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**CDC HEALTH ADVISORY**

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## **Outbreak of Life-threatening Coagulopathy Associated with Synthetic Cannabinoids Use**

**\*\*\*Missouri health care providers and public health practitioners: Please contact your local public health agency, or the Missouri Department of Health and Senior Services (DHSS) at 573-751-6095 or 800-392-0272 (24/7), to report possible cases of life-threatening coagulopathy associated with synthetic cannabinoids use.\*\*\***

### **Summary**

The Centers for Disease Control and Prevention (CDC) is providing information on: 1) the current status of a multistate outbreak of coagulopathy from exposure to synthetic cannabinoid products containing a vitamin K-dependent antagonist agent, such as brodifacoum; 2) signs and symptoms of presenting patients from this outbreak and which patients are at risk; 3) laboratory testing options that are available to help identify and classify cases; 4) available resources that may help clinicians make decisions; and 5) to whom to report possible cases.

### **Background**

#### ***General Background***

Synthetic cannabinoids are not one drug. Hundreds of different synthetic cannabinoid chemicals are manufactured and sold (1). New ones with unknown health risks become available each year. These chemicals are called *cannabinoids* because they act on the same brain cell receptors as tetrahydrocannabinol (THC), the main active ingredient in marijuana; however, synthetic cannabinoids may affect the brain in different and unpredictable ways compared to THC (2). Synthetic cannabinoids are used in a variety of ways including: 1) sprayed onto plant material and then smoked; 2) used in electronic nicotine delivery devices (such as e-cigarettes); or 3) ingested when added to herbal tea or food.

Synthetic cannabinoids are widely available. Consumers can buy synthetic cannabinoids in convenience stores, from individual drug dealers, friends, or online as incense or natural herbal products. They are sold under many different brand names, but are commonly referred to as synthetic marijuana, fake weed, legal weed, K2, and Spice. Adverse effects from synthetic cannabinoids use vary and can include neurological (e.g., agitation, confusion), psychiatric (e.g., hallucinations, delusions), and other physical (e.g., tachypnea, tachycardia, gastrointestinal distress) signs and symptoms (1-3).

#### ***Outbreak Background***

In March 2018, the Illinois Department of Public Health reported cases of unexplained bleeding among patients who reported using synthetic cannabinoids. Subsequent testing of drug and biological samples from case-patients detected the presence of brodifacoum, a long-acting vitamin K-dependent antagonist that is used as a rodenticide (4).

CDC is currently coordinating national surveillance activities for possible cases of vitamin K-dependent antagonist coagulopathy associated with synthetic cannabinoids use. Since the index case was identified in Illinois on March 3, 2018, state health departments have reported 202 cases, including five deaths, to CDC. Case patients have been identified in nine states with the majority being reported from Illinois (n=164). Maryland has reported 20 cases. Florida, Indiana, Kentucky, Missouri, Pennsylvania, Virginia, and Wisconsin have reported six or fewer cases per state. More than 95 of case-patient biological samples have tested positive for brodifacoum. The current working hypothesis is that brodifacoum was mixed with synthetic cannabinoids products.

Case-patients from this outbreak have presented with a variety of signs and symptoms of coagulopathy (e.g., bruising, nosebleeds, excessively heavy menstrual bleeding, hematemesis, hemoptysis, hematuria, flank pain, abdominal pain, and bleeding gums or mouth). In addition, some patients have been asymptomatic or presented with complaints unrelated to bleeding but have had numerical coagulopathy that may put them at risk for bleeding complications resulting from injuries and invasive or surgical procedures. Patients should be considered high-risk for coagulopathy if they have reported use of or are suspected of using synthetic cannabinoids.

The most helpful and commonly available laboratory test to help identify cases is the International Normalized Ratio (INR) that is part of a routine coagulation profile. An abnormal INR is defined as being outside the reference laboratory value. For case reporting purposes, an INR > 2 is being used as a criteria to help identify and classify possible cases. Case confirmation requires detection of brodifacoum in blood, serum, plasma, or urine, as determined by reference laboratory testing. Clinicians and healthcare providers should work with their healthcare facility's laboratory to determine what options are available to them for brodifacoum testing.

## **Recommendations**

### ***Recommendations for Clinicians***

1. Maintain a high index of suspicion for vitamin K-dependent antagonist coagulopathy in patients with a history or suspicion of using synthetic cannabinoids. Patients may present with clinical signs of coagulopathy, bleeding unrelated to an injury, or bleeding without another explanation. Some patients may be asymptomatic or present with complaints unrelated to bleeding but have numerical coagulopathy. NOTE: Some patients may not divulge synthetic cannabinoids use.
2. Ask all patients about history of illicit drug use. All high-risk patients (e.g., those reporting synthetic cannabinoids use or those who are suspected of synthetic cannabinoids use within the last three months), regardless of their presentation, should be screened for vitamin K-dependent antagonist coagulopathy by checking their coagulation profile (e.g., INR).
3. Possible cases should be asked if they have recently donated plasma or blood (e.g., in the last three months). Clinicians treating possible cases who have recently donated plasma or blood should notify their state health department, who can then notify the FDA.
4. Proceduralists (e.g., trauma/general/orthopedic/oral/OB-GYN/cosmetic surgeons, dentists, interventional cardiologists/radiologists, and nephrologists) should be aware that patients with a history of using synthetic cannabinoids may be anti-coagulated without clinical signs of coagulopathy. These patients should be screened for vitamin K-dependent antagonist coagulopathy **prior** to their procedure.
5. Patients sent home from surgeries or other procedures that could result in bleeding should be told not to use synthetic cannabinoids because of the risk that the product may be contaminated with an anticoagulant.
6. Contact your local poison control center (1-800-222-1222) for questions on diagnostic testing and management of these patients.
7. Promptly report possible cases to your local or state health department.

### ***Recommendations for Public Health Officials***

1. Promptly report possible cases to CDC via [NCEHOutbreak@cdc.gov](mailto:NCEHOutbreak@cdc.gov)
2. Contact CDC for case classification criteria, reporting guidelines, case investigation forms, and other questions at the above email.
3. Consider conducting case-finding activities that leverage existing data sources such as your local poison control center, coroner/medical examiner's office, and other applicable surveillance systems.
4. In an effort to better understand the scope of this outbreak, ask your Medical Examiners' office to report possible cases, especially those without an alternative, likely diagnosis. If individuals are identified after death or at autopsy showing signs of suspicious bleeding as described above, coroners are encouraged to report the cases to their local health department.

### **Recommendations for the Public**

1. CDC recommends that people do not use synthetic cannabinoids. Synthetic cannabinoids are always dangerous because it is impossible for people to know what chemicals are in the product, how much they are being exposed to, and how their body will react to the chemicals. The synthetic cannabinoid products associated with this outbreak are especially dangerous because they contain brodifacoum, a chemical used as rat poison that can cause uncontrolled bleeding.
2. People who have used synthetic cannabinoids in the past three months and are concerned about their health should contact their healthcare provider. Synthetic cannabinoid users who develop any unusual bruising or bleeding should seek medical attention immediately.

### **For More Information**

- Synthetic cannabinoids: What are they? What are their effects?  
<https://www.cdc.gov/nceh/hsb/chemicals/sc/default.html>
- Synthetic cannabinoids: An Overview for Healthcare Providers  
<https://www.cdc.gov/nceh/hsb/chemicals/sc/healthcare.html>
- CDC Clinical Outreach and Communication Activity: Outbreak Alert Update: Potential Life-Threatening Vitamin K-Dependent Antagonist Coagulopathy Associated With Synthetic Cannabinoids Use.  
<https://emergency.cdc.gov/coca/clinicalaction/2018/index.asp>

### **References**

1. Castaneto MS, Gorelick DA, Desrosiers NA, Hartman RL, Pirard S, Huestis MA. Synthetic cannabinoids: epidemiology, pharmacodynamics, and clinical implications. *Drug Alcohol Depend* 2014;144:12-41.
2. Gurney SM, Scott KS, Kacinko SL, Presley BC, and Logan BK. Pharmacology, toxicology, and adverse effects of synthetic cannabinoid drugs. *Forensic Sci Rev* 2014;26:53-78.
3. Tai S, Fantegrossi WE. Pharmacological and toxicological effects of synthetic cannabinoids and their metabolites. *Curr Top Behav Neurosci* 2017;32:249-262.
4. King N, Tran MH. Long acting anticoagulant rodenticide (superwarfarin) poisoning: A review of its historical development, epidemiology, and clinical management. *Transfus Med Rev* 2015;29:250-258.

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