**Joe Lombardo**
***Governor***

**Richard Whitley**
***Director***

# Management of Psychiatric Emergencies Associated with Acute Agitation

## Division of Public and Behavioral Health

Leon Ravin, MD
Statewide Psychiatric Medical Director

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## Department of Health and Human Services

*Helping people. It's who we are and what we do.*

# Objectives

1. Define mental health crisis
2. Identify common causes of acute agitation in patients in mental health crisis
3. Review evidence-based FDA-approved treatment options for patients presenting with psychiatric emergencies associated with acute agitation
4. Identify concerns related to off-label administration of treatment interventions

# Mental Health Crisis

**NRS 433A.0175 "Person in a mental health crisis" defined.**

1. "Person in a mental health crisis" means any person:

(a) Who has a mental illness; and

(b) Whose capacity to exercise self-control, judgment and discretion in the conduct of the person's affairs and social relations or to care for his or her personal needs is diminished, as a result of the mental illness, to the extent that the person presents a substantial likelihood of serious harm to himself or herself or others, as determined pursuant to NRS 433A.0195.

2. The term does not include any person in whom that capacity is diminished by epilepsy, intellectual disability, dementia, delirium, brief periods of intoxication caused by alcohol or drugs, or dependence upon or addiction to alcohol or other substances, unless a mental illness that can be diagnosed is also present which contributes to the diminished capacity of the person.

# Acute Agitation in Patients in Mental Health Crisis (Part 1)

**Schizophrenia Spectrum Disorders**

- Delusional disorder
- Brief psychotic disorder
- Schizophreniform disorder
- Schizophrenia
- Schizoaffective disorder
- Psychotic disorder secondary to substances or a general medical condition

**Key symptoms**

- Delusions
- Hallucinations
- Disorganized speech
- Grossly disorganized or catatonic behavior

# Acute Agitation in Patients in Mental Health Crisis (Part 2)

**Catatonia symptoms**

- Stupor
- Catalepsy
- Vaxy flexibility
- Mutism
- Negativism
- Posturing
- Mannerism
- Stereotypy
- Agitation, not influenced by external stimuli
- Grimacing
- Echolalia
- Echopraxia

# Acute Agitation in Patients in Mental Health Crisis (Part 3)

**Manic symptoms in the context of bipolar and related disorders**

A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy associated with

- Inflated self-esteem or grandiosity
- Decreased need for sleep
- More talkative than usual
- Flight of ideals/Racing thoughts
- Distractibility
- Increase in goal-directed activity or psychomotor agitation
- Excessive involvement in activities that have a high potential for painful consequences

# Acute Agitation in Patients in Mental Health Crisis (Part 4)

**Other psychiatric disorders that can present with acute agitation**

- Anxiety disorders (i.e., phobia or panic disorder)
- OCD particularly with absent insight or delusional beliefs
- Trauma- and stress-related disorders with key symptoms of:
  - flashbacks that can involve a complete loss of awareness of present surroundings, or
  - intense psychological distress and marked physiological reactions when exposed to internal or external cues that symbolize or resemble an aspect of the traumatic event

# Restraint or treatment? (Part 1)

**NRS 433.5456 "Chemical restraint" defined.**

"Chemical restraint" means the administration of drugs to a person for the specific and exclusive purpose of controlling an acute or episodic behavior that places the person or others at a risk of harm when less restrictive alternative intervention techniques have failed to limit or control the behavior.

The term does not include the administration of drugs prescribed by a physician, physician assistant or advanced practice registered nurse as standard treatment for the mental or physical condition of the person.

# Restraint Reporting Requirements

In accordance with NRS 433.534 all facilities including hospitals, clinics or other institutions operated by a public or private entity, for the care, treatment and training of consumers must submit any and all consumer denial of rights reports to the Commission on Behavioral Health.

Use of physical (NRS 433.5493(3)), mechanical (NRS 433.5496(3)) and chemical (NRS 433.5503(2)) restraints on a consumer must be reported as a denial of rights to the Commission on Behavioral Health.

All facilities are encouraged to submit all denial of rights reports to the Division of Public and Behavioral Health by email at DORsubmission@health.nv.gov

# Restraint or treatment? (Part 2)

**NRS 433.5456 "Chemical restraint" defined.**

"Chemical restraint" means the administration of drugs to a person for the specific and exclusive purpose of controlling an acute or episodic behavior that places the person or others at a risk of harm when less restrictive alternative intervention techniques have failed to limit or control the behavior.

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# Standard Treatment

**Examples of sources of the information that establish standards of care**

- Prescribing information provided by the Food and Drug Administration
- Practice guidelines developed by the professional organizations
- Point-of-care information tools (i.e., UpToDate or DynaMed)
- Textbooks
- Scientific journals and other peer-reviewed publications
- AMA PRA CME certified activities

# Why Medications?

**A number of brain regions and pathways are associated with aggression and violence**

- In the prefrontal cortex of aggressive patients, 5HT is decreased, whereas both DA and NE are increased.
- In amygdala of aggressive patients, Glu and ACh are hypothetically increased, whereas GABA is decreased.
- Dopamine is involved in the initiation and performance of aggressive behavior.
- During aggressive confrontations, 5HT levels in the PFC may decrease by as much as 80%. Increasing 5HT levels bring about increased activity in the PFC as well as diminished aggression.

# Why Medications? (continue)

**Proposed mechanisms of action**

- First- and second-generation antipsychotics reduce dopaminergic transmission.
- Second-generation antipsychotics also block 5HT2A and can also act at 5HT1A receptors either as full or partial agonists modulating dopamine and glutamate release.
- Lamotrigine decreases Glutamatergic neurotransmission.
- Valproate, Topiramate, Carbamazepine, Oxcarbazepine increase GABAergic and decrease Glutamatergic neurotransmission.
- Lithium increases GABAergic and decreases Glutamatergic and Dopaminergic neurotransmission.
- Phenytoin increases 5HT- and GABAergic, and decreases Glutamatergic neurotransmission.

# Why Medications?

**Proposed mechanisms of action**

- Antidepressants increase prefrontal 5HT thereby facilitating the inhibition of subcortical areas.
- Sustained treatment with a stimulant down-regulates NE and DA receptors ultimately causing a reduction in excessive baseline dopaminergic and noradrenergic neurotransmission.
- β-blockers (Propranolol, Pindolol) and α2-blocker (Clonidine) decease NE transmission.
- Opiate antagonists (Naltrexone) block release of Glutamate, leading to less excitation of DA neurons in ventral tegmental area and less DA release in the PFC.
- BNZ potentiate GABA in hyperactive limbic regions, including amygdala.

# Medications Recently Approved by the FDA

**Management of acute agitation associated with schizophrenia or bipolar I disorder**

Olanzapine 10 mg IM x 1, may repeat the dose 2 hours after initial dose, then 4 hours after the second dose, max 30 mg/day

**Management of acute agitation associated with schizophrenia**

Ziprasidone 10 mg IM every 2 hours or 20 mg IM every 4 hours, max 40 mg/day

Dexmedetomidine 120 mcg buccally/SL x 1. May give additional 60 mcg for up to 2 doses if hemodynamically stable (SPB >90, DBP >60, HR >60). Max 240 mcg/day

# Acute Psychotic/Manic Agitation

**IM options used at the DPBH inpatient psychiatric facilities**

First generation (typical antipsychotics)

- Haloperidol
- Fluphenazine
- Chlorpromazine

- Second generation (atypicals)
- Olanzapine
- Ziprasidone

# Off-label Medication Prescribing

- Implies that the practice is not supported by randomized, blinded, placebo-controlled trials typically required by the FDA to approve a medication for a particular indication
- Is reserved for situations when on-label options failed or don’t exist
- Requires a different level of consent
- Is harder to defend in malpractice lawsuit or actions threatened by the licensing board

# Ketamine Use for Management of Acutely Agitated and Violent Patients in Mental Health Crisis

- Ketamine has been used to manage the acutely agitated and violent patient in the prehospital and hospital settings.
- Not approved by the FDA (Off-label).
- Not recommended by the American Psychiatric Association.
- Studies have been small, methodology has varied, and subject were adults.
- As per NRS, it is a form of a chemical restraint when used for acute agitation (used for sedation rather that treatment of a specific psychiatric syndrome or diagnosis). Reporting requirements apply.

# Ketamine Use Additional Considerations

- Schizophrenia spectrum disorder is a contraindication.
- When used to facilitate painful emergency department procedures in children, Ketamine has been associated with an increased risk of airway obstruction as well as a higher prevalence of vomiting in teen-age population.
- IM or IV Ketamine administration must be done in proper medical settings with constant observation, pulmonary and cardiac monitoring, and ability to provide cardio-pulmonary support in case of adverse reactions.
- Special precautions for safety should be considered because the patients may experience an increase in agitated behavior if they experience dissociative or psychotic symptoms following the administration of Ketamine.

# Questions?

# Contact Information

Leon Ravin, MD
Statewide Psychiatric Medical Director
Division of Public and Behavioral Health
lravin@health.nv.gov
702-486-4400

# Acronyms

5HT – Serotonin
ACh – Acetylcholine
AMA – American Medical Association
BNZ – Benzodiazepine(s)
CME – Continuous Medical Education
DA – Dopamine
DBP – Diastolic Blood Pressure
DPBH – Division of Public and Behavioral Health
DSM – Diagnostic and Statistical Manual
FDA – Food and Drug Administration
GABA – γ-Aminobutyric Acid
Glu – Glutamate
HR – Heart Rate
IM – Intramuscular
IV – Intravenous
NE – Norepinephrine
OCD – Obsessive Compulsive Disorder
PFC – Prefrontal Cortex
PRA – Physician's Recognition Award
SL – Sublingual
SPB – Systolic Blood Pressure

# References (Part 1)


- Green SM, Roback MG, Kennedy RM, Krauss B. Clinical practice guideline for emergency department ketamine dissociative sedation: 2011 update. Ann Emerg Med. 2011 May;57(5):449-61. doi: 10.1016/j.annemergmed.2010.11.030. Epub 2011 Jan 21. PMID: 21256625.

- Barbic D, Andolfatto G, Grunau B, Scheuermeyer FX, MacEwan W, Honer WG, Wong H, Barbic SP. Rapid agitation control with ketamine in the emergency department (RACKED): a randomized controlled trial protocol. Trials. 2018 Nov 26;19(1):651. doi: 10.1186/s13063-018-2992-x. PMID: 30477544; PMCID: PMC6258312.

- Riddell J, Tran A, Bengiamin R, Hendey GW, Armenian P. Ketamine as a first-line treatment for severely agitated emergency department patients. Am J Emerg Med. 2017 Jul;35(7):1000-1004. doi: 10.1016/j.ajem.2017.02.026. Epub 2017 Feb 13. PMID: 28237385

# References (Part 2)


- Sepulveda Ramos C, Thornburg M, Long K, Sharma K, Roth J, Lacatusu D, Whitaker R, Pacciulli D, Moredo Loo S, Manzoor M, Tsang YY, Molenaar S, Sundar K, Jacobs RJ. The Therapeutic Effects of Ketamine in Mental Health Disorders: A Narrative Review. Cureus. 2022 Mar 30;14(3):e23647. doi: 10.7759/cureus.23647. PMID: 35505747; PMCID: PMC9053551.

- American Psychiatric Association. (2022). Diagnostic and statistical manual of mental disorders (5th ed., text rev.). https://doi.org/10.1176/appi.books.9780890425787

- Assessment and emergency management of the acutely agitated or violent adult UpToDate https://www.uptodate.com/contents/assessment-and-emergency-management-of-the-acutely-agitated-or-violent-adult?search=psychotic%20agitation&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1