Behaviour Management in Dementia
Where Do Antipsychotics Fit?

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Guidelines/Reviews

Dementia

- CCCDTD$_3$ [2006]: http://www.cccdtd.ca/
- Tx Mild-Mod [2008]: http://www.cmaj.ca/content/179/10/1019.full.pdf+html [1]
- Tx Severe Alzheimer's [2008]: http://www.cmaj.ca/content/179/12/1279.full.pdf+html [2]
- NICE (UK) [2006]: http://www.nice.org.uk/nicemedia/live/10998/30318/30318.pdf

Other Reviews

Cognitive Impairment:
http://www.rxfacts.org/professionals/CognitiveImpairment.php

Pt/Caregiver Resources

First Link Program Alzheimer's
- http://alzheimer.ca/saskatchewan/
- http://www.alzheimer.ca/english/society/FirstLink.htm

RxFiles Related

Anticholinergic Drug List[3]
Antipsychotic Chart[4]
BPSD Tx Chart[5]
CATIE-AD Trial Summary[6]
Hypersexuality Tx Chart[7]
Psychotropics Newsletter[8]

Highlights

1) Assess for medical causes (eg. Infection [UTI], constipation, urinary retention, delirium).
2) Look for drug causes (esp. recent med Δ's, but also anticholinergic load)
3) Implement non-drug tx before initiating drugs if patient/caregiver in no immediate harm.
4) Unrecognized pain? Try oral acetaminophen (650mg q6h while awake, or 1300mg LA am & hs).
5) Only certain symptoms are likely to respond to antipsychotics:
   - severe agitation
   - aggression
   - psychosis
6) Reassess need for antipsychotics after ~ 3 months as behaviours stabilize (stopping ↓s risk of adverse events)
7) Caution with combo & PRN overuse of APs

Background Issues

Behavioural and psychological symptoms of dementia (**BPSD**) create a significant caregiver challenge. Key symptoms include aggression, agitation, psychosis and mood disorders.

Table 1: Common BPSD Neuropsychiatric symptoms

agitation*	resistive	emotional lability
apathy	wandering	paranoid behaviours
aggression*, verbal/physical	intrusiveness	**psychosis*, hallucinations /delusions**
calling out, screaming	repetitive behaviours	
hostility	vocalizations	
sexual dis-inhibition	hoarding	
	nocturnal restlessness	

*symptoms with some evidence for benefit of antipsychotics

Approach to Managing BPSD

- Document the target symptom (e.g. DOS [form 9])
- Assess for any triggering factors (See Table 2)
- Identify if symptom requires treatment (e.g. is family/caregiver disturbed or in danger?)
- Use non-pharmacological measures whenever possible (See Table 4, next page.)
- **Is pain a possible contributing factor?**
  - Try regular acetaminophen; reassess at 1 wk
- **If drug treatment required:**
  - Tailor to the target symptom(s)
  - Consider potential harms
  - Start low, go slow; **reassess in 3-7 days** for both beneficial and any adverse effects
  - Try tapering the dose or stopping drug every **3+ months** [taper by 25% every 1-2 weeks]. Some behaviours decline as disease worsens.

{If treating acute delirium, stop upon resolution!}

Table 2: Common Triggering Factors in BPSD

Psychosocial		
Distress	Feeling abandoned	Loss of autonomy
Fear of danger		Paranoia
Misinterpretation		
Environmental		
"Bad company"	Excessive demands	Lighting - inadequate
Boredom	Change/lack of routine	Loneliness
Confusing surroundings		Noise
Medical		
B12 /folic acid deficiency	Hypo-thyroidism	Metabolic
Hunger/thirst	Infection (UTI, pneumonia)	Nocturia
Hypercalcemia		Pain
		Constipation
Medications (e.g. rule out drug induced delirium)		
Anticholinergics [10]	Cholinesterase inhibitors	Opioids
Benzodiazepines		Substance abuse
	Digoxin	*…& many others*

What do we know about the benefits and risks of psychotropic meds in BPSD?

- Evidence for psychotropic use is limited and all classes have limited efficacy and serious adverse event (**SAE**) concerns. (See Table 3) For an overview see *BPSD chart* (Page 4).[5]

Where do Antipsychotics (APs) Fit?

AP effectiveness in BPSD is modest & their role is limited due to SAEs.[11,12,13,14] See CATIE-AD Trial Summary.[6]

- APs, both typical (e.g. haloperidol) & atypical (risperidone Risperdal, olanzapine Zyprexa & quetiapine Seroquel), have been studied in BPSD.
- Placebo response rates often ~40%, reflecting high rates of spontaneous resolution & the value of psychosocial input in such trials.[15] [The *more severe* patients may *respond better* to APs.]
- Of these atypical agents risperidone has the most evidence for efficacy (aggression ≤1mg/day & psychosis ≤2mg/day).[13,16]

Serious Adverse Events (SAEs) for all APs.

- SAEs with APs include stroke(OR: 1.3-3.1)[13,17], seizures, EPS effects, ↑ falls, drowsiness, cognitive decline, pneumonia & death.
- Death may be ↑ with atypical & conventional APs in dementia based on RCTs (OR:1.2-1.6; AR ≥1% /12 wks; NNH=87/12wks).[13,18,19,20,21] However observational data is equivocal; some suggest no increase in death for APs typical or atypical.[22,23,24]

Stopping long-term antipsychotics reduced mortality by ~25% at 2 years in long-term follow-up to the **DART-AD** RCT.[25] {n=165, age ~85; Alzheimer's patients MMSE~11 on APs for ≥ 3months for BPSD; 2 arms: stop AP & switch to placebo vs AP use x12months; no significant difference in survival at 12 months; survival at 2yrs: 71% vs 46%; NNT=4/2yrs; survival over 2-4.5yrs: 54% vs 38%, NNT=8, CI: 5-42}

- BPSD outcomes: no statistical difference except verbal fluency better in patients who stopped at 6 mos.[26] There may have been individual differences (e.g. in the more severe).
- Remember, if antipsychotic use is restricted, alternative drugs could be just as harmful!

Table 3: Risks of Various Psychotropic Meds

- Benzodiazepines: falls, fractures, confusion
- Carbamazepine: falls, many DIs & side effects
- Antidepressants: ↓sodium, falls, osteoporosis
- Opioids: delirium; constipation, fractures, ?CV [27]

Avoid the use of psychotropic meds for BPSD if at all possible. When needed, assess for tolerability in ≤3-7 days & reassess for possible taper and/or discontinuation every 3 months.

Table 4: Select Non-drug Treatment Tips

- Allow **behaviours** that are not problematic
  - Ok to wander within limits; delusions can be ok
- Institute a patient centered or relaxed **schedule** that allows flexibility for the preferential routines of each patient:
  - ⇨e.g. medication times, meals, bathing, sleep times, activities
  - ⇨Assess daytime naps: limit/avoid in most, but may be ok to allow aggressive patient to sleep while others are awake
  - ⇨Make time for regular exercise to ↓ restlessness; refer to daytime programs if available
  - ⇨Encourage daily activities to minimize *sun-downing* (eg. playing cards, gardening)
- Make a positive **environment** that avoids triggering factors:
  - ⇨aromatherapy
  - ⇨play music suitable to the individual
  - ⇨reduce noise or number of persons in room
  - ⇨remove keys from view if no longer driving
  - ⇨distract person with snack or activity
  - ⇨if wandering, ensure house/room etc. is safe, put buzzers on doors, provide light, ↓ fall risk
  - ⇨provide clock & calendar if confused regarding time & date
  - ⇨if inappropriate sexual behaviour, consider room placement changes to minimize interactions of concern
- Minimize unnecessary & problem **drugs**. Tools to review include the Beer's list[28], or the START / STOPP Criteria.[29,30,31,32]
  - ⇨Difficulty swallowing can cause severe agitation. If drug necessary, look for better formulations (e.g. dissolvable tablets)
  - ⇨As disease advances toward the end of life, transition over to comfort care, rather than curative/preventative
    - ⇨Review meds with consideration for stopping statins, vitamins, herbals, bisphosphonates
    - ⇨Review BP & blood sugar goals; too low can lead to falls
- Only do **lab work** when necessary
- Providing access to false teeth, hearing aids & glasses may reduce agitation in some patients, although the opposite may be true if patient is sound sensitive, or if these aids are considered bothersome by the patient (esp. hearing aid)

AE=adverse events AP=antipsychotic BG=blood glucose BP=blood pressure CI=confidence interval ChEIs=cholinesterase inhibitors CV=cardiovascular CVAE=cerebrovascular adverse events DI=drug interaction DIN:drug identification number HS=bedtime OR=odds ratio pt=patient NNT=number needed to treat NPN=natural product number RCT=randomized controlled trial SAE=serious adverse events TX=treatment

"First Link"® patient/family support program for Alzheimer's

- Healthcare professionals can refer patients/families to the program
- RCT evidence found a 28% ↓ in rate of nursing home placement over 9.5yrs (HR=0.717; p=0.25) or about a 1.5yr delay in placement median.[33a,b]

Sleep *Insomnia* & Dementia

- Sleep patterns naturally change as you get older. Older adults:
  - Sleep fewer hours & take longer to fall asleep
  - Sleep less deeply & wake up more often during the night
  - Have more trouble adjusting to changes in sleeping conditions, such as a new bed
  - Have changes in their sleep cycle → Older adults spend less time in the most restful stage of sleep
- Sleep disturbance in Alzheimer's Disease (AD) is very common; nocturnal sleep disturbance in AD patients is often accompanied by increased daytime napping, frequently in direct association with the extent of dementia [7]
- An after dinner walk may help in promoting nighttime sleep
- In the later stages of AD, patients may spend ~40% of their time in bed awake and a significant proportion of day-time hours asleep. This ↑ day-time sleep consists almost exclusively of stage 1 & 2 sleep; it does not replace or compensate for the night-time loss of slow-wave sleep (SWS) or REM sleep [6]
- Cholinesterase inhibitors can cause insomnia (& nightmares) [3]
- The presentations of abnormal nocturnal behavior in AD often exceed the limits of what might otherwise be termed insomnia in a nondemented geriatric population [7]
- Behavioural intervention should be tried before pharmacological interventions whenever possible
- Limit drug tx to short term/intermittent use whenever possible

Agents sometimes used for insomnia, and their limitations[34]

Melatonin (1 – 3 – 5mg po HS) ✗⊗ [Look for product with NPN or DIN.]
- Limited short-term evidence (over 3-8wks) for benefit. [35,36]

Trazodone DESYREL (12.5 – 25 – 50 – 100mg po HS)
- Limited evidence. Historically used for "sundowning". Sedating without anticholinergic effects. Minimal effect on sleep architecture. AEs include hypotension, especially in those with interacting drugs or comorbidities.

Mirtazapine REMERON (7.5 – 15 – 30mg po HS)
- Useful when antidepressant effect desired. AEs: weight gain, anticholinergic

Zopiclone IMOVANE / RHOVANE (3.75 – 7.5mg po HS) ✗⊗
- Similar in effect to benzodiazepines. Some consider safer, but evidence lacking. AEs include tolerance, dependence, bitter taste.

Benzodiazepines (e.g. temazepam, lorazepam; clonazepam long-acting)
- Effective for short term use (e.g. ≤3 weeks); however, AEs include tolerance, dependence, falls, confusion, disinhibition, etc. Generally discouraged! {Avoid long-acting agents (e.g. clonazepam) unless daytime anxiety or tapering protocol}

Quetiapine SEROQUEL (12.5 - 50mg po HS)
- No official indication & limited evidence. May be effective in some, but also associated with AE concerns (weight gain, diabetes, hypotension, etc.).
- Has anticholinergic effects and may worsen cognition, especially in elderly.

Methotrimeprazine NOZINAN (2 – 10mg po HS)
- Poorly tolerated in elderly; highly anticholinergic. May be useful in severe insomnia associated with pain and drug withdrawal.

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Reference List of Drugs with Anticholinergic Effects – February 2012 [1, 2, 3, 4]

WHENEVER POSSIBLE, AVOID DRUGS WITH HIGH ANTICHOLINERGIC ACTIVITY IN THE ELDERLY

Antidepressants

TCA

amitriptyline	Elavil	☒
clomipramine	Anafranil	☒
desipramine	Norpramin	☒
doxepin	Sinequan	☒
imipramine	Tofranil	☒
nortriptyline	Aventyl	☒

-less anticholinergic effects than amitriptyline & imipramine

trimipramine	Surmontil	☒

SSRI

citalopram ☆	Celexa	☑
escitalopram ☆	Cipralex χ ⊗	☑
fluoxetine	Prozac	☑
fluvoxamine	Luvox	☑
paroxetine	Paxil	☒
sertraline ☆	Zoloft	☑

Other

bupropion ☆	Wellbutrin ✆, Zyban	☑
desvenlafaxine	Pristiq χ ⊗	☑
duloxetine	Cymbalta ☎ ✆	☑
maprotiline	Ludiomil	☑
mirtazapine ☆	Remeron	☑
moclobemide ☆	Manerix	☑
phenelzine	Nardil	☑
trazodone ☆	Trazorel	☑
venlafaxine ☆	Effexor	☑

In the elderly, citalopram & sertraline are the preferred SSRIs.

Antiparkinsonian

amantadine	Symmetrel	☑
benztropine mesylate	Cogentin	☒
bromocriptine	Parlodel	☑
carbidopa/levodopa ☆	Sinemet	☑
entacapone	Comtan	☑
ethopropazine	Parsitan	☒
pramipexole	Mirapex	☑
procyclidine	Kemadrin	☒
selegiline	Eldepryl ☎	☑
trihexyphenidyl	Artane	☒

Antiemetics/Antivertigo

dimenhydrinate	Gravol OTC	☒
meclizine	Bonamine	☒
promethazine	Phenergan OTC χ ⊗	☒
scopolamine	Transderm V OTC ⊗	☒

Antibiotics

ampicillin	☑	*All Available as Generic
cefoxitin χ	☑	
clindamycin	☑	
gentamicin	(Oint & Sol'n NIHB covered) ☑	
piperacillin χ ⊗	☑	
vancomycin ☎ ⊗	☑	

Antihistamines/Antipruritics

brompheniramine	cough&cold products OTC χ	☒
chlorpheniramine	Chlor-Triplon OTC χ	☒
cyproheptadine	Periactin OTC χ ⊗	☒
dimenhydrinate	Gravol OTC	☒
diphenhydramine	Benadryl OTC χ	☒
hydroxyzine	Atarax	☒
pyrilamine	Midol, Pamprin OTC χ ⊗	☒
trimeprazine ◇	Panectyl ⊗	☒

Preferred Alternatives: **certirizine (Reactine) χ, fexofenadine (Allegra) χ, loratidine (Claritin) χ.**

Respiratory Meds

fluticasone/salmeterol	Advair ☎ ✆	☑
theophylline	Theolair, Uniphyl	☑

Antipsychotics

aripiprazole ☆	Abilify ☎ ⊗	☑
chlorpromazine	Largactil	☒
clozapine	Clozaril ☎	☒
flupenthixol	Fluanxol	☒
fluphenazine	Moditen	☒
haloperidol ☆	Haldol	☑
loxapine	Loxapac	☒
methotrimeprazine	Nozinan	☒
olanzapine	Zyprexa ☎	☒
paliperidone ◇	Invega (☎ on injection only)	☑
pericyazine	Neuleptil	☒
perphenazine	Trilafon	☒
pimozide	Orap	☒
pipotiazine ◇	Piportil	☑
quetiapine	Seroquel	☒
risperidone ☆	Risperdal (☎ on injection only)	☑
thioproperazine ◇	Majeptil χ	☒
thioxthixene	Navane	☒
trifluoperazine	Stelazine	☒
ziprasidone ☆	Zeldox ✆	☑
zuclopenthixol ◇	Clopixol ☎ ⊗	☒

Antimuscarinics

darifenacin	Enablex ☎	☒
flavoxate	Urispas χ	☒
oxybutynin	Ditropan (☎ on CR only)	☒
solifenacin	Vesicare ☎ ✆	☒
tolterodine l-tartrate	Detrol ☎ ✆	☒
trospium	Trosec ☎ ✆	☒

Antispasmotics

dicyclomine	Formulex, Bentylol ⊗	☒
glycopyrrolate	Robinul χ ⊗	☒
hyoscine butylbromide	Buscopan ⊗	☒

Antiseizure Drugs

carbamazepine	Tegretol	☑
divalproex ☆	Epival	☑
oxcarbamazepine	Trileptal ☎ ⊗	☑
valproic acid ☆	Depakene	☑

Preferred Alternatives: **divalproex (Epival), gabapentin (Neurontin), lamotrigine (Lamictal).**

Benzodiazepines

alprazolam	Xanax half-life: ~12 hr	☑
chlordiazepoxide	Librium half-life: ~100 hr	⊗☑
clonazepam	Rivotril half-life: ~34 hr	☑
clorazepate	Tranxene half-life:~100 hr	⊗☑
diazepam	Valium half-life: ~100 hr	☑
flurazepam	Dalmane half-life:~100hr	⊗ ☑
lorazepam ☆	Ativan half-life: ~15 hr	☑
midazolam	Versed half-life: ~3 hr χ	⊗ ☑
oxazepam ☆	Serax half-life: ~8 hr	☑
temazepam ☆	Restoril half-life: ~11 hr	☑
triazolam	Halcion half-life: ~2 hr	☑

Avoid long- & ultra-short acting agents in the elderly.
(Clonazepam ok, if long-acting required eg. chronic anxiety)

Muscle Relaxants

baclofen	Lioresal (☎ on intrathecal only)	☑
cyclobenzaprine	Flexeril ☎ ✆	☒
methocarbamol	Robaxin OTC χ ⊗	☒
orphenadrine	Norflex OTC χ ⊗	☒
tizanidine	Zanaflex ☎	☒

Baclofen is the preferred agent of the above listed muscle relaxants however, it does display moderate to high anticholinergic activity.

Immunosuppressants

azathioprine	Imuran	☑
cyclosporine	Neoral ☎ ✆	☑

Cardiovascular Agents

atenolol	Tenormin	☑
captopril	Capoten	☑
chlorthalidone	generic only	☑
digoxin	Lanoxin, Toloxin	☑
diltiazem ☆	Cardizem	☑
diospyramide	Rythmodan	☒
furosemide	Lasix	☑
hydralazine	Apresoline	☑
isosorbide ◇	Isordil	☑
metoprolol ☆	Lopresor	☑
nifedipine	Adalat	☑
quinidine χ ⊗	generic only	☑
triamterene	Dyrenium	☑

Gastrointestinal Agents

belladonna	generic only χ ⊗	☒
chlordiazepoxide/clidinium	Librax χ ⊗	☒
cimetidine	Tagamet	☒
dicyclomine	Bentylol ⊗	☒
diphenoxylate/atropine	Lomotil ⊗	☒
famotidine ☆	Pepcid OTC & Rx	☑
loperamide	Imodium OTC	☒
	☑ if used short term	
metoclopramide	Maxeran	☑
nizatidine	Axid	☑
prochlorperazine	Stemetil	☒
	☑ if used short term	
ranitidine	Zantac OTC & Rx	☑

-low anticholinergic activity if adjusted for renal function

Preferred Alternatives: **bisacodyl χ, PPIs ☎, domperidone; ranitidine if ≤150mg/day**

Opioids

meperidine	Demerol *Not for chronic use ✆	☒
codeine	(☎ on controlled release only, ✆, inj & liquid)	☑
fentanyl	Duragesic ☎ ✆	☑
hydromorphone ☆	Dilaudid, Hydromorph Contin ✆ on CR only	☑
morphine ☆	Statex, M.O.S., Kadian	☑
oxycodone	Supedol, Oxy IR, OxyContin, OxyNeo ✆ on CR only	☑
tramadol ☆	Ultram, Ralivia, Tridural, Zytram XL χ ⊗	☑

Preferred Alternatives:
acetaminophen χ, NSAIDs (eg. ibuprofen, naproxen)

Miscellaneous

buspirone ◇	Buspar ⊗	☑
colchicine	generic only	☑
dipyridamole	Persantine, Aggrenox ☎ ✆	☑
ketotifen ophthalmic	Zaditor ☎ ⊗	☑
lithium	Carbolith, Duralith	☑
pancuronium	generic only χ ⊗	☑
warfarin ☆	Coumadin	☑

Moderate/High anticholinergic activity
Low anticholinergic activity
_____ = Possible preferred alternatives
☆ = Denotes agents with anticholinergic activity that may be better tolerated than others. Whenever possible, anticholinergic drugs should be avoided, & the preferred agents used.
◇ = Unable to confirm anticholinergic activity
☎ = **EDS** (exception drug status) in Saskatchewan
χ = **non-formulary** in Saskatchewan
✆ = **prior approval** NIHB
⊗ = **not covered** by NIHB
CHEI = Cholinesterase Inhibitor (eg. donepezil)
CR = Controlled Release Formulation
PPI = Proton Pump Inhibitor (eg. rabeprazole)
OTC = Over-the-counter
☑ = Saskatchewan Health finds co-administration of this agent **with a CHEI acceptable**
☒ = If patient is currently on this medication, Saskatchewan Health will **NOT cover CHEI**

Rx FILES

Management of Behavioural & Psychological Symptoms of DEMENTIA (BPSD) [118] Oct/11

Background: very common ≤90% in dementia; a major cause of distress to pts/families/caregivers; harm to self & others; huge cost e.g. institutionalization. -not just agitation but non-agitated Sx (apathy, withdrawal, daytime somnolence {circadian rhythm disturbances}, depression, disinhibition, etc.)

Diagnosis: (Evaluate behaviour→**ABC's** **A**ntecedents (causes: **P**hysical **I**ntellectual **E**motional **C**ultural **E**nvironmental **S**ocial), **B**ehaviours & **C**onsequences), ⇨ Assess history unique factors like Down's Sx, physical exam, cognitive tests Feldman CMAJ'08 & nurse observations; collateral family info essential!

Lab Tests: Recommend CBC, electrolytes, calcium, B12, glucose & TSH; Optional: BUN & SCr, ferritin, magnesium, LFTs, arterial blood gases, ECG, CT/MRI if suggestion of structural lesion eg. renal failure, brain tumor, normal pressure hydrocephalus, subdural hemorrhage ◆Eliminate delirium source Young BMJ'07– eg. **meds** eg. opiates, benzos, anticholinergics **/withdrawal rxs/DI's**, dehydration & infections (if indicated: urinalysis/C&S, chest x-ray, lumbar puncture if suspicion of meningitis)

Tx 1: **Assess for and treat any comorbitities** (eg. **infection, pain, constipation**, depression, psychosis}

Tx 2: **Explore environmental, exercise & behavioural measures** COPE trial! Reserve **drug therapy for situations** where non-pharmacological interventions have been fully explored & implemented or in cases of **significant dangerous risk**. Specify problem behaviour (eg. "agitation" is less useful than "screaming", "hitting when bathed"). Identify what brings it on & what makes it go away. Identify whom the behaviour is bothering (pt, caregiver/staff or other pts). Human interactions eg. activiy, adequate staff eg. nursing home & proper environment most critical.

Tx 3: **Drug Treatment:** consider if Sx having no physical cause, are unrelated to other drugs or unresponsive to non-pharmacological interventions, generally start with **1/3 to 1/2 of usual adult** dose & titrate up slowly; individualize dose

Start Low, Go Slow!

Tx 4: **Reevaluate drug regimen after 3 months**; may attempt to **taper/withdraw** meds after **3 months of behavioural stability**!

MAJOR DEPRESSION
↓ mood, apathy, amotivation

Mild→ non pharmacologic

Moderate to *severe*→ **ANTIDEPRESSANT Tx**

Anxiety often coexists thus use antidepressants with anxiolytic properties
e.g. citalopram, sertraline, venlafaxine

CANMAT 09 suggests:
SSRI's, venlafaxine, mirtazapine, duloxetine, moclobemide, bupropion.
See also RxFiles Charts book pg 104-5.

In general →may be good for depression, depression assoc. agitation, emotionality & irritability. May help behaviours / disinhibition (May worsen apathy in some patients)

Allow >6 week for adequate trial at an adequate dose

⇩

SSRIs: SE: nausea, vomiting, restlessness, falls, insomnia, ↓weight, agitation initially, hyponatremia & bleeding <0.5%
Citalopram 10-30mg/d, **escitalopram**✘⊗ 10-20mg/d, **sertraline** 25-100mg/d, **fluvoxamine** 25-150mg/d, **paroxetine** 10-30mg/d etc.
Venlafaxine: 37.5-225mg XR od {Similar SE as SSRI, but high GI SE & may ↑ BP); **XR** cap: can sprinkle on food.
Bupropion ☎ ✆100-150mg bid or 150-300mg XL ☎ ✆ to activate pt with withdrawal or psychomotor retardation
TCA's: Avoid anticholinergics →less with **nortriptyline** 10-75mg hs & desipramine 25-150mg/d;
SE: hypotension, blurred vision, urinary hesitancy, cardiac conduction changes
Mirtazapine: consider if anorexia/anxiety/sleep problem; **RD** rapid dissolve form if difficulty swallowing; ≤7.5-45mg/d
Moclobemide: role in anxiety & mood dx but may ↑ stimulation; 100mg od-300mg bid
Trazodone: low doses used for sedation & some anxiolytic effect;
monitor for hypotension, serotonin syndrome & rare priapism in ♂
Consider **ECT** in management of treatment resistant or severe depression

Start Low, Go Slow, But go!

PSYCHOSIS/AGITATION
delusions, hallucinations; agitation, aggression

-use non-pharmacological intervention where possible!

Psychosis: Positive Sx delusions, hallucinations or paranoia,
Negative Sx poverty of thought, apathy, social withdrawal

Agitation: aggression, shouting, pacing, psychomotor

Start Low, Go Slow… Then Taper!

ANTIPSYCHOTIC Tx
-first designate target Sx (**not wandering or mild Sx**)
-try to minimize **sedation**,↑confusion,hypotension & **EPS;**
(titrate no more frequent then q1-2wks)

-**target Sx** (hallucinations, delusions, hostility, **aggression**, severe agitation, & violent/high risk behaviour)
risperidone 0.25-2mg/day
quetiapine 12.5-200mg/day
olanzapine ☎ ▼1.25-10mg/day
} monitor for SE may attempt med tapering q**3**month
haloperidol 0.25-2mg/day (especially useful in delirium)
[**aripiprazole** ☎⊗ & **ziprasidone** ✆: caution stimulating agents]

◆Newer agents as effective but generally better tolerated.
Monitor for **SE**: sedation, hypotension, falls [119], EPS (drooling, rigidity & akinesia), anticholinergic SE dry mouth, delirium, constipation, ??ECG, ↑weight/lipids/diabetes , ? ↑stroke OR 2.5-3/death OR 1.5-1.8 Class effect & tardive dyskinesia ⇒ this highlights need to **reevaluate ongoing use**.
◆Pts with **Lewy bodies** (often visual hallucination symptoms) have ↑sensitivity to neuroleptics (quetiapine low dose an option)

ANXIETY
pacing, chanting, psychomotor agitation, etc.

-use non-pharmacological intervention
-minimize provocation
-consider **antidepressant** therapy if anxiety is secondary to depression or very chronic in nature

ANTIANXIETY Medication
- consider **short term as needed**
lorazepam 0.5-2mg/day
oxazepam 5-30mg/day
clonazepam 0.125-2mg/day
(Caution long-acting!)

Benzodiazepines-caution!
SE: sedation, ataxia, altered sleep architecture, motor & **cognitive** impairment & propensity to cause withdrawal Sx when D/C. Paradoxical excitation, **disinhibition** & **falls** may occur. An intermediate acting such as temazepam/oxazepam/lorazepam can be best used for short term, if possible sleep/anxiety states or before planned anxiety provoking situations (eg. bathing, dental work)

Trazodone 12.5-100mg/day considered option by some
50-100mg po hs

Buspirone: ✆ 10-30mg/day; ↓sedation, ↓DI's, ↓ withdrawal & ↓ impairment of motor fx; option→chronic anxiety but delayed onset ~3wk

APATHY
Tx with external activity & environmental measures. **Possible drug options (not without concerns)**: methylphenidate, dopamine agonists or cholinesterase inhibitors.

Sexually Inappropriate Behaviour: assess for **medical reason** eg. UTI & any **drug causes** eg. lorazepam, dopamine agonists. Remove disinhibiting drugs including benzo's & alcohol.
Behavioural interventions 1st redirection, distraction, avoiding stimulants, limited data on drug tx antidepressants, antipsychotics, cholinesterase inhibitor (see also RxFiles Hypersexuality Chart).

Sleep Disturbances: assess for **medical reason** eg. heart failure, sleep apnea, **drug cause** eg. stimulants, Options: **behavioural, trazodone** 25-50mg HS, **zopiclone**✘⊗ 3.75-5mg HS, **Limit to 3-4wk**

Pain: consider trial of **acetaminophen ≤ 3.2g/day** (e.g. 650mg po QID; or long-acting 1300mg BID AM & HS) to reduce **agitation & pain** Husebo'11; opiates if necessary in select individuals

Cholinesterase Inhibitors (ChEIs) -modest cognitive, functional & behavioural benefit; may help apathy, hallucination & delusion?-post hoc analyses; **unlikely to help agitation & aggression** - not better than placebo for agitation Howard'07, may help **Lewy Body dementia** ↓ visual sx's
Consider **cholinesterase inhibitors** in Alzheimer's (**donepezil**, **galantamine**, **rivastigmine**) ☎ ✆; but SE: nausea/vomiting, fatigue, anorexia, ↓ heart rate, urinary incontinence

Memantine ✘⊗ NMDA receptor antagonist, may help agitation, aggression, irritability, disinhibition & psychosis case reports, only post-hoc analysis of RCT. Option: combo with ChEIs in mod-severe AD.

Anticonvulsants: some use short term (<6weeks) in agitation, aggression, hostility, sleep-wake disturbance cycle & mania
◆ **carbamazepine** 100-600mg/day ≤400mg/day in BPSD **SE**: sedation, ataxia, falls, rash, headache, leukopenia & ↑ liver tests & **DIs.** ✓Good for impulsivity or if brain injury.
◆ ? **topiramate** 25-50mg/day cognitive difficulties ◆ **valproate** no longer recommended dose required associated with significant sedation, diarrhea, tremor, nausea, hair loss, ↑ liver tests; useful if manic
◆ other agents gabapentin, lamotrigine-rash, levetiracetam benefit unknown – concerns re: worsening existing behaviour gabapetin-worsening agitation if Lewy Body dementia

BETA BLOCKER: propranolol 10-80mg/d; possible ↓ aggression but diminishes over time; SE:↓ heart rate & hypotension Caution: asthma, PVD & possibly depression Hx

BP=blood pressure **CI**=contraindication **DI**=drug interaction **Dx**=disorder **fx**=function **HR**=heart rate **Hx**=history **n/v**=nausea/vomiting **Pt**=patient **PVD**=peripheral vascular disease **SE**=side effect **Sx**=symptom
Tx=treatment ☎=Exception Drug Status Sask. ✘ =non-formulary in Sask. ⊗=not covered by NIHB ▼=covered by NIHB ✆=prior approval NIHB

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