PSYCHOPHARMACOLOGY & CLINICAL ISSUES
IN CL PSYCHIATRY

1. ON-CALL CLINICAL PEARLS

1. **Avoid IM administration** of medications in the anticoagulated patient (try IV Haloperidol if refusing oral) and **ALL** PMH patients.

2. **Form 1** - While all agree that patients should be placed on a Form 1 if they are a threat to themselves, others or are unable to care for themselves with resulting imminent and serious physical impairment of the person, there is controversy about what should be done when an incapable patient wants to leave hospital and they are in need of urgent medical treatment. At this time we are recommending that patients who are being detained for treatment be certified on a Form 1. Furthermore, some patients on existing Form 1’s may require completion of a Form 3 (i.e. transferred from inpatient psychiatry or QSMHC for an acute medical problem).

3. **QTc intervals** - Be cognizant of QTc intervals in patients receiving antipsychotic medications. Look for concomitant agents that may be contributing to a prolonged QTc (e.g. amiodarone) or documentation of a congenital QTc prolongation syndrome (these patients should not receive antipsychotics except with the active involvement of cardiology). Assess and remind the referring team of the need to optimize other risk factors including low Mg or K levels for Torsades de Pointe ventricular arrhythmias that may occur in the context of QTc prolongation. Repeat the ECG and hold or avoid antipsychotic treatment in patients with increased QTc intervals (typically there is concern if there is an increase of > 25% in 24 hours while on an antipsychotic or a baseline QTc of >500 msec). The risk/benefit balance in patients whose agitation poses a danger to themselves or health care givers and who have a QTc in the range of 500-550 may in fact favour the cautious use of an antipsychotic. You should involve the referring team in a discussion of the risk/benefit ratio – most patients will be controlled with low doses of antipsychotic medications and not experience difficulties.

4. **Follow-up patients treated with antipsychotics for delirium** - If following up on a C-L patient that either you or the primary C-L team has started on an antipsychotic, reassess ECG (QTc), if required constant observation should be considered, monitor EPS (much less frequent with IV haldol than with p.o) and note the number of prns given in a 24 hour period to facilitate decisions around adjustments to standing treatment doses.

5. **Constant observation** – A constant observer (“sitter”) should be included as part of the treatment plan for: (1) delirious patients with safety concerns; (2) patients at high risk of suicide; (3) hypomanic/manic/psychotic patients who are disruptive to the functioning of the inpatient ward. This must be written in the orders and communicated to the treatment team.

6. **Start low and go slow** – Similar to the geriatric population, patients with co-morbid medical conditions (including oncology patients) require lower starting dosages and slower titration of pharmacological treatments.

7. **Micromedex** - If you are unclear about drug interactions with chemotherapeutic or immunosuppressive agents, there are a number of resources. You can check Micromedex through the UHN intranet (it is available under “Clinical Tools” and “Virtual Library”), contact the unit pharmacist (most have coverage until 9 or 10 pm on weekdays and on weekends) or the on-call pharmacist at the respective site.

**Dosing of antipsychotics** - see treatment dosing of antipsychotic medications in delirium later in this handout

8. **Parkinson’s Disease, Lewy Body & HIV dementia** - The best antipsychotic to use in patients with Parkinson’s disease, Lewy Body dementia or HIV dementia is quetiapine as it has the least likelihood of precipitating parkinsonian side-effects.
2. PSYCHOPHARMACOLOGY IN THE MEDICALLY ILL

CANCER PATIENTS

1. Common causes of delirium in cancer patients are:
   a. Medications: corticosteroids, opiates
   b. Hypercalcemia: bone mets
   c. Dehydration & electrolyte abnormalities
   d. Infection: immunocompromised patients, especially bone-marrow transplant patients
   e. CNS lesions: primary (i.e. CNS lymphoma) and secondary (lung, breast, melanoma commonly metastasize to brain)
   f. Paraneoplastic syndrome: rare cause

2. Drug interactions
   a. Procarbazine (antineoplastic agent is a weak MAOI – consider risk with antidepressants and serotonin syndrome
   b. Dopamine agonists (Stemetil)
   c. If unsure, refer to a pharmacist, P450 tables, etc.

3. Avoid the use of physical restraints in this population. The use of restraints in oncology patients with abnormal blood work places them at higher risk for life-threatening complications (i.e. bleeding, sequelae of seizures).
   a. Management of agitation in PMH patients can consist of:
      i. Security
      ii. Use of nursing or family for behavioural management of the patient (family can stay overnight in certain rooms)
      iii. Use of a sitter (constant observation)

4. Be aware of comorbid medical conditions (especially in this population)
   a. Check labs for etiology (see attached Table for causes of delirium)
   b. Medical co-morbidity requires lower starting dosages of medications and slower dose titration
   c. Cancer patients may be at increased risk of thromboembolic events, which can present as anxiety, restlessness or agitation
      i. Check O2 stats and note any pleuritic chest pain

5. If there are serious concerns or questions regarding a PMH consult, Dr. Mary Elliott can be reached through locating at PMH (16-3155)

CARDIOVASCULAR SURGERY PATIENTS

1. Avoid physical restraints in the cardiovascular surgery population, as there is the possibility of disrupting the sternal sutures if the patient fights against the restraints. In the CVICU, if physical restraints are required to maintain the integrity of the lines, then chemical restraints should also be used liberally to ensure patient safety. Check with the patient’s nurse to determine if there are any concerns regarding the impact of medications on the patient’s ventilation - in general IV haldol or atypical antipsychotics are safe to use unless the patient has shown undue sedation that has negatively impacted on care (e.g. difficulty weaning from the ventilator because of sedation). In post-operative patients recovering on the post-operative floor it is helpful to use chemical restraints (typically haldol or haldol + lorazepam) and to get them in either through IV access, convincing the patient to take them or administering oral haldol mixed with orange juice.

2. Do not administer IM medications to patients on anticoagulants – there are a variety of experimental anticoagulants being used in the unit so ask the patient’s nurse about any medications that you are not familiar with.

3. Haldol dosage – the CVICU is quite comfortable with using IV haldol for post-operative delirium. They have protocols to initiate therapy. Psychiatry is usually only called if patients are not responsive to lower doses. Most patients respond to total daily doses in the range of 2.5 – 10 mg/day but there is a subset of patients who have quite high requirements in order to obtain behavioural control (up to 300 mg in 24
hours). QTc prolongation is monitored with ECGs as clinically indicated but the CVICU team are in general less concerned about this as they are monitoring the patients carefully and optimizing other risk factors for arrhythmias that could potentially develop secondary to QTc prolongation (e.g. Mg, K⁺)

**TRANSPLANT PATIENTS**

1. Medication side effects, particularly immunosuppressants (e.g. tacrolimus, cyclosporine, interferon) or steroids with acute psychiatric presentations including delirium, mania and depression
2. Organ specific issues:
   a. Liver
      i. Avoid benzodiazepines in liver failure or in the first few weeks following liver transplantation (“LOT” mnemonic for benzodiazepines bypassing first-pass metabolism – lorazepam, oxazepam, temazepam)
      ii. Delirium post-liver transplant is common – can use IV haloperidol in patients with IV access or an oral atypical in patients without IV access (olanzapine is generally avoided because of its potential impact on glycemic control in this group who are receiving multiple medications that can alter glycemic control)
      iii. Avoid valproic acid
   b. Kidney
      i. Use short-acting benzodiazepines if possible in patients with renal failure
      ii. Dose adjustments are required for some antidepressants in patients in renal failure (e.g., mirtazapine has approximately 50% reduced clearance in renal disease)
      iii. Avoid lithium because of additive nephrotoxicity with many of the immunosuppressant medications
   c. Lung
      i. If hypoxia is contributing to delirium, avoid benzodiazepines
      ii. Can use atypical antipsychotics for anxiety with CO2 retention
      iii. Delirium post-lung transplant is common – can use IV haloperidol in patients with IV access or an oral atypical in patients without IV access (olanzapine is generally avoided because of its potential impact on glycemic control in this group who are receiving multiple medications that can alter glycemic control)
3. Emergency evaluation of the suitability for transplant or suitability to act as a living donor – psychiatry may be asked for an opinion in patients who have end-stage liver disease because of a suicide attempt (most commonly acetaminophen) in terms of whether there are likely to be problems post-transplantation with compliance with lifelong, daily immunosuppressive therapy or whether there is a significant risk of further suicide attempts. Very occasionally there is a potential emergency transplant using a living donor and in these cases the donor needs to be assessed regarding their suitability. Please feel free to page Dr. Abbey for assistance through locating or ask locating to contact Dr. Esther Elliott if Dr. Abbey is out of town.

**Appendix I: Suggested Dosing of Antipsychotic Medications**

Table 1-7  Initial haloperidol doses for the treatment of delirium
Initial adult dose of haloperidol\(^b\) (po,im, iv\(^c,d\))

<table>
<thead>
<tr>
<th>Level of agitation</th>
<th>Young or healthy</th>
<th>Elderly or frail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>0.5 – 1.0 mg</td>
<td>0.5 mg</td>
</tr>
<tr>
<td>Moderate</td>
<td>2.0 – 5.0 mg</td>
<td>1.0 mg</td>
</tr>
<tr>
<td>Severe</td>
<td>5.0 – 10.0 mg</td>
<td>2.0 mg</td>
</tr>
</tbody>
</table>

\(^a\) May repeat at regular intervals, but not before 30 minutes, until the patient is calmer.
\(^b\) Small doses of intravenous (iv) lorazepam (e.g., initially, 1mg of iv lorazepam over 1 minute, repeated again after 30 minutes if agitation persists) may be useful in patients who have not responded to haloperidol alone.
\(^c\) 10mg im or iv is equivalent to 5mg po.
Flush iv line with 2mg of normal saline before using iv form.

Source: Wise et al. 2002

Note: Clinically, IV haloperidol is used first line due to its reduced incidence of EPS and lack of impact on heart rate, blood pressure or respiratory rate.

*As above, avoid PO and IM haloperidol when possible.*

**Table 1-8.** Atypical antipsychotics for the treatment of mild to severe agitation in delirium

<table>
<thead>
<tr>
<th>Agent</th>
<th>Initial dose (oral preparation)</th>
<th>As needed dose (prn)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risperidone (Risperdal)</td>
<td>0.25 – 0.5 mg twice daily</td>
<td>0.25 – 0.5 mg every 4 hours; up to 4mg/day</td>
</tr>
<tr>
<td>Olanzapine (Zyprexa)*</td>
<td>2.5 – 5.0 mg at bedtime</td>
<td>Increase in divided doses; up to 20mg/day</td>
</tr>
<tr>
<td>Quetiapine (Seroquel)</td>
<td>12.5 – 50 mg twice daily</td>
<td>12.5 – 50 mg every 4 hours; up to 600 mg/day</td>
</tr>
</tbody>
</table>

*a Available in an orally disintegrating tablet, Zydis

* Adapted from Wyszynski & Wyszynski. Manual of psychiatric care for the medically ill.*

**Selected etiologies of delirium***

**Drug intoxication**
- Alcohol
- Sedative-hypnotics
- Opiates
- Psychostimulants
- Hallucinogens
- Inhalants

**Intracranial infection**
- Meningitis
- Encephalitis
- Abscess
- Neurosyphilis
- Human immunodeficiency virus

**Drug withdrawal**
- Bacteremia/sepsis
- Fungal
- Protozoal
- Viral

**Metabolic and endocrine disturbance**
- Volume depletion or volume overload
- Acidosis or alkalosis
- Hypoxia
- Uremia
- Anemia
- Hepatic Failure
- Hypoglycemia or hyperglycemia
- Hypokalemia or hyperkalemia
- Hyponatremia or Hypernatremia
- Hypomagnesemia or hypermagnesemia
- Hypophosphatemia
- Thyroid storm
- Hypopituitarism
- Other metabolic disorders (e.g. porphyria, carcinoid syndrome)

**Cerebrovascular**
- Stroke, transient ischemic attack
- Subarachnoid hemorrhage
- Other central nervous system disorders
- Cerebral edema
- Seizures
- Hypertensive encephalopathy
- Eclampsia

**Systemic infection**
- Central nervous system vasculitis
- Systemic lupus erythematosus
- Acute graft rejection
- Acute graft vs. host disease

**Autoimmune**
- Heart failure
- Endocarditis

**Cardiac**
- Hyperthermia: heatstroke, neuroleptic malignant syndrome, malignant hyperthermia

**Other systemic etiologies**
- Postoperative state
- **Hypoxic**
Pulmonary insufficiency  Hypothermia
Pulmonary emboli  Disseminated intravascular coagulation and other
                    hypercoagulable states
Neoplastic disease
Intracranical primary/metastasis/meningeal
                    carcinomatosis
Paraneoplastic syndrome

* Adapted from the American Psychiatric Publishing Textbook of Psychosomatic Medicine

<table>
<thead>
<tr>
<th>Life-threatening Causes of Delirium</th>
<th>Common Causes of Delirium</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WHHHIMP</strong></td>
<td><strong>I WATCH DEATH</strong></td>
</tr>
<tr>
<td>Wernicke’s encephalopathy</td>
<td>Infection</td>
</tr>
<tr>
<td>Hypoperfusion</td>
<td>Withdrawal - alcohol &amp; drugs</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>Acute metabolic</td>
</tr>
<tr>
<td>Hypertensive encephalopathy</td>
<td>Trauma</td>
</tr>
<tr>
<td>Intracerebral hemorrhage</td>
<td>CNS pathology</td>
</tr>
<tr>
<td>Meningitis/encephalitis</td>
<td>Hypoxia</td>
</tr>
<tr>
<td>Poisoning</td>
<td></td>
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<tr>
<td><strong>Deficiencies</strong></td>
<td></td>
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<tr>
<td>Endocrinopathies</td>
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<tr>
<td>Acute vascular</td>
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<tr>
<td>Toxins or drugs</td>
<td></td>
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<tr>
<td>Heavy metals</td>
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</tbody>
</table>

Table 6-8. Selected drugs causing delirium

**Analgesics**
- Opiates (especially meperidine, pentazocine)
- Salicylates

**Antimicrobials**
- Acyclovir, ganciclovir
- Aminoglycosides
- Amphotericin B
- Antimalarials
- Cephalosporins
- Chloramphenicol
- Ethambutol
- Interferon
- Isoniazid
- Metronidazole
- Rifampin
- Sulfonamides
- Vancomycin

**Anticholinergic drugs**
- Antihistamines H1 (e.g., diphenhydramine)
- Antispasmodics
- Atropine and atropine-like drugs (e.g., scopolamine)
- Benztpropine
- Biperiden
- Phenothiazines (especially thioridazine)

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**Antiparkinsonian drugs**
- Amantadine
- Bromocriptine
- Levodopa

**Cardiac drugs**
- Beta-blockers
- Captopril
- Clonidine
- Digitalis
- Disopyramide
- Lidocaine
- Methyl dopa
- Mexiletine
- Procainamide
- Quinidine
- Tocainide

**Sedative-hypnotics**
- Barbiturates
- Benzodiazepines

**Stimulants**
- Amphetamines
- Cocaine
- Ephedrine, epinephrine, phenylephrine
- Theophylline
<table>
<thead>
<tr>
<th>Category</th>
<th>Drugs</th>
</tr>
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<tbody>
<tr>
<td>Tricyclics (especially amitriptyline)</td>
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<tr>
<td>Trihexyphenidyl</td>
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<tr>
<td>Anticonvulsants</td>
<td></td>
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<tr>
<td>Phenobarbital</td>
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<tr>
<td>Phenytoin</td>
<td></td>
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<tr>
<td>Valproic acid</td>
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</tr>
<tr>
<td>Anti-inflammatory drugs</td>
<td>Miscellaneous drugs</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Antihistamines H$_2$ (e.g., cimetidine, ranitidine)</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs</td>
<td>Baclofen</td>
</tr>
<tr>
<td>Antineoplastic drugs</td>
<td>Bromides</td>
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<tr>
<td>Aminogluthethimide</td>
<td>Chlorpropamide</td>
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<tr>
<td>Asparaginase</td>
<td>Disulfiram</td>
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<tr>
<td>Dacarbazine (DTIC)</td>
<td>Ergotamines</td>
</tr>
<tr>
<td>5-Fluorouracil</td>
<td>Lithium</td>
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<tr>
<td>Hexamethylenamine</td>
<td>Metrizamide (intrathecal)</td>
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<tr>
<td>Methotrexate (intrathecal)</td>
<td>Podophyllin (by absorption)</td>
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<tr>
<td>Procarbazine</td>
<td>Propylthiouracil</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>Quinacrine</td>
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<tr>
<td>Vinblastine</td>
<td>Timolol ophthalmic</td>
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<tr>
<td>Vincristine</td>
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