# The ToxIC NOSE (Novel Opioid and Stimulant Exposure)

Report #3 from ToxIC's Rapid Response Program for Emerging Drugs of Abuse

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## Deadly Adulterants: Another Threat from the Opioid Epidemic

### Introduction

**The ToxIC Novel Opioid Stimulant Exposures (NOSE) Reports**

As a project of the Opioid Response Network (ORN), the American College of Medical Toxicology (ACMT) Toxicology Investigators Consortium (ToxIC) is using the enhanced sentinel detector field to identify and report on novel and emerging opioid and stimulant exposures reported in ToxIC every quarter over a 2-year period.

The goal of this project is to disseminate this novel information to the medical toxicology community as well as the ORN as part of a Rapid Response program.

Adulteration and contamination of illicit drugs has long been a potential hazard for people who use both sporadically and chronically. Over the centuries, clusters of illness tied to specific adulterants can be found in historical descriptions. For example, in 1982 four young adults living around San Jose, California developed Parkinson's like movements after intravenous illicit opioid drug use. The substance was tested and found to be 1-methyl-4-phenyl, 1,2,3,6 tetrahydropyridine (MPTP) and 1-methyl-4-phenyl-4-propionoxypiperidine (MPPP), both byproducts of the production of a synthetic "street heroin" that was newly emerging in northern California at the time. MPTP was eventually found to be the neurotoxin responsible for this irreversible drug induced Parkinsonism.[1]

Motivation for the adulteration of illicit drugs is diverse and often multifactorial. In addition to evasion of local regulations and financial considerations, contributing factors include drug supply interruptions, enhancement of desired drug effects, and unintentional contamination of drugs during the manufacturing process. Adulterants can be chemically similar to the marketed product (fentanyl in heroin) with intended effects of use or be completely distinct and unrelated chemicals (MPTP in "street heroin") with unintended effects. Consequences of drug adulteration can result in significant morbidity and mortality.

It is widely known that fentanyl has been used as an adulterant in illicit opioids including heroin and oxycodone.[2] Due to its high potency, even those with tolerance to other opioids may experience life threatening opioid toxicity after inadvertent fentanyl exposure. More surprising, fentanyl has also been found in non-opioid illicit drugs including benzodiazepines and stimulants.[2,3] Individuals using benzodiazepines and stimulants may have little or no tolerance to opioids, increasing the risk of overdose after inadvertent exposure to fentanyl in adulterated products.

This NOSE report highlights specific issues associated with adulterants and opioids using ToxIC data, including results from an ongoing ToxIC study of patients presenting to the Emergency Department (ED) with opioid toxicity.

## The Case and ToxIC Data

### The Case

A young woman was brought to the ED after being found down with decreased respirations by EMS. Another individual found with her was pronounced dead at the scene. After receiving naloxone from EMS, she had return of consciousness and began breathing on her own. Upon arrival to the ED, the patient reported snorting cocaine intranasally with her friend prior to losing consciousness. This was a drug they used regularly. In the hospital, she complained of chest pain and shortness of breath and was found to be tachycardic (HR 135) and hypoxic (oxygen saturation 79% on room air). Her work up was significant for an aspiration pneumonia and stress cardiomyopathy, both of which improved during her hospitalization.

A drug screen was obtained which was positive for fentanyl. Though she confirmed cocaine use, she reported no known use of opioids.

### ToxIC Data

The case above highlights a recent submission to the ToxIC Core Registry, identified by the NOSE enhanced sentinel detector field within the registry. In addition to the ToxIC NOSE project, ToxIC has developed other data streams to evaluate opioid use and outcomes. As part of a grant from the National Institute on Drug Abuse, ToxIC and the Icahn School of Medicine launched a 5-year study entitled "Predicting Medical Consequences of Novel Fentanyl Analog Overdose Using the Toxicology Investigators Consortium (ToxIC)." The study includes nine geographically diverse ToxIC sites around the country that submit cases of suspected opioid overdose presenting to the ED. These cases are being utilized to characterize the novel synthetic opioids used, evaluate the optimal treatments, and track regional trends in fentanyl analog overdoses.

To date, this ongoing study has revealed intriguing data on adulteration and contamination of recreational drugs. Quarterly laboratory analysis of cases describes biological testing from patients presenting with suspected opioid overdose.[4] Of cases analyzed between 10/6/20-3/9/21, 61 cases involved illicit opioids with over 90% of the samples containing

adulterants. The two most common adulterants are quinine, a class 1a anti-dysrhythmic, and levamisole, an anthelminthic. Both agents have the possibility of causing significant clinical toxicity unrelated to opioid effects. Quinine can result in vomiting, hypoglycemia, blindness, and tinnitus. Levamisole can result in agranulocytosis and a disfiguring vasculitis. Neither drug has opioid-like effects.

A recent publication from the Fentalog study describes benzodiazepine adulteration of opioids. This study found etizolam, flubromazolam, and clonazolam, all designer benzodiazepines, to be detected in samples from patients presenting with opioid overdose.[3] This finding is clinically concerning as benzodiazepines can have synergistic effects with opioids, and notably will not be reversed by naloxone. When combined, benzodiazepines can increase CNS and respiratory depressant effects of opioids and heighten potential toxicity.[5]

## Discussion

The high prevalence of adulteration in illicit drugs has significant clinical implications, adding another layer of concern to the opioid epidemic. When caring for opioid users, physicians should be aware that unintentional overdoses may occur when synergistic adulterants such as benzodiazepines and more potent opioids are encountered. Additionally, unexpected opioid overdoses may occur when patients intending to use stimulants unintentionally encounter opioid adulterants. Finally, clinicians should maintain vigilance for unusual side effects after "run of the mill" opioid overdoses, such as a hypoglycemia from quinine adulteration.

## Conclusion

Adulteration of illicit drugs, such as opioids and stimulants, is common and can have unpredicted potentially serious clinical effects.

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### References


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## About the *Opioid Response Network (ORN)*:

*ORN* provides free, localized training and education for states, communities, organizations and individuals in the prevention, treatment and recovery of opioid use disorders and stimulant use. Learn more and submit a request at www.OpioidResponseNetwork.org.

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