Geriatric Delirium: Translating Guidelines into Practice

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Learning Objectives

- To identify geriatric delirium in long-term care settings
- To review the pharmacological and non-pharmacological approaches to managing delirium
- To discuss evidence-based preventative measures

Disclosure for Dr. Chan

- Speaker honouraria from:
  - Astra-Zeneca
  - Eli-Lilly
  - Janssen-Ortho
  - Lundbeck
  - Organon

None in past 7 years

Delirium: The Myths

1) Delirium is a cross-sectional diagnosis
   - Requires 24 hour observation
2) Delirium leads to agitation and behaviour problems
   - Watch for "Apathetic" (hypoactive) Delirium
3) Delirium always has an identifiable cause
   - May not find a single cause; multiple factors with geriatric delirium
4) Delirium is a transient phenomenon
   - May persist or lead to permanent cognitive and/or functional sequelae in elderly

Delirium (DSM-5) criteria

A. A disturbance in attention (ie: reduced ability to direct, focus, sustain, or shift attention) and awareness (reduced orientation to the environment).
B. The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.
C. An additional disturbance in cognition (eg: memory, orientation, language, visual-spatial, perception)
D. The disturbances in A and C are not better explained by another 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 examination, or laboratory findings that the disturbance is a direct physiological consequences of another general medical condition, substance intoxication or withdrawal, or exposure to toxin, or is due to multiple etiologies.

Screening

- Under-recognition, esp. in those:
  - Over 80 y.o. with hypoactive delirium with visual impairment and/or pre-existing dementia
    - Inouye et al. Arch Int. Med 2001
- No reliable screening tool to differentiate delirium and dementia
- Practically, acute-onset and/or fluctuation in cognition/function/abnormal behaviours

How Good Are Long-Term Care Nurses at Screening?

- Voyer et al. (J Am Med Direc Assoc 2012; Int J Geri Psyc 2011)
  - 7 LTC Facilities in Montreal and Quebec
  - N=202 residents
  - CAM-identified delirium in 21.3% by RA's
  - Nursing observation identified 51% of cases identified by Research Assistant
  - Under-recognition of symptoms varied from 25-66.7% by nursing observation
  - More likely delirium in mod-severe Dementia; under-recognized if depressive symptoms

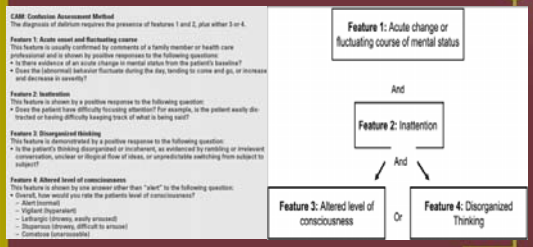
Confusion Assessment Method (CAM) (Inouye et al. Ann.Int.Med. Dec.15/90)

- acute onset and fluctuation AND
- inattention AND
- disorganized thinking OR
- altered level of consciousness

- excellent sensitivity, good specificity

Screening: CAM-Short Form

CAM Short Form **CAM Algorithm**



Delirium, Dementia, Lewy Body Dementia: Cole Am J Geri P 2004

Feature	Delirium	Dementia	Lewy Body Dis
Onset	Acute	Insidious	Insidious
Duration	Hours, Days	Months, Years	Months, Years
Consciousness	Variably alert	Alert	Alert
Attention	Impaired	Intact	Frequently impaired
Cognitive Fluc.	Frequent	Infrequent	Frequent
Symptom Fluc.	Frequent	Infrequent	Infrequent
Visual Hallucinate	Frequent, transient	Occasional	Frequent, complex, persistent
Thinking	Disorganized	Impoverished	Impoverished
Insight	May be present in lucid intervals	Usually absent	Usually absent
Parkinsonism	Usually absent	Occasional	Frequent
Neuroleptic sensitivity	Infrequent	Infrequent	Frequent
EEG	Marked slowing	Usually normal or mild slowing	Can show slowing

Delirium: Subtyping

- Hyperactive (agitated)
  - Differentiate from anxiety
  - Differentiate from dementia

- Hypoactive (apathetic)
  - Differentiate from depression
  - Less sleep-wake reversal

General considerations: Diagnosing Geriatric Delirium

- 24 hr. observation, including sleep-wake cycle
- anxiety
- new incontinence
- unsteady gait, falls
- dysarthria/incoherence
- mood/affect lability
- subtle paranoia and hypervigilance
- sleep disturbance

Practical tip #1: Ask specifically about vivid dreams or nightmares!

Geriatric Delirium

- Predisposing
- Precipitating
- Perpetuating
- Protective/Preventive

Predisposing Factors

Inouye, SK et al. A predictive model for delirium in hospitalized elderly medical patients based on admission characteristics. Ann Intern Med 1993; 119:474-481

- cognitive impairment
- sleep deprivation
- immobility
- visual impairment
- hearing impairment
- Dehydration

Practical tip #2: Ask about use of visual and hearing aids! Carry a voice amplifier

Differential Dx of Causes: DIMS-R

DIMS-R (Drugs, Infection, Metabolic, Structural, Retention): Common precipitating factors for delirium

Drugs
- Prescribed (narcotics, steroids, anticholinergic, NSAIDs)
- Over-the-counter (dimenhydrinate, diphenhydramine)
- Drug intoxication or withdrawal (alcohol, sedative-hypnotics, narcotics

Infection (urinary tract, lungs, skin, blood)

Metabolic disturbances
- Fluid (dehydration, hypovolemia)
- Electrolyte (sodium, potassium, magnesium)
- Nutrition (malnutrition, thiamine deficiency, anemia)

Structural insults
- Cardiovascular (angina, infarction, congestive heart failure)
- Central nervous system (stroke or ischemia, concussion)
- Pulmonary (hypoxia [e.g., COPD exacerbation])
- Gastrointestinal (bleeding with anemia, *C. difficile*, colitis)

Retention problems (urinary retention, constipation)

- Practical Tip #3:
  Check for urinary retention with a bladder scanner!

Medications which may precipitate or perpetuate delirium in the elderly patient

Analgesics	Anti-histamines	Anti-Nauseants	Anti-Parkinsons	Anti-Convulsants	Cardiovasc
Narcotics: •Codeine •Meperidine (Demerol®) •Morphine	Chlorpheniramine Diphenhydramine (Benadryl®) Hydroxyzine (Atarax®)	Scopolamine Dimenhydrinate (Gravol®)	Amantadine Benztropine Trihexyphenidyl Procyclidine Levo-dopa Bromocriptine	Phenobarbital Phenytoin	Beta-blockers (some) Digoxin
Gastrointest	**Genitourinary**	**Psychiatric**	**Pulmonary**	**Sedatives**	**Other**
Cimetidine Ranitidine	Oxybutynin (Ditropan®) Tolterodine (Detrol®) Solifenacin (Vesicare®) Darifenacin (Enablex®) Flavoxate (Urispas®) Trospium (Trosec®)	**Some Tricyclic anti-depressants (TCA)** •Amitryptiline •Doxepin •Clomipramine •Imipramine **Older anti-psychotics** •Chlorpromazine •Thioridazine **Other:** Lithium	Theophylline	Barbituates Chloral Hydrate **Benzodiazepine** Diazepam Lorazepam Oxazepam Triazolam Alprazolam Clonazepam	Alcohol Steroids Warfarin B-lactam and Quinolone Antibiotics (eg: Cipro)

Reducing the Medication Load

- Discontinuing/substituting anticholinergic medications
  - Diphenhydramine (Benadryl), Dimenhydrinate (Gravol), Hydroxyzine (Atarax)
  - Benztropine (Cogentin), etc.
  - Urinary anticholinergics
  - Avoid Amitriptyline (Elavil) Nortriptyline better tolerated
- Avoid the use of Cimetidine (Tagamet) in the elderly!
- Monitoring the effects of Steroids (Prednisone equivalent ≥40mg/d)
  - Fardet Am J. Psych 2012
- Switching Narcotics to (Avoid Meperidine=Demerol):
  - Hydromorphone (Dilaudid)
  - Oxycodone
  - Fentanyl (chronic pain)

Precipitant: Physical Restraints in the Medically Ill Elderly

Pitfall #1: Restraints are necessary to prevent morbidity such as falls, and help with managing delirious pts.

- Physical restraints increase risk of *developing* delirium by 4.4x Precipitating Factors in Hospital-Acquired Delirium, Inouye and Charpentier, JAMA 1996; 275: 852-57
  - Additional morbidities (eg: pneumonia, DVT, stasis ulcers) and mortality risk
  - In 2001, the Ontario government passed Bill 85, the *Patient Restraints Minimization Act*

Avoid limb or posey restraints in the frail elderly!

Perpetuating Factors in LTC

McCusker et al. Environmental factors predict the severity of delirium symptoms in long-term care residents with or without delirium. JAGS 2013

- Severity of Delirium Predicted by 6 Factors:
  - Absence of reading glasses
  - Absence of aids to orientation
  - Absence of family member
  - Absence of glass of water
  - Presence of bed rails and other restraints....
  - ....And the prescription of two or more new medications

Pharmacological Management of Delirium

- When to use Antipsychotics? (CCSMH's National Guidelines, 2006: The Assessment and Treatment of Delirium)

"Psychotropic medications should be reserved for older persons with delirium that are in distress due to agitation or psychotic symptoms, in order to carry out essential investigations or treatment, and to prevent older delirious persons from endangering themselves or others. ***[D]"***

Pharmacological Management of Delirium

- "Haloperidol as treatment of choice"
  - APA Guidelines 1999
- Other conventional antipsychotics
  - Loxapine (Loxapac)
  - Chlorpromazine (Largactil)
  - Methotrimeprazine (Nozinan)
  - Perphenazine
- Atypical antipsychotics
  - Risperidone, Olanzapine, Quetiapine

Atypical vs. Typical Antipsychotics for Delirium

"Higher Potency"	"Medium Potency"	"Lower Potency"
• Haloperidol	• Loxapine	• Methotrimeprazine (Nozinan)
• Risperidone	• Olanzapine	• Quetiapine

"Newer Atypicals": Ziprasidone, Aripiprazole

Haloperidol in Delirium Management

- Comparator to atypicals (3 RCT's in Cochrane)
- Prolonged QTc, especially I.V.– baseline ECG
- Risk of Extrapyramidal Symptoms, esp. elderly
  - >4.5 mg/day in Cochrane Review

Pitfall #2: Haloperidol is best treatment as best evidence

CPG's: Delirium Management

Country	Year	Antipsychotic Recommendations
Canada (Geriatric Delirium)	2006	Haldol; alternative Risperidone, Olanzapine, Quetiapine
Australia	2006	Haldol, Olanzapine, Risperidone
NICE (UK)	2010	Haldol, Olanzapine
United States	1999	Haldol

Antipsychotic	RCT's number of patients (pooled, 2013)
Haldol	258
Chlorpromazine	13
Risperidone	68
Olanzapine	125
Quetiapine	60
Aripiprazole	21 (prospective case-matched)
Ziprasidone	30

WWW.CCSMH.CA

To promote seniors mental health by connecting people, ideas and resources.

Promouvoir la santé mentale des personnes âgées en reliant les personnes, les idées et les ressources

CCSMH
Canadian Coalition for Seniors Mental Health
English Welcome

CCSMPA
Coalition Canadienne Pour la Santé Mentale des Personnes Âgées
Français Bienvenue

Pharmacological Management

We recommend...

- Antipsychotics are the treatment of choice to manage the symptoms of delirium (with the exception of alcohol or benzodiazepine withdrawal delirium). (B)
- Haloperidol is suggested as the antipsychotic of choice based on the best available evidence to date. (B) Initial dosages are in the range of 0.25 mg- 0.5 mg. Od-bid (D)
- Atypical antipsychotics may be considered as alternative agents as they have lower rates of extra-pyramidal signs. (B)
- Benztropine should not be used prophylactically with haloperidol in the treatment of delirium. (D)

Pharmacological Management

We recommend...

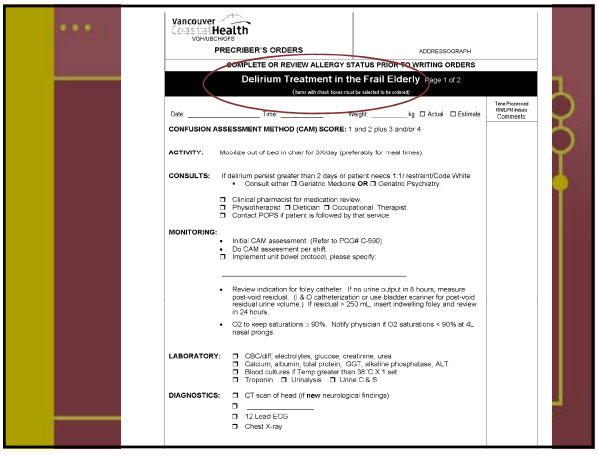
- In older persons with delirium who also have Parkinson's Disease or Lewy Body Dementia, atypical antipsychotics are preferred over typical antipsychotics. (D)
- Sedative-hypnotic agents are recommended as the primary agents for managing alcohol withdrawal delirium (B). Their use in other forms of delirium should be avoided (D).

Antipsychotics for Geriatric Delirium
from: Chan, BC Med J. Oct 2011

Medication	Trade Name	Category	Starting Dose (mg)	Usual Dose Range (mg)	Routes of Administration
Loxapine	Loxapac	Conventional	5-15	5-100	IV, IM, SC, PO
Methotrimeprazine	Nozinan	Conventional	2.5-10	2.5-100	IV, IM, SC, PO
Chlorpromazine	Largactil	Conventional	6.25-12.5	2.5-100	IM, SC, PO
Perphenazine	Trilafon	Conventional	1-2	2-16	IV, IM, PO
Haloperidol	Haldol	Conventional	0.5-1.0	0.5-5	IV, IM, SC, PO
Risperidone	Risperdal	Atypical	0.5-1.0	0.25-3	PO liq/tabs, SL
Olanzapine	Zyprexa	Atypical	1.25-5	2.5-15	PO, SL, IM
Quetiapine	Seroquel	Atypical	12.5-50	12.5-200	PO (IR, XR)

Pharmacologic Management: Guidelines

- Frequency:
  - Regular vs. Prn; nighttime dosing
- Route:
  - PO (tabs, sl, liquid) vs. SC vs. IM vs. IV
- Dosages:
  - haloperidol 0.25-0.5 bid
  - risperidone initiated at 0.25 mg od-bid
  - olanzapine at 1.25-2.5 mg per day
  - quetiapine at 12.5-50 mg per day



Vancouver Coastal Health

PRECRIBER'S ORDERS — ADDRESSOGRAPH

COMPLETE OR REVIEW ALLERGY STATUS PRIOR TO WRITING ORDERS

Delirium Treatment in the Frail Elderly Page 1 of 2

(Items with check boxes must be selected to be ordered)

Date _____ Time _____ Weight _____ kg ☐ Actual ☐ Estimate

CONFUSION ASSESSMENT METHOD (CAM) SCORE: 1 and 2 plus 3 and/or 4

AGTIVITY: Mobilize out of bed in chair for 3/24day (preferably for meal times).

CONSULTS: If delirium persist greater than 2 days or patient needs 1:1/ restraint/Code White
- Consult either ☐ Geriatric Medicine **OR** ☐ Geriatric Psychiatry.

☐ Clinical pharmacist for medication review.
☐ Physiotherapist ☐ Dietician ☐ Occupational Therapist
☐ Contact POPS if patient is followed by that service

MONITORING:
- Initial CAM assessment. (Refer to POG# C-590)
- Do CAM assessment per shift.
- ☐ Implement unit bowel protocol, please specify:

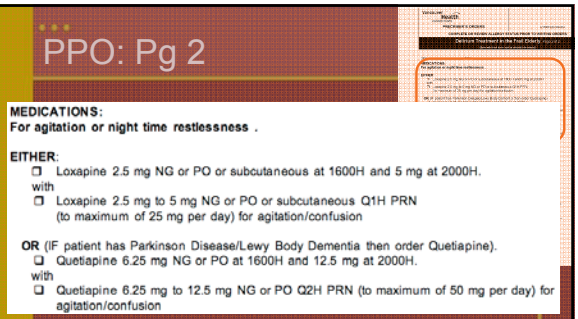
_____

- Review indication for foley catheter. If no urine output in 8 hours, measure post-void residual. (I & O catheterization or use bladder scanner for post-void residual urine volume.) If residual > 250 mL, insert indwelling foley and review in 24 hours.
- O2 to keep saturations ≥ 90%. Notify physician if O2 saturations < 90% at 4L nasal prongs.

LABORATORY: ☐ CBC/diff, electrolytes, glucose, creatinine, urea
☐ Calcium, albumin, total protein, GGT, alkaline phosphatase, ALT
☐ Blood cultures if Temp greater than 36°C X 1 set
☐ Troponin ☐ Urinalysis ☐ Urine C & S

DIAGNOSTICS: ☐ CT scan of head (if **new** neurological findings)
☐ _____
☐ 12 Lead ECG
☐ Chest X-ray

PPO: Pg 2



MEDICATIONS:
For agitation or night time restlessness .

EITHER:
- ❒ Loxapine 2.5 mg NG or PO or subcutaneous at 1600H and 5 mg at 2000H.

with
- ❒ Loxapine 2.5 mg to 5 mg NG or PO or subcutaneous Q1H PRN (to maximum of 25 mg per day) for agitation/confusion

OR (IF patient has Parkinson Disease/Lewy Body Dementia then order Quetiapine).
- ❒ Quetiapine 6.25 mg NG or PO at 1600H and 12.5 mg at 2000H.

with
- ❒ Quetiapine 6.25 mg to 12.5 mg NG or PO Q2H PRN (to maximum of 50 mg per day) for agitation/confusion

If unable to give Quetiapine NG or PO then:
- ❒ Methotrimeprazine (Nozinan®) 2.5 mg subcutaneous at 1600H and 5 mg at 2000H

with
- ❒ Methotrimeprazine (Nozinan®) 2.5 mg to 5 mg subcutaneous Q1H PRN (to maximum of 25 mg per day).

Consent to Treat Geriatric Delirium in LTC Facilities

- Substitute Decision-Maker's Consent to Treatment with Antipsychotics is Desirable, especially in those with pre-existing Dementia
- 1.5-2X risk of serious adverse events resulting in hospital admission or death that occurred within 30 days of initiating atypical or conventional antipsychotic therapy in the nursing home (n=20,559, pharmacovigilance). Rochon et al. Arch Int Med. 2008.
- Explanation of alternatives and the avoidance of physical restraints

Prognosis of Geriatric Delirium

Witlox, Meta-analysis, JAMA July 28, 2010

- Increased mortality in hospital and up to 2 year post (Leslie et 2005, McCusker 2003, McAvay 2006)
- Increased morbidity: LOS, functional decline, institutional care (Leentjens 2005, Rockwood 2001, McCusker 2003, McAvay 2006)
- More cognitive deficits: Up to 30-60% at 1 month (Levkoff 1992, Rockwood 1993, McCusker 2003, Marcantonio 2003); Lingering impairment at 6 months post-cardiac surgery (Saczynski, NEJM July 5, 2012)
- Those with Dementia and Delirium are less likely to achieve pre-Delirium cognitive and functional baseline status (McCusker 2001) and have a longer course of delirium (Dasgupta 2010, Boettger 2011)

Prognosis in LTC Resident

(Cole et al. **The course of delirium in older long-term care residents** Int J. Geri Psychiatry 2012)

- 14.7% delirium rate in 279 LTC residents in Montreal and Quebec
- Mean 11.3 +/- 10.1 days of delirium
- Range 7-63 days
- Recovery Rate at 4 weeks: 77.1%
- Recovery Rate at 24 weeks: 80.3%

Prognosis of Geriatric Delirium

- Increased risk of developing Dementia? (Rockwood 1999)
- Witlox, Meta-analysis, JAMA July 28, 2010
  - Odds Ratio=12.52 (1.86-84.21), mean follow-up= 4 yrs
  - 2 studies: Bickel *Dement Geriatr Cogn Disord. 2008;*26(1):26-31. Lundström *J Am Geriatr Soc. 2003;51(7):1002-1006.*
- Krogseth, Dement Geriatr Cogn Disord. 2011
  - Odds Ratio=10.5 (1.6-76.3), follow-up= 6 months
- Davis, Vantaa 85+, Brain, August 9, 2012 (epub)
  - Cohort of 553 seniors, aged 85 or over, Vantaa, Finland
  - Odds Ratio=8.7 (2.1-35), followed up to 10 years.
  - Delirium was associated with worsening Dementia severity

Prognosis

- Independent risk factor to mortality and morbidity in and after hospitalization
- Persistent cognitive and functional deficits common in geriatric delirium
- General anesthesia, independent of delirium, may lead to lingering cognitive impairments (Postoperative Cognitive Dysfunction=POCD)
  - Mason J. Alz Dis 2010; Deiner Br. J. Anaes 2009

The continuum between delirium and dementia….

- Pitfall #3: Delirium is reversed quickly once physical factors addressed

Protective/Prevention

Flaherty Med Clin North Am 2011

- Summary of Non-Pharmacological Mult-Component, Interdisciplinary-based, Prevention or Management Measures
- HELP = Hospital Elder Life Program
  - ...estimated at more than $7.3 million per year during 2008 at a community hospital! (Rubin, JAGS, 2011)
- Antipsychotics
- Melatonin

Prevention: HELP

Inouye, SK et al. A multicomponent intervention to prevent delirium in hospitalized older patients. N Engl J Med 1999; 340: 669-676

- 850 elderly patients, intervention (target 6 predisposing factors) vs. usual care group
- Incidence of delirium developed in 9.9% of the intervention group compared to 15% of the usual care group (OR 0.6)
- The days of delirium and number of episodes were also reduced in the intervention group
- However, the severity and recurrence rate was not reduced in comparison to the control group.

Prevention: Risk Stratification and Antipsychotics

- Kalisvaart study (Haloperidol prophylaxis)
  - 4 risk factors
    1. Visual Impairment
    2. Cognitive Impairment
    3. Dehydration (BUN: Creat ratio 18 or more, US units)
    4. APACHE II: Score 16 or higher
  - Risk stratification in developing Delirium
    - Intermediate risk: 1-2 risk factors
    - High risk: 3-4 risk factors

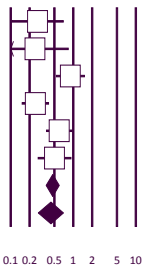
Antipsychotic Prophylaxis of Delirium

Author	TX	Pla-cebo	Site	Age	Dose	Outcome
Wang 2012	229	228	ICU	≥65	Haldol IV O.5 mg load then 0.1 mg/hr IV x 12 hrs, on ICU admission	Lower incidence of delirium (15.3% vs. 23.2%)
Kalisva-art 2005	212	218	Hip Sx	≥70	Haldol po 1.5 mg/d preoperative and up to 3 days postoperative	-Similiar incidence of delirium (15.1% vs. 16.5%) -Less # delirium days (5.4 days vs. 11.8 days) -Less # days in hospital (17.1 days vs 22.6 days) -Less severity of delirium
Kaneko 1999	38	40	GI Surg	X̄=72	Haldol IV 5 mg/d x 5 days postoperative	Lower incidence of delirium (10.5% vs. 32.5%)
Prakanr attana 2007	63	63	CAB G	X̄=61	Risperidone sl 1 mg/d on 1st postop day only	Lower incidence of delirium (11.1% vs. 31.7%)
Larsen 2010	196	204	Hip, Knee	X̄=74	Olanzapine 5 mg/d preop and postop (2d)	Lower incidence of delirium (14.3% vs. 40.2%); longer and

Forest Plot of All Included Studies

Fok et al. Do Antipsychotics Prevent Postoperative Delirium? A Systematic Review and Meta-analysis. Submitted for publication

Model	Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
	Prakanrattana et al 2007	0.269	0.104	0.694	-2.716	0.007
	Kaneko et al 1999	0.244	0.071	0.835	-2.247	0.025
	Kalisvaart et al 2005	0.899	0.535	1.510	-0.403	0.687
	Larson et al 2010	0.248	0.152	0.404	-5.598	0.000
	Wang et al 2012	0.596	0.371	0.956	-2.145	0.032
	Borger van der Burg-H1	0.502	0.273	0.920	-2.228	0.026
Fixed		0.467	0.366	0.596	-6.122	0.000
Random		0.437	0.275	0.696	-3.489	0.000



Melatonin Prophylaxis for Geriatric Delirium

- Al-Aama et al. ***Melatonin decreases delirium in elderly patients: a randomized, placebo-controlled trial*. Int J Geriatr Psychiatry. 2011.**
  - **145 geriatric pts from ER admitted to Int. Med Units**
  - **Mean age= 84 y.o.**
  - **Randomized to placebo or melatonin 0.5 mg/d for 14 d.**
  - **Reduction in incidence of delirium from 31% (placebo) to 12% (melatonin). P=0.014**
  - **Odds Ratio= 0.19 (adjusted for Dementia)**

Pearls and Pitfalls

Practical tips

- Ask specifically about vivid dreams or nightmares!
- Ask about use of visual and hearing aids! Optimize sensory input. Carry a voice amplifier.
- Check for urinary retention with a bladder scanner!

Pitfalls

- Restraints are necessary to prevent morbidity such as falls, and help with managing delirious pts.
- Haloperidol is best treatment as best evidence
- Delirium is reversed quickly once physical factors addressed

Web Resources

- Care for Elders Interactive Delirium Module
  - UBC Division of Geriatric Psychiatry
  - www.careforelders.ca
- VIHA Delirium information
  - www.viha.ca/mhas/resources/delirium
- Canadian Coalition of Seniors Mental Health
  - Clinical practice guidelines (2006)
  - www.ccsmh.ca
- Chan, "Clarifying the Confusion about Confusion: Current Practices in Managing Geriatric Delirium"
  - www.bcmj.org (October 2011)