HHS Public Access

Author manuscript

J Public Health Manag Pract. Author manuscript; available in PMC 2024 March 11.

Published in final edited form as:

J Public Health Manag Pract. 2020 ; 26(6): E1–E7. doi:10.1097/PHH.0000000000001002.

The Public Health Response to a Large Poisoning Outbreak Involving an Illicit Substance: Synthetic Cannabinoids Contaminated With a Long-Acting Anticoagulant Rodenticide, Illinois, March-July, 2018

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Abstract

During March-July 2018, the Illinois Department of Public Health responded to an acute outbreak of severe coagulopathy among patients with recent synthetic cannabinoid use. Toxicological testing indicated that cases were exposed to brodifacoum, a long-acting anticoagulant rodenticide. A total of 174 confirmed and probable cases, including 5 deaths, were linked to this outbreak. On the basis of the experience of responding to this complex outbreak, we recommend several steps for consideration to improve health department preparation for acute outbreaks involving illicit substances including strengthening communication between public health and law enforcement agencies, reviewing legal authority to investigate noninfectious acute disease outbreaks, continuing strong partnerships with state poison control centers, partnering with substance abuse and mental health agencies to provide services to patients, and determining health department ability to rapidly enter into public-private partnership agreements.

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Keywords

illicit drugs; law enforcement; outbreak investigation; public health

On March 22, 2018, the Illinois Department of Public Health (IDPH) was notified by the Illinois Poison Center (IPC) of 4 patients seen in emergency departments (EDs) during the preceding 2 weeks with unexplained bleeding and evidence of prolonged coagulation (high international normalized ratios by the prothrombin time assay). All patients reported synthetic cannabinoid (SC) use within 3 days of illness onset. On the basis of presenting clinical signs and improvement after treatment with high doses of vitamin K and/or fresh frozen plasma, exposure to a long-acting anticoagulant rodenticide (LAAR) through SC use was suspected.[1]

As hospitals in Illinois reported a rapidly increasing number of patients with similar clinical presentations, an investigation was initiated by IDPH, IPC, the Centers for Disease Control and Prevention (CDC), Illinois local health departments (LHDs), and law enforcement agencies to identify additional patients, understand the epidemiologic links among patients, and implement control measures. In addition, there was a concerted effort to educate health care providers on presenting clinical signs and symptoms to ensure rapid patient identification and initiation of appropriate treatment.

By mid-July 2018, a total of 174 confirmed and probable cases were identified in Illinois, with 96 of 97 patients who had specimens tested for the presence of LAARs positive for brodifacoum, a commercially available rodenticide. Five deaths due to bleeding among Illinois residents have been linked to this outbreak. This is the largest cluster of LAAR poisoning cases reported in the literature.[2–4]

Synthetic cannabinoids, also known as K2 and spice, are heterogeneous psychoactive compounds originally developed to study the structure and function of cannabinoid receptors, but in recent years, SCs have emerged as drugs of abuse. They first appeared for sale in European countries around 2005 before becoming available in the United States in 2008.[5] In 2017, 26 SCs were listed as Schedule I substances under the Controlled Substances Act and all 50 states have taken legislative or administrative actions to curb SC use.[6,7] SCs are manufactured illegally, and producers continuously alter the chemical structures to create compounds that evade laboratory testing.[5]

To understand how often outbreaks related to illicit drugs are reported, using a PubMed query, we reviewed “Notes From the Field” articles in CDC’s *Morbidity and Mortality Weekly Report*, a publication used by local, state, and federal public health agencies to report outbreak investigations.[8,9] During January 2011 to June 2018, of 287 published articles, 35 (12%) were related to noncommunicable disease (CD) outbreaks; of these, 13 (37%) were related to public health investigations involving illicit or counterfeit substances.[1,10–21]

Although infrequent, outbreaks involving illicit substances can escalate rapidly. For example, an outbreak of severe illness (sweating, severe agitation, or psychosis) occurred

among SC users in Mississippi in 2015 that resulted in 721 suspected cases and 9 deaths in a 1-month period.[21] Given the infrequency of these types of outbreaks, the concomitant lack of experience by public health agencies, and the potential for a large number of cases, in this article, we discuss how we managed this complex investigation, issues we encountered, and provide suggestions for how health departments can prepare for outbreaks involving illicit substances.

The Public Health Investigation

Language in Illinois statutes and regulations provides legal authority for IDPH "[*t*]o make investigations and inquiries with respect to the causes of disease and death […] and to make other investigations that it may deem necessary for the preservation and improvement of health."[22] IDPH does not have a unit that responds specifically to acute health events that involve illicit substances, which necessitated an internal discussion to determine which section within IDPH would lead the response. The CD section investigates cases of reportable CD including tuberculosis, vaccine-preventable diseases, enteric diseases, and arboviral diseases. Annually, this section helps LHDs throughout Illinois respond to more than 200 CD outbreaks. This section has a strong relationship with Illinois LHDs—CD staff regularly provide guidance and tools to help LHDs investigate outbreaks—and has well-established communication channels with hospitals and health care providers. In addition, the CD section has strong case tracing and data analytic capability. Therefore, although this was not an infectious disease outbreak, IDPH leadership determined that the CD section would lead the investigation in close collaboration with the IPC, which would provide toxicological expertise.

The CD section rapidly developed an outbreak investigation tool to collect epidemiologic data, including patient clinical data, history and frequency of SC use, specific SC products used, locations where SCs were purchased, and environmental exposure to rodenticides. Data were collected through patient interviews, by medical chart abstraction, and from IPC clinical consultations. Despite asking questions about illicit activity, patient cooperation with the public health investigation was high; 131 of the 141 patients (93%) reached by phone completed the patient interview.

Initially, all patient interviews were conducted by IDPH but as the volume of cases increased, LHDs in jurisdictions with cases were asked to assist with the investigation. During the investigation, patients were reported in 16 Illinois LHD jurisdictions; 3 jurisdictions accounted for 72% of patients. Patients were clustered in 3 distinct geographic areas—the Chicago area, including Cook County and neighboring counties; the Peoria area in central Illinois; and around the City of Rockford, located near the border with Wisconsin.

In all, 28 IDPH staff members worked on the SC response. The majority (57%) of the staff were from the CD section. IDPH leadership, legal staff, public information officers, as well as public health preparedness staff played key roles in this investigation and response. In addition, CDC sent a team of 3 scientists for a 14-day period to assist with the investigation. IDPH and the deployed CDC staff reported a total of 1965 person-hours working on the response during March 22 to May 15, 2018. Time worked on the response by IPC and LHD

staff is not included in this report but was substantial. Although the CD section was able to monitor for concurrent outbreaks, the number of staff needed to coordinate and carry out this investigation resulted in the need for overtime and reassignment of the staff away from routine work duties.

Information Sharing

This investigation was complex and required IDPH to share information with multiple entities including clinicians, SC users, the public, LHDs, law enforcement agencies, IPC, CDC, other states reporting cases, and the media (Figure). Coordination with law enforcement was essential to prevent additional exposures and deaths.

Illinois Poison Center

Clinicians treating potential cases could report them either directly to public health (IDPH or LHDs) or to the IPC. A large proportion of cases (76%) were first reported to the IPC, primarily when clinicians sought treatment guidance. At the beginning of the outbreak, the appropriate vitamin K treatment regimen was unknown. As clinicians shared lessons learned from treating patients, the IPC developed and disseminated standard clinical treatment guidelines. To ensure complete case reporting and address any acute issues, IPC and CD section staff held daily phone calls for the duration of the public health investigation.

Clinicians

Throughout the investigation and outbreak response, frequent communication with clinicians was a high priority. Efforts involved alerting them to the existence of these unusual cases, providing information to enable rapid identification of suspect cases, and supporting them in effective clinical management of cases. In addition to clinical guidance disseminated by the IPC, memoranda with messages specific to each clinical audience were developed by IDPH and sent to Illinois EDs, emergency medical service providers, surgeons, dentists, pharmacists, and coroners through electronic distribution lists.

Patients sought care at 50 health care facilities in Illinois. During the course of this investigation, some health care facilities were reluctant to share patient information with public health. In general, Illinois health care facilities associate public health reporting with infectious disease and given that law enforcement was involved in the investigation, the facility staff were hesitant to disclose patient information to IDPH and LHDs. A memo was sent out by the IDPH general counsel to all Illinois hospitals on April 3, 2018, outlining the applicable Illinois statutes and assuring facilities of the legal basis for public health investigation of this outbreak.

Law enforcement

At the time of this outbreak, many SCs were classified as illegal in Illinois and because the route of SC contamination with brodifacoum was unknown, a law enforcement investigation was initiated. The goal of both the public health and law enforcement investigations was to prevent additional cases. The objectives of the public health investigation were to understand patient risk factors including SC exposure and use, to characterize clinical presentation, and

to identify whether there were common products used by patients (Table). The objectives of the law enforcement investigation were to identify locations and persons from which SC products were purchased, to rapidly remove product from the supply chain, and to test seized products for SC composition and the presence of LAARs.

As part of the public health investigation, LHD and IDPH staff asked each interviewed patient about SC product(s) utilized and whether the patient had any utilized SC product(s) remaining. If the patient reported having product available, the patient was asked about willingness to surrender it for testing. Given the illicit nature of these substances, law enforcement was responsible for obtaining SC products from patients to maintain chain of custody and for testing products for SC composition and presence of LAARs. Product testing results were not directly shared with IDPH, given the active law enforcement investigation.

Through designated liaisons, a subset of information obtained from the public health investigation patient interview, specifically information regarding where and how a patient obtained SC products, was shared by IDPH with Illinois State Police. In addition, limited patient information was shared to allow for separate law enforcement interview of cases. This collaboration resulted in the seizure of SC products from the supply chain.

The public and SC users

All entities involved in the investigation worked on media outreach to alert the public about this outbreak and the substantial risk associated with SC use (Figure). IDPH issued 7 press releases that discouraged SC use and encouraged anyone with a serious reaction after using SCs to seek immediate medical attention.[23] Despite high media coverage of the outbreak, it was not clear how best to target messaging to individuals who use SCs.

Several strategies were utilized to communicate information to potential SC users. IDPH created shareable infographics that could be widely disseminated.[23] These infographics included information about SCs and the dangers associated with their use. One LHD that had a high volume of patients posted messaging at convenience stores, which were reported as a source of SC purchase by some patients. During the epidemiologic interview, patients were encouraged to share information with their social network. When patients who presented for care to EDs were asked about how they first heard about contaminated SC products (n = 59), 46% indicated hearing about it from friends or family, 25% had not heard about the risk prior to seeking care, and 22% reported receiving information from a newspaper or television.

CDC and other state health departments

At the same time as the outbreak was occurring in Illinois, smaller clusters and some sporadic cases were reported by states across the country. CDC helped coordinate information sharing among states with suspect cases. Concurrently, IDPH shared investigation tools, including the epidemiologic interview tool and case definitions, directly with states experiencing cases.

Unusual Challenges Encountered

Treatment

Coagulopathy associated with LAAR exposure requires high initial doses of intravenous vitamin K (phytonadione), in addition to other treatments such as fresh frozen plasma or 4-factor prothrombin complex to stabilize acutely ill patients.[3] Long-term (3-6 months) high-dose prescription oral vitamin K is needed to manage patients once stable.[3] Given the large number of patients, there were initial concerns about the vitamin K supply chain and the potential for localized treatment shortages. Contingency plans were developed for sharing of vitamin K between hospitals in areas with high numbers of cases. However, the supply chain proved to be robust and there were no substantial shortages of oral or intravenous vitamin K.

The most significant challenge related to treatment was the combination of the high cost of prescription oral vitamin K and the extended duration of treatment. Many patients in this outbreak were underinsured or uninsured and, even among patients with insurance, high co-payments resulted in several patients foregoing treatment. Without appropriate vitamin K treatment, these individuals were in danger of developing severe outcomes such as fatal hemorrhage and often returned to EDs for additional care to manage bleeding. As a result, IDPH implemented a telephonic process for patient follow-up to identify challenges in accessing vitamin K. The initial follow-up call was attempted 10 days after a patient first presented for care, with a second follow-up call scheduled for 7 days after the first phone call was completed. Two attempts were made at each time interval to contact a patient. Conducting these calls (n = 326) was labor-intensive, with a relatively low patient response rate (54%); however, gaps in access to treatment were identified, and IDPH staff attempted to address identified needs by communicating directly with patients' providers or referring cases to available clinical resources.

One solution offered to patients who identified issues accessing vitamin K due to financial reasons was a prescription assistance program available from a vitamin K manufacturer. Patients who were reached for follow-up reported difficulty completing the required paperwork. IDPH successfully worked with this pharmaceutical manufacturer to obtain a large donation of oral vitamin K that could be distributed to patients at no cost. It took several weeks to finalize the legal agreement and to establish mechanisms to securely accept, store, track, and distribute the donation.

Once the donation was received, patients who had reported issues with obtaining vitamin K were contacted to alert them to the availability of the free medication. In partnership with 2 large health care systems, vitamin K was placed strategically at pharmacies located in areas with high numbers of patients. For patients who were unable to physically access these pharmacies, a free prescription mail service was established. As of August 15, 2018, a total of 51 039 vitamin K pills had been dispensed to 86 patients.

Plasma donation

Some patients (n = 7) reported donating plasma at for-profit donation centers, leading to concerns about whether donated plasma contaminated with LAARs could adversely affect

recipients, as well as lead to uncontrolled bleeding from the venipuncture site in donors. A question was added to the patient interview questionnaire about plasma donation; if donation during the preceding 3 months was reported, the collecting plasma center was notified. In turn, the plasma center was responsible for notifying the US Food and Drug Administration (FDA) to allow for adverse event monitoring. Plasma and blood donation centers in Illinois were made aware of this outbreak and the potential risk associated with donations from SC users and advised by IDPH to seek guidance from the FDA, the regulating authority, regarding enhanced screening protocols.[24]

Discussion

We summarize here our experience as a state public health department investigating an acute poisoning outbreak involving an illicit substance. On the basis of our experience, there are several lessons learned that may aid other health departments increase preparedness for this type of complex and rapidly escalating investigation.

Because public health and law enforcement investigations have overlapping information needs, establishing communications channels among state and local public health and law enforcement agencies can minimize duplicate data collection and improve situational awareness among agencies.[25] Although there are preestablished relationships between Illinois public health and law enforcement agencies that facilitate sharing of aggregate data, we faced challenges, given the limitations of information sharing during an active investigation due to both patient privacy concerns and law enforcement limitations of sharing details of an active criminal investigation. Determining law enforcement product testing capability and secure channels by which forensic laboratory product testing results could be disclosed to public health may have facilitated information sharing during this response. Our experience in Illinois suggests that a shared data platform for public health and law enforcement agencies that would allow for secure data sharing and joint situational analysis may be a useful tool in future outbreaks involving illicit substances to improve bidirectional data sharing.

During the course of this investigation, some health care facilities were reluctant to share patient information with IDPH despite state statutes establishing legal authority to conduct this type of investigation. To avoid similar issues during rapidly unfolding investigations of acute non-CD outbreaks, public health agencies may want to establish legal authority for such investigations in advance and work to educate health care facilities in their jurisdictions on public health reporting and disclosure requirements.

To be able to rapidly respond to this type of outbreak, health departments can identify in advance what capabilities are needed internally and predetermine which health department section or group has the most applicable experience and skill set to lead a response. The experience in Illinois suggests that an effective response will likely involve expertise across disciplines including CD, environmental health, and behavioral health. Implementing an organizational structure that allows for effective internal collaboration and data sharing early in the response can also contribute to a more effective response.

The importance of partnerships in a complex response cannot be understated. In Illinois, there is a strong history of collaboration between IDPH and IPC. During this response, IPC was able to take initial reports of suspect patients, thereby reducing the reporting burden to both clinicians and LHDs, provide treatment guidance to clinicians, and share patient management lessons learned in real time across health care facilities. Health departments can consider working closely with their poison control centers to strengthen existing relationships and to determine the level of toxicological and clinical guidance they can provide.

Given that this outbreak involved individuals who used illicit substances, partnering with state and local agencies that have behavioral health expertise may have helped better address the needs of this population. The experience in Illinois suggests that having preestablished referral mechanisms between health departments and agencies that provide mental health and substance abuse services may allow for better provision of services to patients in future outbreaks. Based on the lack of clear communication channels to reach Illinois individuals who used SCs, these agencies may also be a potential avenue for providing targeted educational messaging.

Although public-private partnerships have increasingly been encouraged as a way to improve public health services, at the time of this outbreak, IDPH had limited capacity for accepting donations, particularly of prescription drugs. Having preestablished legal templates and protocols to facilitate public-private partnerships, including a process for material donation, might have reduced the time it took IDPH to obtain the vitamin K donation. The Illinois experience suggests that engaging health department legal staff may help facilitate the development of public-private partnerships by preparing documents and procedures in advance and negotiating unanticipated issues during the response itself.

The reason brodifacoum was present in the SC products consumed by cases is unknown, although it may have been deliberately added to potentiate the physiological effects of the products.[4,26,27] Sporadic patients with coagulopathy associated with SC use continue to be reported in Illinois and in a number of other states. Given the unknown provenance and composition of SC products, ongoing public health messaging of the risks associated with SC product use is needed. The lessons learned from this complex outbreak response can be utilized by other health departments to better prepare for acute non-CD outbreaks, particularly those associated with illicit substances.

Acknowledgments

Dr Nirav Shah, Donald Kauerauf, Molly Lamb, Kelly Walblay, Judy Kauerauf, Dawn Nims, Julie Dow, and Alexandra Barger affiliated with the Illinois Department of Public Health at the time of the outbreak were key to carrying out the public health response. Staff from the following local health departments contributed to the outbreak response: Tazewell County Health Department, Peoria City/County Health Department, Cook County Department of Public Health, City of Chicago Department of Public Health, Winnebago County Health Department, Woodford County Health Department, DuPage County Health Department, Fulton County Health Department, Kankakee County Health Department, Mason County Health Department, Kane County Health Department, Madison County Health Department, Mclean County Health Department, Stephenson County Health Department, and Will County Health Department. Illinois Poison Center staff including Carol DesLauriers and the Toxikon fellows, Drs Arkady Rasin, Jason Devgun, Theresa Kim, and Maxim Dzeba, provided invaluable toxicological support and patient clinical follow-up.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

No authors report any conflicts of interest or sources of funding from nonpublic sources.

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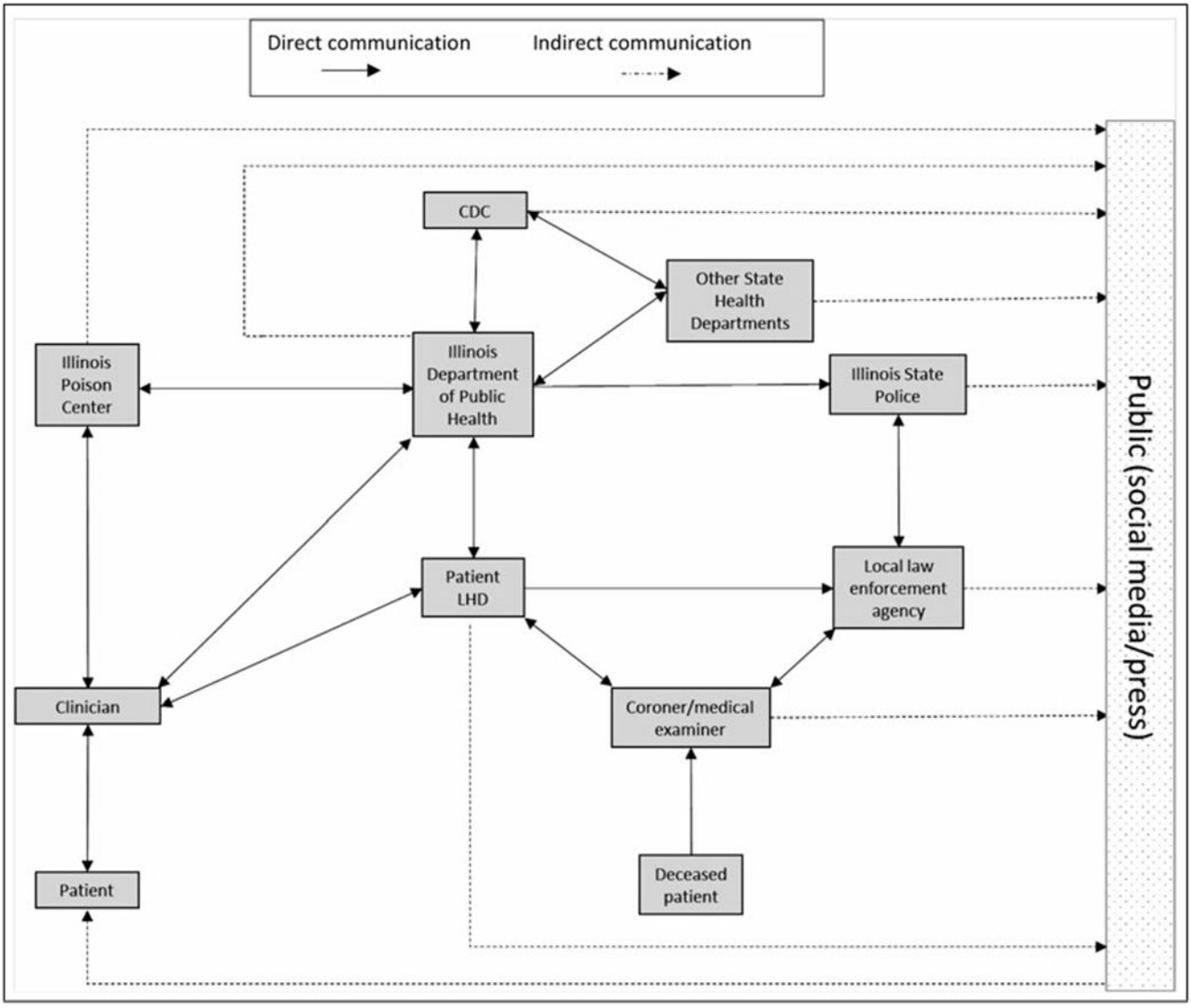

FIGURE.

Information Sharing During an Outbreak Response Involving Synthetic Cannabinoids Contaminated With a Long-Acting Anticoagulant Rodenticide, Illinois, 2018

Abbreviations: CDC, Centers for Disease Control and Prevention; LHD, local health department.

TABLE

Information Needed for the Public Health Investigation Compared With the Law Enforcement Investigation During an Outbreak Response Involving SCs Contaminated With a LAAR, Illinois, 2018

Information Needed	Public Health Investigation	Law Enforcement Investigation
Patient-related interview		
Symptoms	X	
SC use (frequency and duration)	X	
Environmental Exposure to rodenticides	X	
Testing		
Blood clotting test—prothrombin time (INR)	X	
Urine toxicology panel	X	
LAAR serum testing	X	
Product-related interview		
SC brands used	X	X
Place of purchase	X	X
Date of purchase	X	X
Remaining product available	X	X
Testing		
SC compounds in product	X	X
LAAR compounds in product	X	X
Other adulterants	X	X

Abbreviations: INR, international normalized ratio; LAAR, long-acting anticoagulant rodenticide; SCs, synthetic cannabinoids.