

Etiologies

- **Medications**
- Fecal impaction
- Pain
- Infections
- Electrolyte disturbances
- Metabolic changes
- Brain lesions
- Postoperative sequelae
- Sensory or sleep deprivation
- Substance intoxication or withdrawal
- Environmental changes
  - Unfamiliar sounds, medication tests, and schedule disruptions in the hospital environment

Pharmacists can have a role in providing medication recommendations to treat many of these etiologies

Mergenhagen, 2008

Delirium Causing Medications

High Risk Medications

- **Analgesics**:
  - Opiods, NSAIDs
- **Anticholinergics**:
  - Atropine, benzotropine, diphenhydramine, scopolamine
- **Antidepressants**:
  - Mirtazapine, SSRIs, TCAs
- **Sedative-hypnotics**:
  - Benzodiazepines, propofol
- **Corticosteriods**:
  - Hydrocortisone, prednisone, methylprednisone, dexamethasone
- **Dopamine agonists**:
  - Amatadine, bromocriptine, levodopa, pergolide,pramipexole, ropinirole

Low Risk Medications

- **Cardiovascular agents**
  - Antiarrhythmics, beta-blockers, clonidine, digoxin
- **Antimicrobials**
  - Acyclovir, aminoglycosides, amphotericin B, cephalosporins, fluoroquinolones, linezolid, macrolides, penicillin, sulfonamides
- **Anticonvulsants**
  - Carbamazepine, phenytoin, valproate
- **Gastrointestinal agents**
  - Antiemetics, H2 receptor antagonists
- **Muscle relaxants**
  - Baclofen, cyclobenzaprine

Mergenhagen, 2008

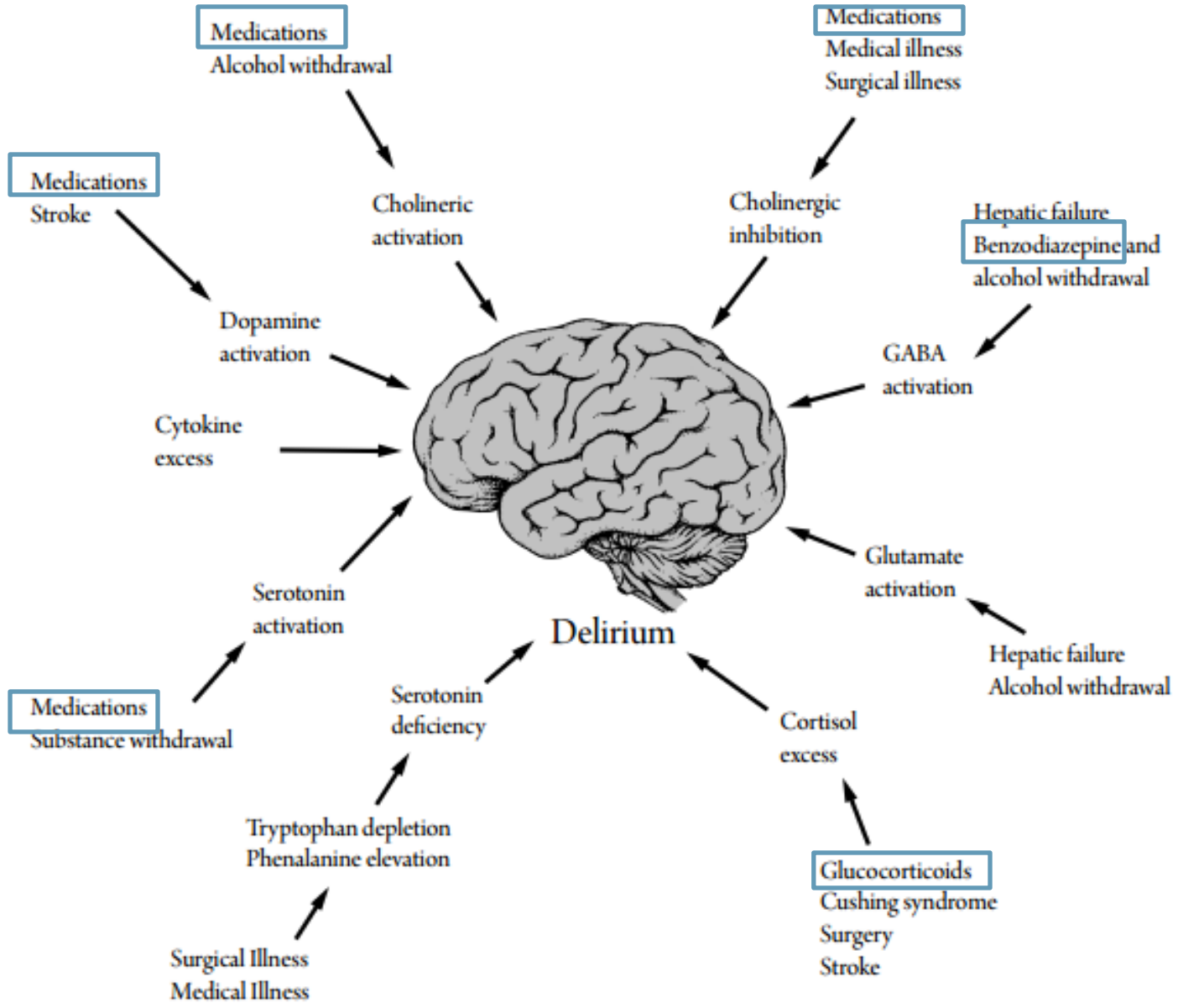


Figure 1-1. Neurotransmitters and biomarkers of delirium.

Reprinted with permission from: Flacker JM, Lipsitz LA. Neural mechanisms of delirium: current hypotheses and evolving concepts. J Gerontol Biol Sci Med Sci 1999;54A:B243.

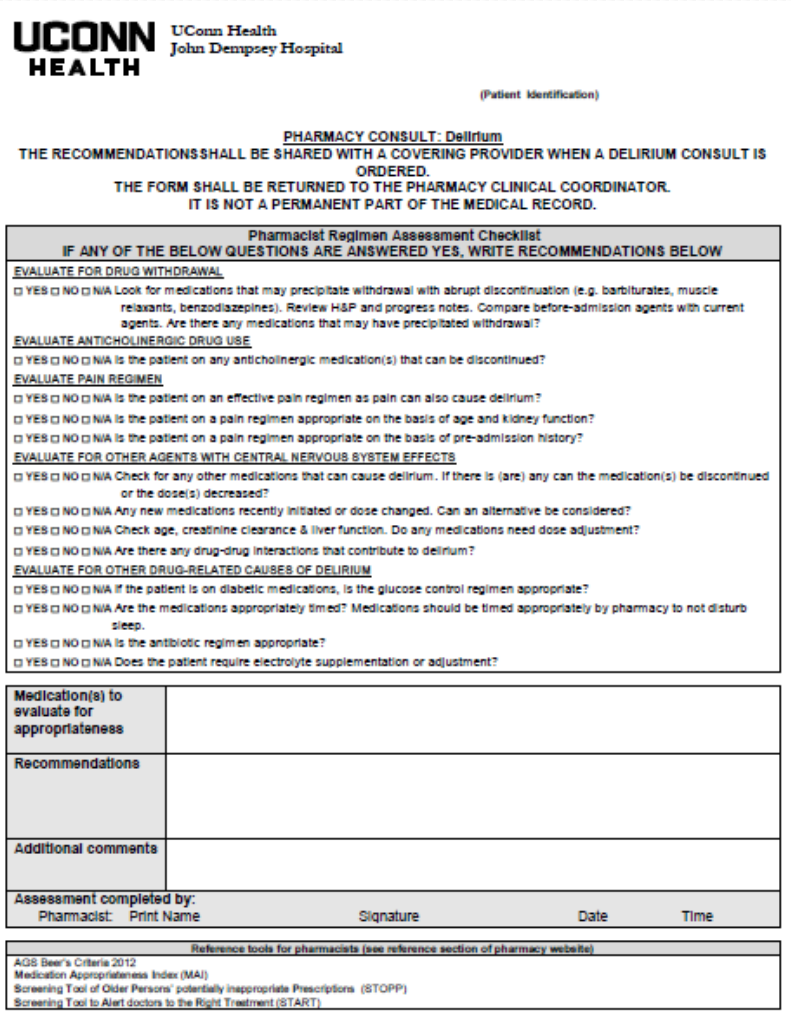
Fosnight

Role of the Pharmacist

- Approximately 40% of delirium cases are caused by medications
- Identifying drug-related causes of delirium
- Reducing polypharmacy
  - STOPP- Screening Tool of Older Persons potentially inappropriate Prescription
  - START- Screening Tool to Alert doctors to the Right Treatment
- Selecting proper pharmacologic treatment for delirium
- Monitoring for side effects and other parameters associated with drug therapy

Pharmacy Consult: Delirium

- Drug withdrawal
- Anticholinergic drug use
- Pain regimen
- Agents with central nervous system effects
- Other drug-related causes of delirium



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UConn Health
John Dempsey Hospital

(Patient Identification)

PHARMACY CONSULT: Delirium

THE RECOMMENDATIONS SHALL BE SHARED WITH A COVERING PROVIDER WHEN A DELIRIUM CONSULT IS ORDERED.
THE FORM SHALL BE RETURNED TO THE PHARMACY CLINICAL COORDINATOR.
IT IS NOT A PERMANENT PART OF THE MEDICAL RECORD.

Pharmacist Regimen Assessment Checklist
IF ANY OF THE BELOW QUESTIONS ARE ANSWERED YES, WRITE RECOMMENDATIONS BELOW

EVALUATE FOR DRUG WITHDRAWAL
☐ YES ☐ NO ☐ N/A Look for medications that may precipitate withdrawal with abrupt discontinuation (e.g. barbiturates, muscle relaxants, benzodiazepines). Review H&P and progress notes. Compare before-admission agents with current agents. Are there any medications that may have precipitated withdrawal?

EVALUATE ANTICHOLINERGIC DRUG USE
☐ YES ☐ NO ☐ N/A Is the patient on any anticholinergic medication(s) that can be discontinued?

EVALUATE PAIN REGIMEN
☐ YES ☐ NO ☐ N/A Is the patient on an effective pain regimen as pain can also cause delirium?
☐ YES ☐ NO ☐ N/A Is the patient on a pain regimen appropriate on the basis of age and kidney function?
☐ YES ☐ NO ☐ N/A Is the patient on a pain regimen appropriate on the basis of pre-admission history?

EVALUATE FOR OTHER AGENTS WITH CENTRAL NERVOUS SYSTEM EFFECTS
☐ YES ☐ NO ☐ N/A Check for any other medications that can cause delirium. If there is (are) any can the medication(s) be discontinued or the dose(s) decreased?
☐ YES ☐ NO ☐ N/A Any new medications recently initiated or dose changed. Can an alternative be considered?
☐ YES ☐ NO ☐ N/A Check age, creatinine clearance & liver function. Do any medications need dose adjustment?
☐ YES ☐ NO ☐ N/A Are there any drug-drug interactions that contribute to delirium?

EVALUATE FOR OTHER DRUG-RELATED CAUSES OF DELIRIUM
☐ YES ☐ NO ☐ N/A If the patient is on diabetic medications, is the glucose control regimen appropriate?
☐ YES ☐ NO ☐ N/A Are the medications appropriately timed? Medications should be timed appropriately by pharmacy to not disturb sleep.
☐ YES ☐ NO ☐ N/A Is the antibiotic regimen appropriate?
☐ YES ☐ NO ☐ N/A Does the patient require electrolyte supplementation or adjustment?

Medication(s) to evaluate for appropriateness	
Recommendations	
Additional comments	

Assessment completed by:
Pharmacist: Print Name Signature Date Time

Reference tools for pharmacists (see reference section of pharmacy website)
AGS Beer's Criteria 2012
Medication Appropriateness Index (MAI)
Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP)
Screening Tool to Alert doctors to the Right Treatment (START)

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Other Delirium Related Pharmacy Consults

- Pharmacist implemented, automatic, delirium pharmacy consult service at an Illinois hospital
- Pharmacist identified drug as a possible cause of delirium in 44.5% of causes and 20.2% as a definite cause
- Total of 1,201 delirium consults between December 2012 and May 2014

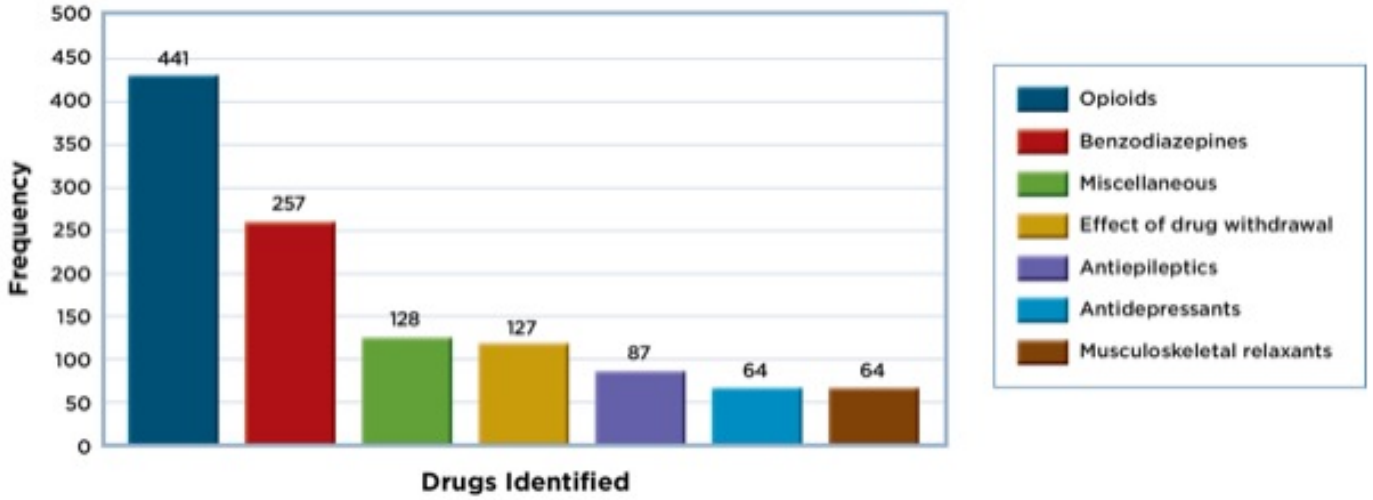

Figure. Common drugs identified as possible or definite causes of delirium[a,b]

[a] For some consults, more than one drug was implicated.

[b] Data derived from 1,201 consults conducted over an 18-month period (December 2012-May 2014).

Wild, 2015

Treatment and Order Sets

Prevention and Non-Pharmacologic Delirium Therapy

- Sleep hygiene
  - Avoid medication and procedures during sleep if possible
  - Reduce noise at night
  - Lights off at night and on during the day
  - Avoid daytime napping
- Orientation
  - Reorient patient as needed
  - Encourage family involvement and regular family visits
  - Use eyeglasses, hearing aids, and interpreters
  - Use music, massage, and relaxation techniques
  - Use sitters
- Maintain patient's mobility and self-care ability
- Promote nutrition and hydration

Order Set

- [ ] WT13280

WT13280

CONFUSION ASSESSMENT METHOD (CAM) SCREEN POSITIVE
Reassess patient to identify reversible contributions to delirium. Screen for potential contributors such as alcohol and psychotropic medication use
-Repeat physical exam and review VS including O2 sat with goal of identifying reversible causes such as hypoxis, CHF, etc.

Consults:

- [ ] PT EVALUATE AND TREAT

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If appropriate, discontinue or reduce the dose of medications with anticholinergic and/or sedative side effects. Consider reviewing with Pharmacist

- [ ] PHARMACY MED REVIEW CONSULT Patient with delirium

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If presentation atypical or patient unimproved in 24 hours...

- [ ] GERIATRICS CONSULT Patient with delirium

Activity:

- [ ] OOB WITH ASSISTANCE
- [ ] AMBULATE WITH ASSISTANCE

Patient Care:

- [ ] ENCOURAGE PO INTAKE
- [ ] REMOVE FOLEY
- [x] AVOID MEDICAL/NSG PROCEDURES during sleep if possible
- [x] REORIENT PATIENT AS NEEDED
- [x] ENCOURAGE FAMILY INVOLVEMENT and regular family visits
- [x] REDUCE NOISE AT NIGHT

Pharmacologic Treatment

- Indicated for:
  - Agitation that is of clear discomfort for the patient
  - Patient is at risk of self-harm or to harm others
- No drugs with FDA-approved labeling for treatment of delirium

Haloperidol

Class	Typical antipsychotic
MOA	Works at cerebral synapses and the basal ganglia by blocking dopamine-mediated neurotransmission to facilitate stabilization of cerebral function.
Place for Use	Most frequently used and best studied medication for delirium Shown to decrease hallucinations, delusions, and disorganized thinking
Clinical Trials	**Han, 2004** •Purpose: Comparison of haloperidol and risperidone in the treatment of delirium •Results •No significant differences in response to haloperidol compared to risperidone for treatment •Memorial Delirium Assessment Scale significantly improved compared to baseline for both drugs •No clinically significant differences in adverse effects compared with both groups **Hu, 2004** •Purpose: Effect of haloperidol on delirium compared to olanazpine or placebo •Results •All groups showed significant decreases in Delirium Rating Scale by the 7th day of treatment (olanzapine 72.2%; haloperidol 70.4%; placebo 29.7%) •Significant increase in dry mouth (16.7 vs. 2.7) and more extrapyramidal symptoms (31.9 vs. 2.7%) among haloperidol patients compared to olanzapine

Mergenhagen,2008, Lexicomp, Lonergan, 2007

Haloperidol

Dosing	0.25-0.5mg PO q8hrs or IM q6hrs No renal or hepatic dose adjustments provided Various administration routes
PK	Few active metabolites Onset of action (IV, IM) 30-60 minutes
Side Effects and Monitoring	QTc Prolongation (Should be discontinued if QT interval increases by 25% or is greater than 450 msec) Anticholinergic effects May cause sedation Orthostatic hypotension Extrapyramidal effects (Parkinson-like symptoms, akathisia, dystonia)
Clinical Pearls	Once a patient's delirium is controlled the patient should be weaned off the scheduled doses 2D6 inhibitor

Mergenhagen,2008, Lexicomp, Lonergan, 2007

Quetiapine

Class	Atypical antipsychotic
MOA	High affinity for alpha1-adrenergic receptors and some affinity for 5-HT2A, histamine, and D2 receptors
Clinical Trials	**Tahir, 2010** Purpose: Clinical utility of quetiapine in the management of delirium vs. placebo Population: 29 patients completed trial (16 quetiapine, 13 placebo) Intervention: Quetiapine Mean dose: 40mg on day 4, 25mg on day 1, 37.5 on day 10 Results: Quetiapine showed a significantly faster response in improvement of DRS-R 98 scores than placebo

Lexicomp; Tahir TA et al. 2010

Quetiapine

Dosing	12.5-25mg PO q12hrs
PK	Rapid absorption Short half life (6 hours) Clearance decreased by 30-50% in the elderly
Side Effects and Monitoring	Vivid dreams Sedation Low incidence of extrapyramidal side effects Short term drowsiness QTc prolongation
Clinical Pearls	Singular administration route

Order Set

Medications:

In cases of severe agitation that is of clear discomfort to patient and/or interferes with care, or if patient is at risk for self injury. Recommended starting doses:

Haloperidol 0.25 -0.5mg PO q8hrs or IM q6hrs

Quetiapine 12.5 - 25mg PO q12hrs

- [x] PHARMACY TO SCHEDULE MEDS Ensure meds are scheduled
- [ ] HALOPERIDOL 0.25 MG PO Q8HRS PRN X 7 Day Severe agitation
- [ ] HALOPERIDOL 0.5 MG PO Q8HRS PRN X 7 Day Severe agitation
- [ ] QUEtiapine 12.5 MG PO Q12HRS PRN X 7 Day Severe agitation
- [ ] QUEtiapine 25 MG PO Q12HRS PRN X 7 Day Severe agitation

.

If unable to take po...

- [ ] HALOPERIDOL 0.25 MG IM Q6HRS PRN X 7 Day Severe agitation
- [ ] HALOPERIDOL 0.5 MG IM Q6HRS PRN X 7 Day Severe agitation

Laxative/Stool Softeners:

If patient has not had a bowel movement in the past 3 days:

- [ ] BISACODYL 10 MG PR x 1 dose now
- [ ] SENNOSIDES 17.2 MG PO x 1 dose now

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Adjust daily bowel regimen

- [ ] SENNOSIDES 17.2 MG PO QDay 8.6 mg = 1 tab
- [ ] DOCUSATE 100 MG PO BID

.

Review Pain Assessment-If pain present and no prior pain medication is ordered, in absence of liver disease order:

- [ ] ACETAMINOPHEN 650 MG PO QID

Additionally Investigated Drugs

- Atypical antipsychotics
  - Amisulpride
  - Risperidone
  - Olanzapine
  - Ziprasidone
  - Aripiprazole
- Physostigmine
- Melatonin

Mergenhagen, 2008; Wang, 2013

Questions?

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