Clinical Implications of Substances in the Unregulated Drug Supply

A Resource for Emergency Department Providers

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ScalaNW

Purpose and Scope

This document serves to:

- Increase clinician awareness of substances with clinical implications identified in Washington's unregulated drug supply through community drug checking programs.
- Offer clinical considerations for potential exposures while emphasizing the complexity of the drug supply, polysubstance use, and atypical presentations.
- Supplement—not replace—standard clinical protocols, toxicology consultation, and broad differential diagnosis.

Key Disclaimers

- **Consult the Washington Poison Center (1-800-222-1222) right away for unknown toxidromes.**
- Always prioritize ABCs and rule out life-threatening non-toxicologic conditions (e.g., sepsis, trauma, metabolic disorders).
- Keep a broad differential diagnosis in mind. Patients may have symptoms unrelated to substance use, even if use is disclosed.
- The clinical implications of many substances in the supply are not fully understood.
- The drug supply is highly variable and rapidly changing.
- Some substances described in this document may be at low prevalence in the local drug supply but common in other regions and have clinical significance. Prevalence is being monitored by the **Washington Community Drug Checking Network** (see next page).

About the Washington State Drug Supply

The Washington Community Drug Checking Network (CDCN) monitors trends in the unregulated drug supply in Washington State. The CDCN:

- Provides on-site drug checking for clients of harm reduction programs.
- Conducts confirmatory lab testing of drug samples and makes results publicly available.
- Identifies whether a substance is present or not present.
- Tracks these most common substances of concern:
  - Benzodiazepines
  - Cocaine
  - Fentanyl and fentanyl analogs
  - Heroin
  - Methamphetamine
- Performs ongoing surveillance and investigation of novel psychoactive substances as they appear in drug checking results and other relevant data sources.
- Views drug checking as a valuable harm reduction tool that can provide limited insight into the unregulated drug supply.

Trends identified by the CDCN, as of June 2025:

- Drug checking samples sold as methamphetamine or fentanyl are the most tested substances.
- Over 90% of drug checking samples sold as methamphetamine contained methamphetamine and no other compounds.
- Samples sold as fentanyl are highly variable, often containing three or more compounds. Powder forms of fentanyl generally have high and widely varying potency.
- >90% of drug checking samples sold as Percocet or M30 pills contained fentanyl.

The unregulated drug supply is highly variable.

- Potency is variable and often unknown.
- Substances of the same form may be confused with one another (e.g., powder fentanyl may be confused with powder cocaine).
- Regional and temporal drug supply trends change rapidly. Refer to the CDCN for the most up-to-date data.

General Approach to Acute Management of Toxidromes

If a patient presents with symptoms concerning for unknown substance exposure, call the Washington Poison Center at 1-800-222-1222 for consult. Prioritize ABCs, rule out life-threatening non-toxicologic conditions (e.g., sepsis, trauma, metabolic disorders), and keep a broad differential diagnosis in mind as patients may have symptoms unrelated to substance use, even if use is disclosed.

The general approach to management is as follows:

Initial Stabilization

- ABCs: Prioritize airway, breathing, and circulation.
- Empiric Treatment for Altered Mental Status:
  - Cardiorespiratory monitoring.
  - Oxygen or advanced airway support as needed.
  - Monitor glucose, treat hyperglycemia/hypoglycemia.
  - Consider empiric thiamine if indicated.
  - Administer naloxone (IV/IM/IN) for suspected opioid involvement.
  - Monitor blood pressure and treat hypotension/hypertension.
- Broad Differential Diagnosis: Evaluate for infection, metabolic derangements, psychiatric etiologies, neurologic events, and trauma.

Assessment of Toxidromes

- While classic toxidromes (e.g., opioid, anticholinergic, sympathomimetic) can guide care, polysubstance exposure is common, and presentations may be mixed or atypical, for example:
  - Opioid toxidrome: respiratory depression, pinpoint pupils, sedation.
    - Consideration: Sedative/hypnotics may mimic or coexist with opioid effects.
  - Sympathomimetic toxidrome: tachycardia, hypertension, agitation, diaphoresis.
    - Consideration: Kratom intoxication or withdrawal states may produce similar symptoms.
  - Sedative/hypnotic toxidrome: somnolence, respiratory depression.
    - Consideration: May mimic or coexist with opioid effects.
    - Caution: Flumazenil is contraindicated in chronic benzodiazepine users due to risk of withdrawal seizures.

Laboratory and Diagnostic Workup

If the clinical picture is clear, additional testing may not be necessary. Consider the following based on clinical judgment:

- Bloodwork: CBC, BMP, LFTs; acetaminophen/salicylate levels if suspected.
- Urine toxicology: Many substances (e.g., fentanyl, xylazine, BTMPS) are not detected on standard urine drug screens.
- Additional testing: ECG (for QRS/QT prolongation), imaging (if trauma or infection suspected).

Special populations

Pregnant persons

- Many substances are lipophilic and cross the placenta.
- **Priority:** Stabilize the parent to protect the fetus (e.g., treat hypoxia, hypotension, hypertension, hypoglycemia, hyperglycemia).
- Left lateral positioning for gravid patients with decreased LOC – shifts weight off the IVC and improves venous return to the heart.
- Substance use or intoxication alone is not a mandatory CPS report.

Children

- Do not induce vomiting.
- Call poison control.
- Exposures may be intentional or unintentional.
- Exposures may be much higher doses on a mg/kg basis.
- Differential diagnosis should include hypoglycemia, sepsis, and non-accidental trauma.
- Very high doses of naloxone are sometimes required for opioid exposures.
- Good supportive care is the mainstay of treatment in the absence of a clear antidote.
- Unintentional ingestion of illicit substances by a child may constitute a mandatory report to CPS in Washington. Reportable incidents include fatalities, near fatalities (serious or critical condition), and use of naloxone.

Substance-Specific Considerations

The following substances of clinical significance have been found in the Washington State drug supply. The drug supply is highly variable. **Refer to the CDCN for the most up-to-date data.**

Brief background information and clinical considerations are listed for each substance; however, the clinical implications of many substances identified in the supply are not fully understood.

Fentanyl and Fentanyl Analogs

Background

- Fentanyl is the predominant opioid in the local drug supply.
- Fentanyl analogs may be more or less potent than fentanyl and are less commonly identified in the local drug supply.

Clinical Presentation

- Opioid toxidrome.
- Overdose/toxicity: unresponsive/unconscious, abnormal respirations, pinpoint pupils, cold/clammy skin, cyanosis.
- Withdrawal: Rapid pulse, sweating, tremor, dilated pupils, runny nose/tearing, bone/joint aches, nausea, vomiting, diarrhea, anxiety, restlessness, irritability, strong urge to use opioids.

Management

- Opioid toxidrome management.
- Overdose/toxicity: Respiration support and naloxone. Naloxone should be titrated to adequate respiratory drive — additional naloxone doses or a naloxone infusion may be indicated, but care should be taken to avoid unnecessarily inducing severe withdrawal.
- Withdrawal and use disorder: medications for opioid use disorder (MOUD; methadone, buprenorphine) and adjunct medications.

Nitazenes

Background

- Potent, novel synthetic opioids.
- Newly identified in the local drug supply. Few samples have tested positive locally.

Clinical Presentation

- Similar to other opioids, plus seizures and prolonged toxicity.
- Overdose/toxicity: seizures, nausea/vomiting, dizziness, unresponsive/unconscious, abnormal respirations, pinpoint pupils, cold/clammy skin, cyanosis. May have prolonged toxicity.
- Withdrawal: Rapid pulse, sweating, tremor, dilated pupils, runny nose/tearing, bone/joint aches, nausea, vomiting, diarrhea, anxiety, restlessness, irritability, strong urge to use opioids.

Management

- Overdose/toxicity: Respiration support and naloxone. Extended monitoring may be necessary. Additional naloxone doses may be indicated, but care should be taken to avoid unnecessary additional doses that induce severe withdrawal.
- Withdrawal: Medications for opioid use disorder (methadone, buprenorphine) and adjunct medications.

Nonpharmaceutical Benzodiazepines

Background

- Variable potency and half-life.
- Often not detected on urine drug screens.
- Most benzodiazepines tested at CDCN sites that looked like pharmaceuticals contained only non-pharmaceutical benzodiazepines.

Clinical Presentation

- Equivalent to other benzodiazepines, with considerable variable potency and half-life.
- Overdose/toxicity: May have profound and/or prolonged sedation.
- Withdrawal: irritability, anxiety/panic, tremor, sweating, nausea/vomiting, palpitations, headache, muscle pain and stiffness, perceptual changes. Severe withdrawal may include seizures and psychosis.

Management

- Equivalent to other benzodiazepines.
- Overdose/toxicity: Supportive care only. CAUTION: Do not use flumazenil due to risk of seizures in benzodiazepine dependency. Flumazenil will make the patient refractory to benzodiazepines.
- Withdrawal: benzodiazepine (diazepam, lorazepam), phenobarbital, or chlordiazepoxide for stabilization. Taper off benzodiazepines.

Medetomidine

Background

- Alpha-2 adrenergic agonist used as a veterinary sedative that is more potent than xylazine.
- Very few samples have been positive for medetomidine in the local drug supply.
  - In July to September 2025, 18 out of 177 substances tested that were sold as fentanyl powder contained medetomidine.
  - Medetomidine is more commonly seen on the east coast.

Clinical Presentation

- Overdose/toxicity: Profound and prolonged sedation, bradycardia, hypotension, respiratory depression, unconsciousness.
- Withdrawal:
  - Withdrawal syndrome is life-threatening with profound autonomic dysfunction, including tachycardia, uncontrollable vomiting, diaphoresis, tremor, and severe hypertension that may lead to end-organ damage.
  - Consider medetomidine withdrawal in patients who do not respond to standard opioid or xylazine withdrawal management.

Management

- Overdose/toxicity: Airway management, fluids, vasopressors. Administer naloxone to treat concomitant opioid overdose.
- Withdrawal:
  - Patients with severe withdrawal symptoms and autonomic dysfunction that is not resolved by standard treatments for fentanyl or xylazine withdrawal should be admitted to the ICU.
  - Patients with suspected medetomidine withdrawal should be given a dexmedetomidine infusion for hemodynamic stability while managing concomitant opioid withdrawal.

Kratom and 7-OH

Background

- Widely available as a dietary supplement despite lack of FDA approval.
- Acts on opioid, adrenergic, serotonergic, and dopaminergic receptors. Classified as an atypical opioid, with stimulant effects at low doses and opioid effects at high doses.
- The Washington Poison Center indicates that the proportion of calls about "kratom" referencing 7-OH have increased in 2025.
- The primary compounds in kratom are mitragynine and 7-hydroxymitragynine (7-OH).
- 7-OH is extracted or synthesized into a much more potent product.
- Overdoses that involve kratom typically also involve other substances like fentanyl.

Clinical Presentation

- Overdose/toxicity:
  - Respiratory depression, confusion, drowsiness, hypertension, agitation, arrythmias, nausea/vomiting.
  - Respiratory depression can be reversed with naloxone.
  - Although rare, hepatotoxicity, seizure, kidney injury, and cardiotoxicity have been reported.
- Withdrawal: Rapid pulse, sweating, tremors, dilated pupils, runny nose/tearing, bone/joint aches, nausea, vomiting, diarrhea, anxiety, restlessness, irritability.

Management

- Overdose/toxicity: Treat as clinically indicated. Contact poison control.
- Withdrawal and use disorder: no established consensus. Consider clonidine and/or low dose buprenorphine.

BTMPS (Bis(2,2,6,6-tetramethyl-4-piperidyl) sebacate)

Background

- Industrial chemical not studied for human consumption.
- Identified in substances sold as fentanyl, including 12% (22/177 samples) of fentanyl powder and 58% (7/12) of fentanyl pills tested from March-May 2025.

Clinical Presentation

- Unknown. BTMPS inhibits calcium channels and nicotinic acetylcholine receptors, so hypotension, bradycardia, altered mental status, and hyperglycemia are possible.

Management

- Uncertain clinical implications. Treat as clinically indicated.

Local Anesthetics

Background

- In March-May 2025, 22% of substances tested that were sold as fentanyl powder contained local anesthetics, predominantly benzocaine and lidocaine.

Clinical Presentation

- Temporary airway numbness when insufflated/inhaled.
- Toxicity: Ardiac toxicity is possible with intravenous use due to Na+ channel blockade, however doses in the supply are unknown and there have been no case reports of toxicity from unregulated substance use.

Management

- Supportive care.

Acetaminophen

Background

- Commonly found in substances sold as fentanyl.
- No known case reports of acute or chronic toxicity from unregulated fentanyl use.

Clinical Presentation

- No known case reports, but acetaminophen toxicity is possible depending on route of administration (i.e., hepatotoxicity, nephrotoxicity).

Management

- Consult Poison Control.

Screening

Patients presenting with acute toxidromes from known or unknown substance exposure should be screened for suicidal ideation, mental health conditions, and substance use disorder, and provided with appropriate interventions.

Conclusion

This resource provides an overview of potential clinical considerations for emerging trends in Washington's unregulated drug supply; however:

- The drug supply is highly variable, and trends change rapidly.
- Several substances included have minimal research on human consumption.
- Polysubstance use and non-toxicologic conditions complicate presentations.
- **Clinical judgment is paramount.**
- **Consult the WA Poison Center (1-800-222-1222) for real-time guidance.**