Morbidity and Mortality Weekly Report (*MMWR*)

Notes from the Field: Suspected Medetomidi Syndrome Among Fentanyl-Exposed Patients Philadelphia, Pennsylvania, September 2024- 2025

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Summary

What is already known about this topic?

Medetomidine, a nonopioid sedative not approved for use in humans, replaced xylazine as th adulterant in the Philadelphia, Pennsylvania, illegal opioid supply during the last 4 months c

What is added by this report?

During September 2024–January 2025, 165 patients at three Philadelphia health systems w fentanyl withdrawal complicated by profound autonomic dysfunction, including severe hype This syndrome was resistant to medications that had previously been effective in managing withdrawal but was responsive to dexmedetomidine.

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Medetomidine, a synthetic alpha-2 adrenoreceptor agonist, is a new drug adulterant that was
opioid samples tested in Philadelphia, Pennsylvania, during the last 4 months of 2024. During
xylazine (previously the most common adulterant) decreased from 98% to 31% of samples (*1*
hospitals in Philadelphia noticed an increasing number of hospitalized patients with a severe c
distinct from fentanyl and xylazine withdrawal, characterized by profound autonomic dysfunct
hypertension and tachycardia. This report aims to increase awareness of the presence of mede
supply, characterize the emerging medetomidine withdrawal syndrome, and describe measure
care for this life-threatening syndrome.

Top

Investigation and Outcomes

During fall 2024, in response to emerging awareness of a newly recognized medetomidine wi
medicine and medical toxicology faculty members at three Philadelphia health systems (healt
maintaining a list of patients identified with the syndrome, including those they had helped ca
for, as well as patients referred by other health care providers. The faculty members reviewed
patients who were admitted to the three health systems during September 1, 2024–January 3
withdrawal syndrome was characterized by severe signs and symptoms that were not resolve
protocols for fentanyl and xylazine withdrawal. Overall, 165 patients were identified who dem
or symptoms such as agitation, anxiety, severe hypertension, tachycardia, tremor without clon
vomiting, resistant to increasing doses of opioids (e.g., fentanyl, hydromorphone, methadone, c
diazepam, droperidol, haloperidol, lorazepam, midazolam, phenobarbital, or propofol), and adj
withdrawal medications (clonidine, ketamine, olanzapine, ondansetron, or tizanidine) (*2*). Medi
33–43 years). This evaluation was reviewed and approved by the institutional review boards o

Among the 165 patients, 150 (91%) required intensive care unit (ICU) care, including 39 (24%
intubation (Table). A total of 137 (83%) patients were treated with and responded to dexmed
eventually recognized as potentially effective; medetomidine is an enantiomer[†] of dexmedeto
dexmedetomidine exposure can induce a withdrawal syndrome manageable with controlled w
Traditional dosages of dexmedetomidine (0.2–1.5 μg/kg/hr) (*3*) were used and titrated to contr
patients with intubation. In a majority of patients requiring dexmedetomidine, the drug was tit
of 1.5 μg/kg/hr. Duration of infusion varied, depending on the patient. Use of oral alpha-2 ago
limited because of vomiting. Patients were also treated with antihypertensive medications titra

however, they were responsive to dexmedetomidine, as described in the management of dexm
(*4*,*5*). Health care providers and public health agencies need to be aware of this life-threatenir
because it can require substantial escalations in care compared with the typical opioid and xyl
Public health agencies should consider testing for medetomidine in their regional drug supplie
Top

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Top

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Top

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Top

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Top

* Dexmedetomidine is an alpha-2 agonist medication that is used for sedation in an ICU and o

† Enantiomer molecules are mirror images of each other and are not superimposable (e.g., righ

§ Posterior reversible encephalopathy syndrome is a neurologic disorder characterized by brai
blood pressure is severely increased. The syndrome is diagnosed by cross-sectional brain ima

4. Pathan S, Kaplan JB, Adamczyk K, Chiu SH, Shah CV. Evaluation of dexmedetomidine wit
J Crit Care 2021;62:19–24. https://doi.org/10.1016/j.jcrc.2020.10.024 PMID:332275
5. Bouajram RH, Bhatt K, Croci R, et al. Incidence of dexmedetomidine withdrawal in adult c
study. Crit Care Explor 2019;1:e0035. https://doi.org/10.1097/CCE.0000000000000035

Top

**TABLE. Characteristics of patients hospitalized with combined opioid and sus
withdrawal syndrome — three health systems, Philadelphia, Pennsylvania, S
January 2025**

Characteristic	No. (%)		
	Health system A (n = 55)	Health system B (n = 48)	He sys (n
Age, yrs, median (IQR)	37 (33–45)	38 (35–41)	3
Sex			
Female	12 (22)	20 (42)	
Male	43 (78)	28 (58)	
Race and ethnicity*			
Black or African American, non-Hispanic	6 (11)	6 (13)	
White, non-Hispanic	44 (80)	34 (71)	
Hispanic or Latino	5 (9)	0 (—)	
Other	0 (—)	8 (17)	
Clinical findings and hospital course			
Maximum heart rate (beats per minute), median (IQR)	144 (125–155)	136 (118–156)	1

Characteristic	No. (%)		
	Health system A (n = 55)	Health system B (n = 48)	He sys (n
Patient-directed discharge	14 (26)	13 (27)	
Residential drug treatment	14 (26)	7 (15)	
Law enforcement custody	12 (22)	0 (—)	

* Persons of Hispanic or Latino (Hispanic) origin might be of any race but are categorized as H non-Hispanic.

Top

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