**PURPOSE:** This protocol specifically addresses how to screen, evaluate and treat delirium.

**DEFINITIONS**

Delirium (DSM IV Criteria):

- Disturbed consciousness with reduced ability to focus, sustain or shift attention.
- Cognitive change such as memory deficit, disorientation, or language disturbance which is not better accounted for by dementia
- Perceptual disturbance (i.e. Hallucinations or visual illusions) not better accounted for by dementia
- Rapid onset (hours to days) and fluctuating daily course
- Evidence of a causal medical condition/substance intoxication/withdrawal
- Classified according to psychomotor symptoms: hyperactive, hypoactive, mixed.
  - **Hyperactive:** agitation, restlessness, attempting to remove catheters, emotional lability.
  - **Hypoactive delirium:** withdrawal, flat affect, apathy, lethargy, decreased responsiveness. (Unrecognized in 66-84% of hospitalized patients.)
  - Rates: 1.6% hyperactive, 43.5% hypoactive, 54.1% mixed.

**IMPORTANCE OF MONITORING DELIRIUM IN THE ICU:**
Delirium is an independent predictor associated with prolonged mechanical ventilation, cognitive abnormalities at hospital discharge, and increased ICU and hospital length of stay. High prevalence: 20-50% of unventilated ICU patients, 60-80% of ICU patients being ventilated. Threefold-higher reintubation rate 10 additional days in the hospital 3x-increased risk of 6 month mortality Median ICU Cost: $22,346 vs. $13,332 "Altered Mental Status" strongest independent predictor of mortality (OR 31, p <0.001)

**PRECIPITATING AND IATROGENIC RISK FACTORS:**

- Hypoxia
- Metabolic disturbances
- Electrolyte imbalances
- Withdrawal syndromes
- Acute infection (systemic and intracranial)
- Seizures
- Dehydration
- Hyperthermia
- Head trauma
- Vascular disorders
- Immobilization
- Restraints
- Sleep deficiency
- Sedation medication
- Intracranial space-occupying lesions

- *Medications* are the most prevalent modifiable risk factor:
1. Morphine and "high"-dose benzodiazepines linked to delirium in unadjusted analysis.
2. Study: Lorazepam = independent risk factor for daily transition to delirium, whereas fentanyl, morphine, and propofol trended toward delirium development but were not statistically significant.

**PREVENTION:**

1. **Modify Risk Factors:** 40% relative reduction in development of delirium
   1. Repeated reorientation of patients
   2. Repetitive provision of cognitively stimulating activities for the patients
   3. Early mobilization
   4. Timely removal of catheters and physical restraints
   5. Goal directed analgesia/sedation

2. **Pharmacologic Prevention and Treatment:**
   1. Optimize quantity/type of sedatives/analgesics
   2. SCCM guidelines: set appropriate target sedation levels using sedation scales (RASS), readdress target levels daily, and titrate to desired clinical end point.
   3. Maintain light sedation; target RASS score of 0 to -1
   4. Daily sedation vacations starting at 0530 unless specifically ordered to continue sedation.
   5. Attempt to transition to PRN sedation meds PRIOR to starting back continuous infusions.
   6. Provide adequate analgesia.

**DIAGNOSIS AND MONITORING OF DELIRIUM**
Confusion Assessment Method for the ICU (CAM-ICU): sensitivity and specificity > 90%; takes < 1min to complete (attached).

Assess agitation/delirium using the RASS & CAM-ICU Scoring tools every shift

1. **RASS Score +2 to +4**
   1. Provide/optimize analgesic if patient is in pain
   2. If RASS remains > 1+, then provide adequate sedation to maintain safety (tube dislodgement, etc)
      1. Propofol IV infusion (max 50 mcg/kg/min; do not increase above max)
      2. QTc ≤ 500 msec: Initiate haloperidol 5 mg IV q2h PRN agitation (max 35 mg/24 hours) and add atypical antipsychotic quetiapine 50 mg PO BID (may titrate up by 50 mg/dose if patient remains on continuous sedation; max 400 mg/day) OR Risperidone 1 mg PO BID (may titrate up by 100% every 24 hours; max dose 8 mg BID)
   3. If propofol AND haldol/atypical antipsychotic are ineffective (or contraindicated), add midazolam 2 mg IV q2h PRN

2. **RASS Score 0 to -1**
   1. Negative CAM-ICU
      1. Re-assess for delirium every shift
   2. Positive CAM-ICU
      1. Discontinue delirium-causing medications (benzodiazepines, diphenhydramine, metoclopramide, promethazine etc.)
      2. QTc ≤ 500 msec
      3. Initiate treatment with Risperidone 1 mg PO BID (may titrate up by 100% every 24 hours; max dose 8 mg BID) or quetiapine 50 mg PO BID & haloperidol 5 mg (35 mg/day) IV q6h PRN agitation/delirium
      4. Continue to assess RASS & CAM-ICU every 6hrs
      5. Persistent delirium after 24h or remains on continuous sedation titrate up quetiapine by 50 mg/dose (max 400 mg/day)
1. Continue with same dose until delirium/agitation resolves, then titrate by 50 mg/dose until off
6. QTc ≥ 500 msec
1. If sedation required AND potential extubation within 72 hours OR maximized atypical antipsychotic therapy, consider switching to dexmedetomidine; minimize other sedative drugs/infusions

3. **RASS Score -2 to -3**
   1. Decrease sedation to achieve RASS goal of 0 to -1; then re-assess for delirium

4. **RASS Score -4 to -5**
   1. Assess if deep sedation is appropriate:
      1. Indications for deep sedation: elevated ICP, dyssynchrony/hypoxia, neuromuscular blocking agent, post-operative management requires deep sedation
      2. Continue current sedation if appropriate; re-assess need for sedation every shift
   2. Deep sedation inappropriate
      1. Minimize sedation to achieve a RASS Score 0 to -1; re-assess for delirium every shift

There are no drugs with regulatory approval for treatment of delirium.

1. SCCM guidelines recommend: Haldol 2-5mg q 6-8hrs; Typically start with low dose
   2. Atypical Antipsychotics also used
1. Current evidence suggests that atypical antipsychotics (olanzapine, risperidone, quetiapine) are as effective as and perhaps safer than haloperidol for treatment of delirium in acutely ill adults

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
<th>NOTES</th>
<th>ADVERSE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol</td>
<td>2-10 mg po, IV, IM q 2h</td>
<td>Less sedating; High incidence of EPS</td>
<td>QTc Prolongation; Orthostatic Hypotension</td>
</tr>
<tr>
<td>(Haldol)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td>0.5-4 mg per day po; IM available</td>
<td>Low incidence of QTc prolongation and low EPS</td>
<td>Orthostatic Hypotension, Sedation, Palpitation</td>
</tr>
<tr>
<td>(Risperdal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>5-30 mg per day po</td>
<td>Less sedating; low incidence of EPS and QTc prolongation</td>
<td>Somnolence, Fatigue, Headache</td>
</tr>
<tr>
<td>(Abilify)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Other recommendations:

1. Baseline EKG should be obtained for **EVERY** patient prior to starting antipsychotics (quetiapine, haloperidol, risperidone) to assess for QTc prolongation
2. Monitor for QTc changes weekly with EKG (order Mondays)
3. If patient is excessively drowsy during the day and up at night; consider switching morning quetiapine to risperidone (starting dose of risperidone 1 mg PO; may titrate up by 1 mg intervals daily, if necessary; max 6 mg/dose). Keep nightly quetiapine; adjust dose as needed

**CAM-ICU**