Care of the Acutely Agitated Patient

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Dealing with combative patients is one of the most difficult challenges an emergency physician encounters. Often brought in against their will, such patients may be agitated, confrontational, and nearly impossible to examine. If not controlled, they may harm themselves or others, including the emergency department staff, other patients, and visitors.

-Rosen's Textbook of Emergency Medicine

Objectives

- Recognize agitation and predict violence
- Prevent escalation
- Tips for De-escalation
- Recommendations for physical and chemical restraints
- Cases

Agitation Defined

- "Excessive verbal and/or motor activity"

-Emergency Psychiatry; Principles and Practice

- **C**ohen-**M**ansfield **A**gitation **I**nventory
- **B**rief **A**gitation **R**ating **S**cale
- **P**ositive and **N**egative **S**ymptom **S**cale - **E**xcited **C**omponent (PANSS-EC)

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PANSS-EC

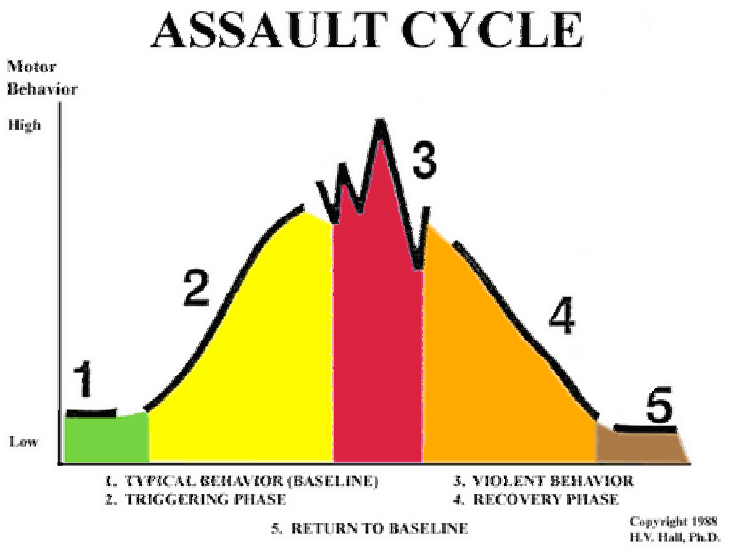
- Poor impulse control
- Tension
- Hostility
- Uncooperativeness
- Excitement

- Each given 1-7, for max total score 35

"Who feels it knows it."

Warning Signs

- Angry
- Pacing, changing positions frequently
- Clenched fists or tight grip on rails
- Loud speech
- Previous history
- Sometimes there is no warning



"A good captain weathers the storms he cannot avoid, and avoids the storms he cannot weather"

-Aaron Longton,
Oregon Fishing Captain

Prevention

- See them fast--long waits make things worse
- Disarm your patients...in a friendly way
- "Private but not isolated" bed if possible
- Don't provide any weapons--safe rooms

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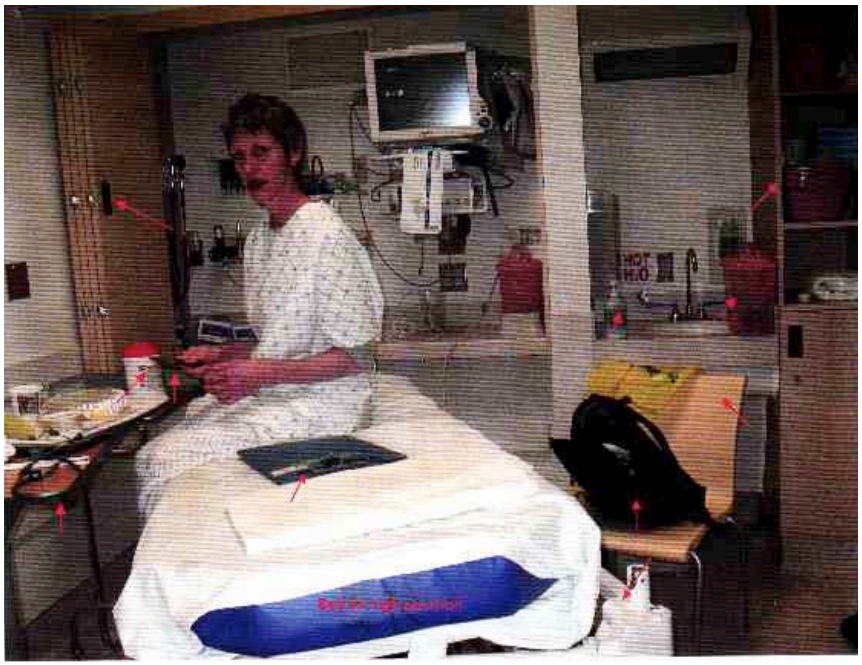

Prevention continued

- Keep door open
- Security nearby
- You and Pt equidistant to door

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De-escalation

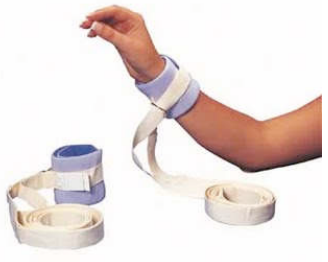
- Act as an advocate
- Make pt comfortable
- Strengthens “therapeutic alliance”
- Saves time, money, adverse outcomes, and injuries
- Under-emphasized in ED training

De-escalation: “10 Domains”

- Respect Personal Space
- Do Not Be Provocative
- Establish Verbal Contact
- Be Concise
- Identify Wants and Feelings
- Listen Closely
- Agree or Agree to Disagree
- Lay Down Law and Set Clear Limits
- Offer Choices and Optimism
- Debrief Pt and Staff

Glick RL et al, *Emergency Psychiatry; Principles and Practice*. Lippincott, 2008.

A Brief Word About Restraints



Take-Down team

- "Code 100"
- 6 staff + 1 physician
- Nurse #1 runs the code
- Nurse #2 gets the meds
- Nurse #3 gets restraints
- 1 staff per limb
- Physician to determine meds.

The Ideal Agitation Medication

- Fast acting
- Minimally labor/time intensive
- Not ***too*** sedating
- Safe for the patient
- Safe for you and staff
- Ethical and legal

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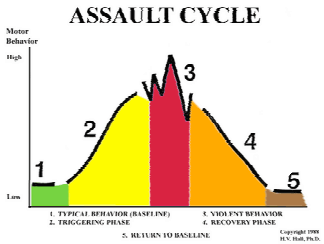
Cast of Characters

Cast of Characters

- Lorazepam (Ativan)
- Midazolam (Versed)
- Diazepam (Valium)
- Haloperidol (Haldol)
- Droperidol (Inapsine)
- Diphenhydramine (Benadryl)
- Benztropine (Cogentin)
- Ziprasidone* (Geodon)
- Olanzapine* (Zyprexa, Zydis)
- Risperidone (Risperdal)
- Aripiprazole* (Abilify)
- Quetiapine (Seroquel)

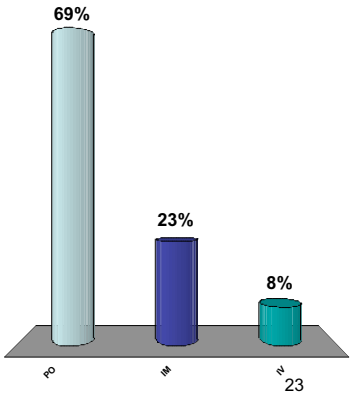
Case 1: The Universal Agitated Patient

- 30 y M, unknown hx, "acting crazy!"
- How crazy?
- A bit agitated<-->Violent



Case 1a: "a bit agitated" What Route?

1. PO
2. IM
3. IV



Strengthen the therapeutic alliance!

"He's a very controlling person"

PO is preferred route

- Offers patient choice and control
- Strengthens therapeutic alliance
- Can be given in elixirs or ODT
- Can even be given to pts in restraints
- Some are quite fast acting
- Generally preferred by patients

CONSUMERS' WANTS AND NEEDS DURING A PSYCHIATRIC EMERGENCY

Figure 2. Medication preferences

34 If you need to take psychiatric medications while being treated for a psychiatric emergency in the future, how would you prefer to take the medication? Please rate each of the following ways you could be given medication, giving a 9 (most preferred) to only one option.

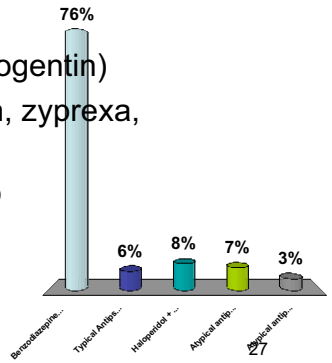
95% CONFIDENCE INTERVALS

	Least preferred	No strong feeling	Most preferred	Avg(SD)	Obs	MP	NSP	LP
Pills or capsules				8.2 (1.3)	63	93	6	2
Liquid medicine				4.9 (2.9)	9	37	26	37
An injection I agree to				4.7 (2.8)	11	25	34	41
An injection forced on me				1.5 (1.5)	2	2	5	93
	1 2 3	4 5 6	7 8 9			%	%	%

Allen et al. What do consumers say they want and need during a psychiatric emergency?. *Journal of Psychiatric Practice* (2003) vol. 9 (1) pp. 39-58

Case 1a: "a bit agitated" What kind of medicine?

1. Benzodiazepine (lorazepam)
2. Typical Antipsychotic (haloperidol, droperidol)
3. Haloperidol + lorazepam (+- cogentin)
4. Atypical antipsychotic (geodon, zyprexa, risperdal)
5. Atypical antipsychotic + benzo



ACEP Clinical Policy Level B Recommendations

- Use a benzodiazepine (lorazepam or midazolam) or a conventional antipsychotic (droperidol* or haloperidol) as effective monotherapy for the initial drug treatment of the acutely agitated undifferentiated patient in the ED.
- If rapid sedation is required, consider droperidol* instead of haloperidol.
- Use a combination of an oral benzodiazepine (lorazepam) and an oral antipsychotic (risperidone) for agitated but cooperative patients.

ACEP Clinical Policy Level C Recommendations

- The combination of a parenteral benzodiazepine and haloperidol may produce more rapid sedation than monotherapy in the acutely agitated psychiatric patient in the ED.

Lukens et al. Clinical Policy: Critical Issues in the Diagnosis and Management of the Adult Psychiatric Patient in the Emergency Department. *Annals of Emergency Medicine*. Vol 47, No 1, January 2006.

Expert Consensus Guideline 2005

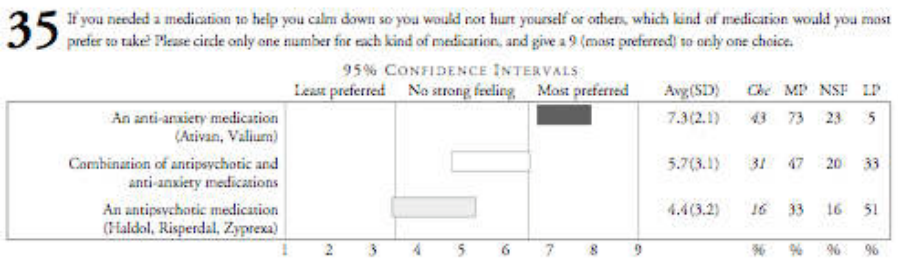
- "BNZs are recommended when no data are available, when there is no specific treatment (e.g., personality disorder), or when they may have specific benefits (e.g., intoxication)."

Allen et al. The Expert Consensus Guideline Series: Treatment of Behavioral Emergencies 2005. *Journal of Psychiatric Practice*. Vol 11, Suppl 1

Why BZNs are Preferred for Undifferentiated Agitation

- Safe. No EPS. No Sz
- Easy to titrate
- Preferred for intoxications
- Preferred for seizure, etoh w/d.
- Works some for psychosis
- Preferred by patients

Consumers' Wants and Needs During a Psychiatric Emergency



Allen et al. What do consumers say they want and need during a psychiatric emergency?. *Journal of Psychiatric Practice* (2003) vol. 9 (1) pp. 39-58

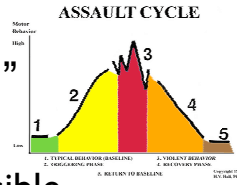
Consumers' Wants and Needs During a Psychiatric Emergency

36 If you needed a medication to help you calm down so you would not hurt yourself or others, are there specific medications you would most prefer to take (for example, are there certain medications that have helped you in the past)? Please circle only one number for each kind of medication, and give a 9 (most preferred) to only one choice. If you are not familiar with any of the medications, just leave that item blank.

95% CONFIDENCE INTERVALS

	Least preferred / No strong feeling / Most preferred	Avg(SD)	Glc	MP	NSF	LP
Ativan (lorazepam)		6.5(2.3)	25	58	33	8
Valium (diazepam)		5.4(2.9)	22	38	32	30
Klonopin (clonazepam)		5.3(3.2)	20	49	17	34
Seroquel (quetiapine)		4.6(3.0)	13	30	33	37
Risperdal (risperidone)		4.1(3.2)	9	31	17	51
Zyprexa (olanzapine)		4.0(3.0)	14	21	29	50
Navane (thiothixene)		3.6(2.7)	4	22	26	52
Prolixin (fluphenazine)		3.5(2.6)	0	16	32	52
Stelazine (trifluoperazine)		3.5(2.9)	12	20	16	64
Loxitane (loxapine)		2.9(2.6)	6	11	28	61
Geodon (ziprasidone)		2.7(2.1)	0	5	37	58
Haldol (haloperidol)		2.5(2.5)	6	12	9	79
Clozaril (clozapine)		2.3(2.1)	0	8	17	75
Mellaril (thioridazine)		2.2(1.6)	0	4	15	81
	1 2 3 4 5 6 7 8 9		%	%	%	%

Case 1b: "really agitated"



- PO still preferred route if possible
- Benzodiazepines still preferred class
- Lorazepam most widely used
  - -Reliable IM absorption
  - -No metabolites
- Consider Midazolam

Midazolam 5mg vs Lorazepam 2mg vs Haloperidol 5mg (IM)

	Time to Sedation	Time to Arousal
Midazolam IM	18 min	81 min
Lorazepam IM	32 min	217 min
Haloperidol IM	28 min	126 min

Nobay et al. A Prospective, Double-blind, Randomized Trial of Midazolam versus Haloperidol versus Lorazepam in the Chemical Restraint of Violent and Severely Agitated Patients *Academic Emergency Medicine* (2004)

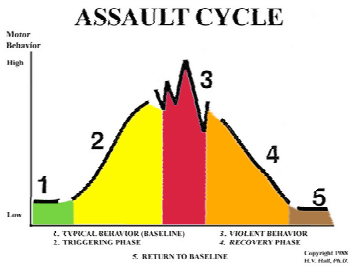
Midazolam 5mg vs Droperidol 5mg vs Ziprasodone 20mg (IM)

	Time to Sedation	Rescue medication	Required oxygen
Midazolam	15 min	24/48	10/48
Droperidol	30 min	5/50	4/50
Ziprasidone	30 min	9/46	7/46

Martel et al. Management of Acute Undifferentiated Agitation in the Emergency Department: A Randomized Double- Blind Trial of Droperidol, Ziprasidone, and Midazolam. *Academic Emergency Medicine* (2005)

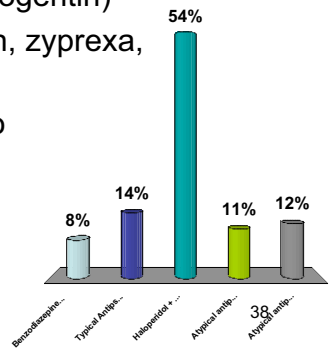
Case 2: 30 y M h/o Schizophrenia

- Off Meds
- Maybe intoxicated
- How agitated? Really Agitated.



Case 2: What kind of medicine?

1. Benzodiazepine (lorazepam)
2. Typical Antipsychotic (haloperidol, droperidol)
3. Haloperidol + lorazepam (+- cogentin)
4. Atypical antipsychotic (geodon, zyprexa, risperdal)
5. Atypical antipsychotic + benzo



ACEP Level B: Known Psych dz

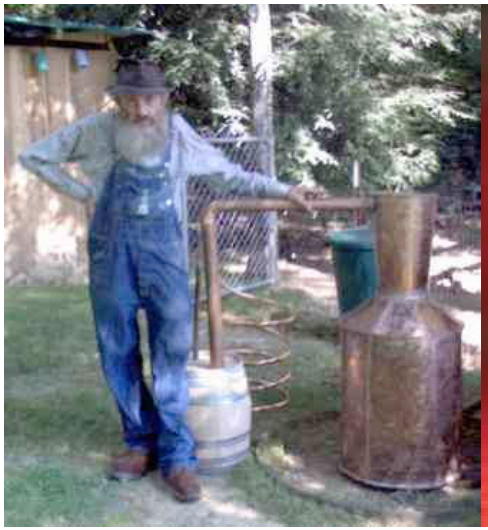
- "Use an antipsychotic (typical or atypical) as effective monotherapy for both management of agitation and initial drug therapy for the patient with known psychiatric illness for which antipsychotics are indicated."
- "Use a combination of an oral benzodiazepine (lorazepam) and an oral antipsychotic (risperidone) for agitated but cooperative patients."

Lukens et al. Clinical Policy: Critical Issues in the Diagnosis and Management of the Adult Psychiatric Patient in the Emergency Department. *Annals of Emergency Medicine*. Vol 47, No 1, January 2006.

Expert Consensus Guideline

- "Within the limits of expert opinion and with the expectation that future research data will take precedence, these guidelines suggest that the SGAs are now preferred for agitation in the setting of primary psychiatric illnesses but that BNZs are preferred in other situations."

Allen et al. The Expert Consensus Guideline Series: Treatment of Behavioral Emergencies 2005. *Journal of Psychiatric Practice*. Vol 11, Suppl 1

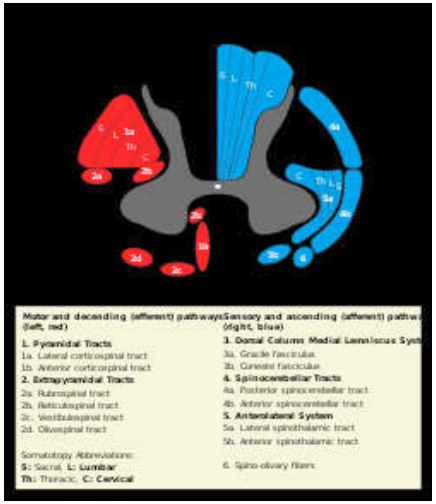


First Generation Antipsychotics

- Powerful, effective, Dopamine antagonists
- Long history
- Cheap
- Narrower range of sx
- Not favored by pts
- Not used long term
- High EPS

Extrapyramidal Symptoms

- Dystonia
- Oculogyric crisis
- Akinesia
- Akithesia
- Parkinsonism
- Tardive dsykinesia

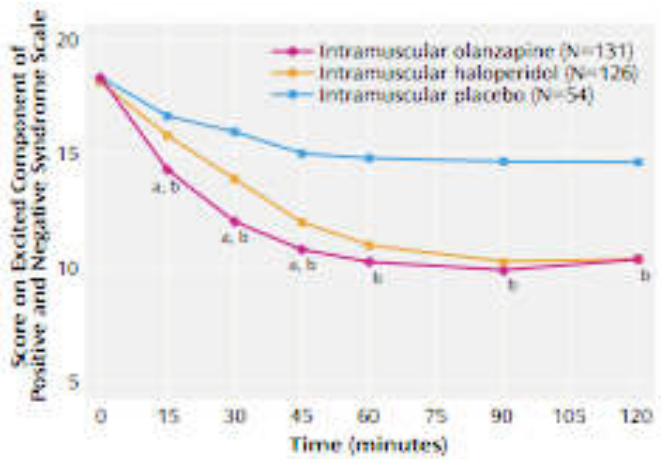


Second Generation Antipsychotics

- Broad range of sx, multiple receptors
- Effective single agent
- Low EPS
- Preferred by pts and psychiatrists
- Shorter history
- Expensive

Drug	Dose	Unit cost ($)	Ratio
Geodon	20mg IM	145	3.3
Zyprexa	10mg IM	369	8
Risperdone	2mg po	100	2.3
Haloperidol	5mg IM	11	
Ativan	2mg IM -	25	
Benadryl	50mg IM-	8	
	Regimen cost	44	1

IM Haloperidol vs IM Olanzapine



Wright et al. Double-blind, placebo-controlled comparison of intramuscular olanzapine and intramuscular haloperidol in the treatment of acute agitation in schizophrenia. *The American Journal of Psychiatry* (2001) vol. 158 (7) pp. 1149-51

Citrome. Comparison of intramuscular ziprasidone, olanzapine, or aripiprazole for agitation: a quantitative review of efficacy and safety. *The Journal of Clinical Psychiatry* (2007) vol. 68 (12) pp. 1876-85

NNT IM Ziprasidone, Olanzapine, Aripiprazole, Halopidol, Lorazepam

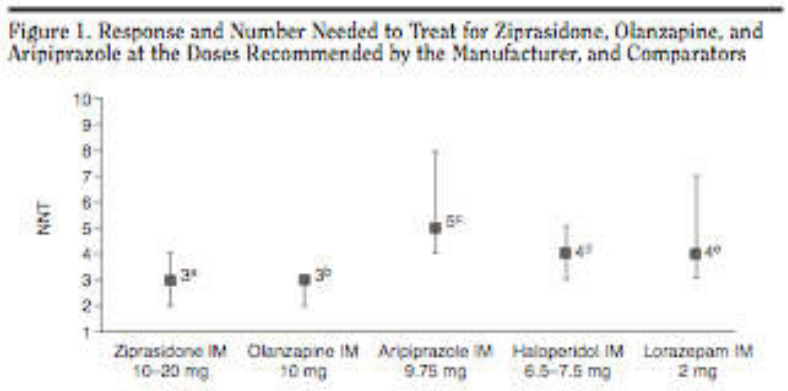


Table 4. Treatment-Emergent Extrapyramidal Symptoms

Antipsychotic	Disease State	Study Reference	Dose of Haloperidol or Lorazepam	Adverse Event	NNH Versus Placebo[a]	95% Confidence Interval[b]	NNH Versus Active Comparator[a]	95% Confidence Interval[b]
Olanzapine	Schizophrenia	Breier et al,[10,11] 2002[f]	Haloperidol, 7.5 mg	Acute dystonia	ND[c]	NS* (−∞ to ∞)	−20	NS* (−9 to −∞ and 57 to ∞)
				Parkinsonism	142	NS* (−149 to −∞ and 49 to ∞)	−7	−4 to −27
				Akathisia	86	NS* (−227 to −∞ and 36 to ∞)	−15	NS* (−7 to −∞ and 50 to ∞)
				Requiring anticholinergic medication	NA		−15	NS* (−7 to −∞ and 79 to ∞)
	Schizophrenia	Wright et al,[12,13] 2001	Haloperidol, 7.5 mg	Acute dystonia	ND[c]	NS* (−∞ to ∞)	−14	−9 to −38
				Extrapyramidal syndrome	−92	NS* (−21 to −∞ and 36 to ∞)	−21	−11 to −191
				Requiring anticholinergic medication	115	NS* (−19 to −∞ and 15 to ∞)	−7	−5 to −13
	Bipolar mania	Meehan et al,[14,15] 2001	Lorazepam, 2 mg	Acute dystonia	ND[c]	NS* (−∞ to ∞)	ND[c]	NS* (−∞ to ∞)
				Akathisia	99	NS* (−105 to −∞ and 34 to ∞)	−106	NS* (−20 to −∞ and 30 to ∞)
				Requiring anticholinergic medication	46	NS* (−17 to −∞ and 10 to ∞)	17	NS* (−218 to −∞ and 8 to ∞)
	Dementia	Meehan et al,[16,17] 2002[f]	Lorazepam, 1 mg	Acute dystonia	ND[c]	NS* (−∞ to ∞)	ND[c]	NS* (−∞ to ∞)
				Parkinsonism	69	NS* (−183 to −∞ and 29 to ∞)	69	NS* (−183 to −∞ and 29 to ∞)
				Akathisia	ND[c]	NS* (−∞ to ∞)	ND[c]	NS* (−∞ to ∞)
Aripiprazole	Schizophrenia	Andreazza et al,[18] 2006	Haloperidol, 6.5 mg	Extrapyramidal symptoms	−167	NS* (−24 to −∞ and 33 to ∞)	−10	−7 to −18
	Schizophrenia	Tran-Johnsen et al,[19] 2007[f]	Haloperidol, 7.5 mg	Acute dystonia	116	NS* (−306 to − and 49 to ∞)	−17	NS* (−8 to −∞ and 172 to ∞)
				Akathisia	47	25 to 349	−12	−6 to −533
	Bipolar mania	Oren et al,[20] 2005[f,g]	Lorazepam, 2 mg	Acute dystonia	−144	NS* (−28 to −∞ and 46 to ∞)	156	NS* (−164 to −∞ and 53 to ∞)
				Parkinsonism	11	7 to 26	10	7 to 18
				Akathisia	20	12 to 62	20	12 to 62
Haloperidol	Schizophrenia	Breier et al,[10,11] 2002[f]	Haloperidol, 7.5 mg	Acute dystonia	20	NS* (−27 to −∞ and 8 to ∞)		
				Parkinsonism	6	4 to 23		
				Akathisia	13	NS* (−27 to −∞ and 8 to ∞)		
	Schizophrenia	Wright et al,[12,13] 2001	Haloperidol, 7.5 mg	Acute dystonia	14	9 to 38		
				Extrapyramidal syndrome	27	NS* (−27 to −∞ and 8 to ∞)		
				Requiring anticholinergic medication	6	4 to 13		
	Schizophrenia	Andreazza et al,[18] 2006	Haloperidol, 6.5 mg	Extrapyramidal symptoms	10	7 to 22		
	Schizophrenia	Tran-Johnsen et al,[19] 2007[f]	Haloperidol, 7.5 mg	Acute dystonia	15	8 to 259		
				Akathisia	10	6 to 40		

*NS = not statistically significant at $p < .05$.
[a]A negative number for NNH implies an advantage for olanzapine or aripiprazole over the comparator.
[b]When not statistically significant, the 95% confidence interval represents both positive and negative numbers. (See text.)
[c]Incidence for the event is zero for the 2 interventions being compared.
[d]Data from all doses of the second-generation antipsychotic were pooled.
[e]Numerical data were determined by physically measuring the printed bar graph on the copy of the poster provided by Bristol-Myers Squibb Company.
Abbreviations: NA = not available, ND = no difference, NNH = number needed to harm.

Citrome. Comparison of intramuscular ziprasidone, olanzapine, or aripiprazole for agitation: a quantitative review of efficacy and safety. The Journal of clinical psychiatry (2007) vol. 68 (12) pp. 1876-85

NNH: Olanzapine vs Haloperidol

- Parkinsonism: Avoided every 7 pts
- Acute Dystonia: Avoided every 14 pts
- EPS: Avoided every 21 pts
- Anticholinergic Rx: Avoided every 7 pts

Citrome. Comparison of intramuscular ziprasidone, olanzapine, or aripiprazole for agitation: a quantitative review of efficacy and safety. *The Journal of clinical Psychiatry* (2007) vol. 68 (12) pp. 1876-85

Case 3: Elderly and Delirious

- Maybe a bit demented, maybe not…
- Pulling out lines, trying to get up
- What do you want to use?

Wait for it….

- Quiet room, low lights
- Language?
- Family and familiarity

Case 3: Elderly and Delirious

- Haloperidol low dose = first line
- Extensive history (but not FDA-labeled)
- Negligible anticholinergic effects
- Minimal hypotension
- BZNs and anticholinergics can worsen sx

QTc?

- All antipsychotics can prolong QTc and predispose to torsades de pointes
- Beware if baseline EKG = QTc >500
- Droperidol received controversial FDA Black Box Warning
- Haldol IV route not FDA approved 2/2 QTc…but everyone uses it.

Based on the evidence and view that IV haloperidol was a highly effective and preferred treatment for delirium, the committee approved the use of IV haloperidol in doses < 2mg with cumulative dose of 20mg/24 hours without 12-lead ECG monitoring. Telemetry and daily ECGs would be required for single doses ≥ 2 mg or cumulative doses of ≥ 20 mg/day.

Pharmacy and Therapeutics Committee
University of California, San Francisco and Mount Zion Medical Center
Wednesday, October 8, 2008

A Tale of Two Black Box WARNINGS

regarding dementia-related psychosis

- In placebo controlled trials with atypical antipsychotics, risk of death 1.6-1.7 times greater than placebo. Most deaths cardiovascular or infectious.
- Observational studies suggest similar problems with conventional antipsychotics
- Haloperidol is not approved for the treatment of patients with dementia-related psychosis (Prod Info haloperidol oral tablets, 2008).

While you're worrying

- EPS, acute dystonia,
- Neuroleptic Malignant Syndrome
- Olanzapine-->hypotension
- Olanzapine + BZN co-administration not advised.
- Ziprasidone-->More QTc prolongation but no recorded bad outcomes

Case 4: Parkinson's dementia Pt with delirium

- What do you give?
- Quetiapine (Seroquel) is most widely used antipsychotic for dopaminergic-induced psychosis.

Summary

- Acute agitation is dangerous for you and pt
- Prevention and de-escalation is key
- Oral route preferred when possible
- BZN's preferred for undifferentiated agitation in healthy adults
- Controversy over atypical vs typical antipsychotics in psychotic agitation
- Haloperidol most widely accepted in elderly with delirium (quetiapine in Parkinson's)