

Michigan Regional POISON CONTROL CENTER

Children's Hospital of Michigan **DMC**

Health Alert

Movement 2019: Detroit Electronic Music Festival Hart Plaza Downtown Detroit May 25-28, 2019

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Michigan Festival Season Summer 2019	
Chevrolet Belle Isle Grand Prix	May 31 – June 2
Hoe Down	June 15
Lakes of Fire (Rothbury)	June 12 – 16
Electric Forest (Rothbury)	June 27 – 30
Detroit River Days	June 21 – 23
Common Ground (Lansing)	June 27 – 30
Faster Horses	July 19 – 21
Mo Pop	July 27 – 28

The Michigan Regional Poison Control Center can be reached at **1-800-222-1222**

The 13th annual Movement draws over 100,000 attendants from around the globe and marks the beginning of the Michigan music festival season. This update highlights the drugs-of-abuse most likely to be encountered by prehospital or hospital providers, including keys to the recognition and management of toxicity resulting from these substances.

The expected circulating drugs are unlikely to be very different from other years. Certain festivals are associated with specific drugs or combinations of drugs/substances. The Movement Festival tends to have more designer agents and the Hoedown is usually associated with heavy ethanol use. Festivals in downtown urban areas will continue to reflect the usual substances found in these locales such as ethanol, marijuana, cocaine, heroin and methamphetamine.

NEW FOR 2019

Fentanyl here to stay!

Heroin adulterated with fentanyl and fentanyl analogs (“fentalogs”) has become the norm in Southeast Michigan and based on Medical Examiner data, approaches involvement in 80% of “heroin” overdoses. It has been suggested that some dealers now advertise their heroin as having “fire,” using it as a selling point to mean the heroin contains or is laced with fentanyl. While most commonly the heroin is cut with fentanyl, some samples of “heroin” contain no actual heroin at all but pure fentanyl. This often baffles health care providers as patients present with an opioid toxidrome but have a **negative urine drug screen for opioids**. **IMPORTANT REMINDER:** Fentanyl itself will not trigger a positive urine drug screen for opioids. Opioids which will lead to a positive urine drugs of abuse include codeine, morphine, heroin, oxycodone, hydrocodone, hydromorphone. Some will pick up oxycodone and oxymorphone. Fentanyl will not trigger the opioid testing unless it is mixed with morphine or heroin. Methadone and buprenorphine require separate specific testing. Fentanyl overdoses *will* respond to naloxone therapy at usual doses. The carfentanil crisis has passed; it no longer seems to be an issue in the Detroit area heroin supply. Fentalogs (e.g. cyclopropyl fentanyl, acetyl fentanyl, and other fentanyl derivatives) and the W class opioids (U-47700 aka “u-4”) are being combined into tablets and substituted for oxycodone and hydrocodone complete with appropriate imprint codes. “Xanax” tablets (alprazolam) have also been found to contain fentanyl and fentalogs.



<http://www.dea.gov/pr/micrograms/2006/mg0106.pdf>

Xylazine

Xylazine is a veterinary sedative, muscle relaxant and analgesic. It is a pre-synaptic α_2 agonist and analog of clonidine. It is not approved for use in the US but is being combined with fentanyl and sold as “heroin”. As a cutting agent, it provides an additive sedative effect but can also cause apnea, hypotension and bradycardia. Mechanistically, naloxone will not reverse the effects of xylazine, which can complicate overdose reversal efforts and clinical management. In Puerto Rico and the East Coast (i.e. Maryland), xylazine has been substituted for opioids in “speedballs” (heroin/cocaine mixtures) and may be moving west.

Gabapentin

The prescription and recreational misuse of gabapentin is becoming more common as restrictions on opioid prescription increase. This GABA_A analog is frequently co-prescribed with NSAIDs for chronic pain relief; however when combined with opioids such as heroin, it causes additive sedation and respiratory depression. Gabapentin is readily bought and sold recreationally. While it infrequently causes significant apnea when taken as a single agent, in combination with other sedative hypnotics it augments the “high” but also increases the risks of respiratory failure and resulting complications.

Kratom

This is a “natural” substance derived from the leaves of a tropical tree in Southeast Asia. Kratom contains the active ingredient *mitragynine* an opioid-receptor agonist. It is frequently available in powder form but also as raw dried leaves and is often brewed as a tea. At low doses, it gives a mild stimulant effect, however at high doses it acts on the μ receptor causing more classic opioid effects **without** profound respiratory depression. Kratom is used recreationally but is also marketed for the treatment of chronic pain disorders and to curb the symptoms of opiate withdrawal. Treatment of intoxication with Kratom is generally supportive with titrating doses of naloxone if necessary for respiratory depression or benzodiazepines for agitation. Kratom is currently a federally unscheduled substance in the US.



Marijuana Edibles

Decriminalization of marijuana has led to the burgeoning industry of cannabinoid edibles. These edibles and potables can contain high concentrations of THC and are poorly regulated. Patients unfamiliar with edible preparations do not realize that the desired “high” effect is *delayed*, so dose stacking is common resulting in an unexpected intense high. Additionally, because the edibles are frequently in the form of candies, cookies, and sugar drinks, children are ingesting them with increasing frequency. Children have unusual responses to THC overdose and can have a variety of presentations including seizures, posturing, hypotension, lethargy, coma, bradycardia, and apnea requiring mechanical ventilation.



Naloxone for the Public

Kits are now prescribed to people at high risk for opioid overdose and are readily available on the street. Your friendly local pharmacist can dispense without a prescription. REMEMBER, you may see “partial reversals” if opioids are mixed with other agents. Patients may still be intoxicated with another agent even though the respiratory depression caused by the opiate is reversed. This is not an indication to give more naloxone as the patient can still be pushed into opiate withdrawal (vomiting) while being intoxicated and sedated with a secondary agent. The naloxone kits come in 3 forms: a syringe with a nasal atomizer (2 mg), a voice actuated needle autoinjector (2 mg) or a preloaded commercial nasal atomizer (4 mg).



Laboratory testing

Many synthetic and “designer” agents **WILL NOT BE DETECTED** by standard drugs of abuse screening. Testing can be done by:

- [Beaumont-Royal Oak](#) contact Dr. Michael Smith in the toxicology laboratory 248-551-8058
- [Redwood Toxicology](#) (Santa Rosa, CA) has several panels of urine drug screens for these substances. A comprehensive GC-MS is also available. 800-255-2159
- [NMS Labs](#) 866-522-2216

PRE-HOSPITAL CONCERNS

The principal pre-hospital concerns with these agents are:

- Airway: Anticipate vomiting and aspiration before and during transport (especially with naloxone administration)
- Respiratory depression and coma
- Hyperthermia and heatstroke – initiate cooling as soon as possible
- Rhabdomyolysis and acidosis
- Dehydration and electrolyte abnormalities (hyponatremia)
- Behavioral changes leading to trauma, sexual assault and other issues

Some indications for transport to the hospital include:

- Tachycardia
- Hypotension or severe hypertension
- Hyperthermia
- CNS depression
- Delirium, agitation, or seizures
- Persistent hallucinations
- Respiratory compromise
- Persistent vomiting
- Trauma

HOSPITAL CONCERNS

1. Patients who arrive unresponsive and apneic should be ventilated with a bag-valve-mask. *Initiate small titrating doses of IV naloxone if ventilation is easily performed. Consider nasal and OP airways to assist with BVM as long as there is no evidence of facial trauma.*

NOTE: The pre-hospital administration of intranasal (IN) naloxone does not guarantee adequate absorption--**especially if several doses were administered in rapid succession**. Volumes over 1 ml given more frequently than every 5-10 minutes leads to nasopharyngeal overflow into the posterior pharynx with swallowing. Swallowed naloxone has no activity in reversing an opioid.

2. Incomplete reversal or no effect from naloxone suggests a polypharmacy overdose where an opioid and another agent were administered or hypoxic brain injury.

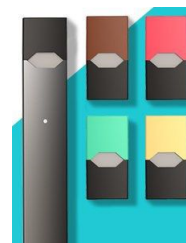
NOTE: In this case, naloxone may actually increase the likelihood aspiration as the patient withdraws without gaining awareness and ability to protect the airway. Other reasons for apparent lack of reversal with naloxone include anoxic encephalopathy and intracranial hemorrhage. These patients should be intubated regardless of whether they are “protecting their airway” since the majority (>90%) will have a significant aspiration detected later in their hospitalization.

3. Most of the newer designer drugs will not show on standard Drugs of Abuse screens. If the UDS is negative, do not be surprised.
4. In contrast to popular belief, most of the fentanyl analogs (fentalogs) including carfentanil, will respond to usual doses of naloxone.
5. We cannot confirm many of the fentalogs in the lab. If you need to try to confirm, please notify the Poison Center and we will help you find an appropriate send-out lab.
6. Please do not forget to fully assess the patients. We have seen significant **rhabdomyolysis** and **compartment syndromes** with these overdoses. Initial CKs may be negative but rise over time. Compartment syndromes have occurred in the buttocks, flanks and abdominal compartments depending upon patient position and activity prior to arrival. Peripheral neuropraxias also occur, especially from pressure effects. Remember that this is in your differential for “stroke”
7. We highly suggest obtaining lactates, ABG/VBG, and core temperatures on any ill-appearing individual. A number of these chemicals can cause a lactate-associated acidosis (Type A and B) with or without associated hyperthermia.

Specific Agents

THC

E-cigarette devices: Originally designed to deliver nicotine, these devices are effective delivery systems for synthetic cannabinoids. Their unassuming appearance allows people to use these chemicals in public places without alerting public safety officers. There is a vaporizer that exactly mimics an albuterol MDI. Additionally, liquid preparations of nicotine can be very concentrated leading to unintentional overdoses if ingested leading to agitated/ nicotinic presentations. A newer version of this is Juuling („jeweling“). The Juul is a very small vaporizer that looks like a USB drive. There have also been reports of battery explosions leading to the tragic loss of many man-buns and pants fires.



Butane Hash Oil: Also known as “Dab” or “Wax”, BHO is extracted THC from ground marijuana using butane (lighter fluid). The butane is later evaporated leaving behind concentrated hash oil. BHO is estimated to contain 60-80% THC (average 52% according to the DEA) and a drop or 2 is as potent as a joint. When combined with powdered sugar, chocolate, and Chex™ cereal, it is called “Puppy Chow”. It has also been added to Cinnamon Toast Crunch™. THC has been also found in transdermal patches and personal lubricants. E-cigarettes and vape pens can be used to smoke BHO with simple alterations.

Cannabis Hyperemesis Syndrome (CHS): Though the pathophysiology is poorly understood, patients who chronically use cannabis for years may develop this syndrome. Symptoms include nausea and vomiting with or without abdominal pain. Many will self-treat with more cannabis, which worsens the situation. Patients report improvement in symptoms with hot showers or baths but symptoms recur. Definitive treatment involves complete cessation of cannabis use. Symptomatic relief may be obtained from IV fluids, antiemetics (which may not work well), haloperidol, and capsaicin cream applied to the abdomen (don't forget to wipe it off after 30 minutes). Try to convince a marijuana user his/her vomiting is from marijuana use. Denial is no longer just a river in Egypt.

THC HOMOLOGS (*designer marijuana or cannabinoid receptor agonists/homologs*)

Herbal blends containing synthetic cannabinoid receptor agonists are extremely popular. They are sold over the Internet, in gas stations, grocery stores and in community “head shops”. Labeled ingredients include blends of herbs designed to cause relaxation, such as *Leonotis leonurus* (Wild Dagga), *Pedicularis densiflora* (Indian Warrior), or *Nymphaea nouchali var caerulea* (Blue Lotus).

Newer Cannabinoid Homologs “Trade Names”	
Bob Marley	Green Giant
Jeffery	Blue Caution
White Tiger Kush	Caution
Ah	WTF
AK-47	AK-47 24kt Gold
Hulk Purple Chronic	Hulk Ultimate
Scoobie Snax Potpurri	Next Generation Herba
Cloud 9 Mad Hatter Incense	Platinum Caution Super Strong Incense 3 rd Generation
Down 2 Earth Climaxxx	Out of this world
Fragrant Potpurri	
Skunk 101	Happy Start
Pretty Woman	Camp Climbing Chalk
Bon Air	Little Secrets Fresh Scents

First Generation THC Homologs	
Spice Silver	Space Truckin
Spice Gold	Solar Flare
Spice Diamond	Moon Rocks
Spice Arctic Synergy	Blue Lotus
Spice Tropical Synergy	Aroma
Spice Egypt	Scope
Smoke	Serenity Now
Sence	Bliss
Skunk	Blaze
Yucatan Fire	Black Mamba
Genie	Zohai
ChillX	JWH-018, -073, -250
Highdi's Almdrohner	K2, K3, K4
Earth Impact	Galaxy Gold
Gorillaz	

In recent years we have seen a decrease in the first-generation cannabinoid homologs (K2, K3, K4, Spice), and an increase in second and later generation cannabinoid homologs (AB- PINACA, AB-FUBINACA, etc.) presenting to emergency departments. These newer agents are ***much more potent*** and capable of causing significant toxicity with associated agitation and delirium. Others may cause coma, respiratory depression,

and bradycardia. In contrast, cathinone derivatives—AKA “bath salts” (mephedrone, methylene, 3,4-methylenedioxypyrovalerone, alpha-PVP [Flakka] or MDPV) are losing popularity.

Some or all of these synthetic cannabinoid homologs are sold as a pure powder to sprinkle on tobacco or other plants such as parsley or other green plant material.

Long-acting anticoagulants in synthetic cannabinoids: There were numerous reported cases in 2018 of **brodifacoum**, diphacinone, and bromodialone contamination of synthetic cannabinoids (i.e. K2/Spice). First reported in the Chicago area, cases spread throughout the Midwest (no reported cases in Michigan). These agents are long acting vitamin K antagonists similar to coumadin. There have been over 160 cases reported to the CDC since March 2018 with at least 5 deaths, however prevalence and geographic involvement seems to have tapered off. Patients presented with bleeding from multiple body sites and back pain in conjunction with an elevated INR. Poisoned patients reported use of the following synthetic cannabinoids:



- | | | |
|-------------|----------------------|---------------|
| • Mind trip | • Yellow Giant | • Kisha Coles |
| • Red Giant | • Blue Giant | • Joker |
| • OMG | • Bling Bling Monkey | • Cloud |
| • Kush | • Sexy Monkey | • Matrix |

Please call the Poison Control Center for cases of unexplained coagulopathy if you suspect this. Urine drug screens may not be positive for cannabinoids as these are often synthetic substances. Brodifacoum requires specialized testing to confirm its presence.

Presentation:

- Smoking 300 mg of an herbal blend can lead to clinical effects including red conjunctiva, tachycardia, dry mouth, and altered mood and perception. The effects persist for six hours with mild after-effects lingering through the following day.

Toxicity:

- Symptoms include agitation, confusion, hallucinations, dizziness, severe tachycardia, hypertonia, dyspnea, vomiting, panic and ECG changes.
- Some of the synthetic cannabinoids have resulted in seizures and persistent psychosis particularly in adolescents

Withdrawal:

- Symptoms include diaphoresis, tremor, palpitations, insomnia, headache, diarrhea, nausea and vomiting

Laboratory:

- THC homologs will NOT show on drugs of abuse screening. There is a **complete lack of cross-reactivity** between these designer synthetic compounds and urine immunoassays for THC (marijuana metabolites). Please see page 3 for more information on lab testing.

Treatment:

- ABC's (note increased secretions)
- Anticipate vomiting
- High dose benzodiazepines for agitation and seizures
 - There is no maximal dose of benzodiazepines
 - Double dose every 5 minutes if using diazepam and 15-20 minutes if using lorazepam (to avoid dose-stacking)
- Non-GABA acting anticonvulsants are ineffective for seizures (phenytoin, levetiracetam)
- Use a barbiturate and/or propofol if an anticonvulsant is needed
- Occasionally a neuroleptic agent may be needed, particularly when psychosis or hallucinations dominate. An ECG is recommended to screen for prolonged QTc before using a neuroleptic agent. We prefer haloperidol because of the lack of multiple receptor activation

STIMULANTS

Phenylethylamines

The phenylethylamine structure is the backbone of excitatory neurotransmitters as well as a variety of abused substances including amphetamines, “bath salts”, the 2C series, and most “designer” drugs. These drugs increase norepinephrine, dopamine, and serotonin levels. Clinical effects and treatment are similar.

Amphetamines: Both stimulants and entactogens (promotes empathy, increase the need to touch, removes fear)

Slang terms for Amphetamines

E	M&M
Ecstasy	Bean
XTC	Roll
ADAM	Love-hearts
Clarity	Doves
Essence	Icebergs
Yellow Kellys	Whizz
Hug drug	Strawberries
Lover's speed	

1. MDMA (methylenedioxymethamphetamine):
 - + LSD= "rolling and trolling", "candy-flipping"
 - + heroin = "rolling"
 - + Viagra = "hammerhead", "Sextasy"
 - + Methamphetamine = "MethX"
 - "Molly" ("the molecule") is supposed to be MDMA. However, many tablets do not contain MDMA but instead are methylone, BZP and TMFPP sometimes combined with caffeine. MDMA is increasingly being detected in combination with methamphetamine (Meth X).
 - MDMA Typical dose 75-100 mg
 - Doses are stacked on each other every 30-60 minutes
 - Onset of action: 30 minutes; duration: 3-6 hours
 - As the dose is escalated, dilated pupils, tachycardia, hypertension hallucinations, and hyperalertness develop
 - MDMA users may have uncontrollable bruxism and therefore place objects in their mouths such as glow-sticks or candy pacifiers
 - Stroking or caressing neighbors is common
2. PMA or PMMA (paramethoxyamphetamine):
 - Slang terms include: Death, Dr. Death, Superman, Mitsubishi, Double Stack
 - possibly more potent than MDMA
 - delayed onset of action relative to MDMA (90 minutes)
 - PMMA was responsible for 27 fatalities in Canada, 4 in Britain, 24 in Israel, 12 in Norway.
3. Bromo DragonFly:
 - Psychedelic
 - Often mistaken for LSD
4. N-bomb: 251-NBOMe, 25C-NBOMe, 25b-NBOMe aka "Legal acid", "Smiles", "Mr. Happy", 25
 - White powder with bitter and metallic taste
 - Snorted, blotted, or laced into food.
 - Often sold under the pretense that it is LSD
 - Single tablet may contain up to 6 effective doses
5. Methamphetamine:
 - Slang terms include: Speed, Ice, Chalk, Meth, Crystal, Crank, Fire, Glass
 - "Smurfing": going to various pharmacies to gather pseudoephedrine
 - "Tweaking": repetitive behaviors while high
 - MDEA, MDA
 - Recently, an increase in "yaba-like substances" which are tablet forms of methamphetamine combined with caffeine

The stimulant effect enables users to dance for long periods of time increasing the risk of heat stroke and dehydration which may in turn lead to rhabdomyolysis, DIC and secondary liver and renal failure

- Severe hyponatremia is not uncommon both as a direct effect of the drug and ingestion of pure water for rehydration
- Cardiovascular collapse, serotonin syndrome, seizures and intracranial bleed may occur
- Urine drug screens may be positive for amphetamines

2C Derivatives: These are purchased on the Internet as “research chemicals” (RC). The most common form is powder or homemade capsules. Slang terms are: Eternity, 2CB, 2CC, 2CI, 2CE, 2CT2, 2CT7, 2CD, 2C21, 2CP, Bees, Nexus, Bromo, CB, CID, blue mystic, trypstacy, 7-up, India, and Beautiful.

- Stimulants with hallucinogenic properties
- May be used in combination with MDMA to prolong effects
- Generally taken orally as a powder-filled capsule, but can be smoked or snorted. 2CI has been sold as a white 16 mg pill with imprint “I”
- Typical dose: 10-60 mg
- Onset of action: 30-60 minutes; duration: 3-6 hours but can be > 16 hours
- As the dose is escalated, dilated pupils, tachycardia, hypertension hallucinations, and hyper-alertness develop
- Laboratory: Urine drug screens may be positive for amphetamines

Cathinones: Herbal products sold as “Bath Salts,” “incense,” “stain remover,” “insect repellants,” “jewelry cleaner,” “phone screen cleaner,” and “plant food.”

- Cathinones are sold in small packets and are labeled “not for human consumption.” They are ingested, inhaled or injected.
- These are stimulants and usually increase the brain neurotransmitter serotonin, but also affect dopamine and norepinephrine.
- Information is available on the MDCH website along with a Health Care Provider FAQ sheet www.michigan.gov/substanceabuseepi
- Presentation
 - Patients present with sympathomimetic findings with hypertension and tachycardia plus signs and symptoms suggesting serotonin excess (hyperreflexia and clonus)
 - The clinical presentation of a newer synthetic cannabinoids and designer stimulants may be similar.
 - Agitation, tachycardia, confusion, diaphoresis, hypertension, agitation, chest pain, anxiety, motor automatisms, bruxism, sleep deprivation are common
 - Paranoia and psychotic behavior may be severe and prolonged and patients may have dysphoric hallucinations
 - Rhabdomyolysis, hyperthermia, metabolic acidosis, and liver failure may occur
 - Some like Sonic, have a prolonged duration of 3-8 hours
 - Interestingly, MDPV does not typically cause seizures but may cause a false positive PCP screen.
- Treatment
 - ABC’s (note increased secretions)
 - Anticipate vomiting
 - Benzodiazepines for agitation/seizures/rigidity.
 - High doses may be needed, there is no maximal benzodiazepine dose
 - Barbiturates or propofol may be needed for seizures
 - As with the cannabinoid homologs, phenytoin and/or levetiracetam (Keppra) will not be effective
 - Fluid resuscitation; many of these patients will be dehydrated
 - Monitor for hyperthermia, rhabdomyolysis, and acidosis
 - Aggressive external cooling
 - Psychotic behavior may require a neuroleptic agent such as haloperidol but check ECG for prolonged QTc first

Slang terms for Cathinones

Meow-Meow	Miaow miaow
Bounce	Neo doves (mephedrone)
Bubble	Sonic (MDPV)
Bubble Love	Woof woof (MDAI)
Plant food	Gravel (alphaPVP)
Drone	Flakka (alpha PVP)
NRG-1 (naphyrone)	Rave (naphyrone)
MCAT	Smokin Slurries Scrubba (alpha PVP)
White Rush	Ocean Snow
Cloud Nine	Charge Plus
Scarface	Hurricane Charlie
Red Dove	White Dove
Sextasy	White lightening
Ivory Wave	

- Consider intracranial bleed or electrolyte disturbance if the mental status is altered or seizures occur

Tryptamines

Schedule I or non-scheduled. These chemicals are derivatives of tryptamine, the endogenous precursor to serotonin. They are purchased on the Internet as “research chemicals”, with the exception of Foxy, which is Schedule I. The most common form is powder or homemade capsules, but tablets have been found. Slang terms are: Foxy, 5-MEO DIPT (5-methoxy diisopropyl tryptamine), AMT (alpha methyl tryptamine), and 5-MEO DMT (5-methoxy dimethyltryptamine).

- These agents are stimulants with hallucinogenic properties
- Foxy is generally taken orally as a powder-filled capsule or yellow, blue or tan round tablet embossed with one of many possible logos (alien, pacman, spider), typically containing 4 mg
- Other tryptamines are generally in powder form
- The typical dose is 10-20 mg
- Onset of action is 30 minutes; duration 3-6 hours
- As the dose is escalated, dilated pupils, tachycardia, hypertension hallucinations, and hyper-alertness develop
- Foxy users may demonstrate catalepsy (limbs moved by the evaluator will stay in place) with temporary inability for voluntary movement
- Stroking or caressing neighbors is common
- Laboratory: Urine drug screens may be positive for amphetamines
- Treatment:
 - ABC's
 - Aggressive cooling best performed with misting and evaporation (fans)
 - Charcoal may be considered for recent ingestions (< 60 minutes) as long as the airway is intact
 - Control of agitation/seizures with benzodiazepines/barbiturates/propofol
 - Rule out intracranial bleed in those with altered MS
 - Anticipate rhabdomyolysis and treat accordingly
 - Benzodiazepines if sedation is necessary

Piperazines

Non-scheduled. “Party pills” or “herbal highs”. Sold as “XTZ”, “COK-N”, “X-plode”. BZP is legal in Canada. BZP (benzylpiperazine): sold as Ecstasy with bull or fly logo or “Legal Cocaine herbal high”

- Amphetamine-like stimulant
- Combined with caffeine, Camelia sinensis, Oxedrine, 5HTP, and other vitamins and minerals
- Also combined with TMFPP (see below) as MDMA substitute

TMFPP- (trimethylfluorophenylpiperazine): entactogenic, like MDMA

- DEA testing of over 1400 “ecstasy” tablets purchased in Detroit revealed no MDMA, but instead, BZP and TMFPP with caffeine
- Some party pills may contain LSA
- Treatment is the same as above

Cocaine

Detroit cocaine is almost uniformly cut with unusual drugs such as levamisole (veterinary de-worming agent). Levamisole may also be used to cut heroin. There are two syndromes associated with levamisole exposures. The first is a profound neutropenia and it has been noted in users who smoked crack contaminated with levamisole. The other syndrome is a vasculitic-type rash leading to skin and deeper tissue necrosis and eventual loss of the underlying structure. Levamisole appears to affect some people and not others and toxicity has been seen in several patients in the downtown Detroit area. There have been a number of deaths reported after smoking cocaine/fentanyl mixtures. Levamisole should be suspected in a patient with unexplained neutropenia or pancytopenia or who develops a purpuric appearing “rash” particularly in appendages such as the nose,



Levamisole vasculitis
N Engl J Med 2011;
364:e52June

ears and fingers. This may be an autoimmune vasculitis and can lead to devastating disfigurement and amputations.

OPIOIDS

In addition to respiratory depression, opioids share QTc prolongation and hearing loss. Some agents may be serotonergic.

Oxymorphone

Red octagonal tablets which can be swallowed or snorted. Treatment is as for other opioids (see below).

Zohydro™ER

Introduced in March 2014, Zohydro is an extended-release formulation of hydrocodone without the addition of acetaminophen or aspirin. Zohydro contains as much as 50 mg of hydrocodone per pill. Zohydro may be crushed, chewed, dissolved, snorted and injected. It is not formulated with any features to prevent diversion.

Heroin

Detroit is seeing an increased ratio of fentanyl and fentanyl analog in “heroin” products. Some products sold as heroin contain exclusively fentanyl and analog. There is increasing market probably driven by opioid users and abusers who switch to heroin because it is cheaper and more available than prescription medications. Newer formulations make some opioids (e.g. OxyContin™) more difficult to abuse. Many of these drugs contain adulterants including quetiapine (Seroquel™), quinine, caffeine, lidocaine, levamisole or fentanyl and analog. Heroin may also be sold in capsules. Capsules may be red/white or blue/white.

W class synthetic opioids

These agents U-47700 and AH-7921 are both mu and kappa agonists and the kappa agonism may lead to dysphoria. These agents are being pressed into tablets and stamped with imprint codes referable to oxycodone. They are ultra-potent agents with onset within 30-90 minutes and duration is dependent upon route of administration. U-47700 is ~7.5x as potent as morphine. Orally, they tend to last several hours but inhaled through a vaporizer, can have extremely rapid onset and short duration. There are case reports of reversal with naloxone. Naloxone is a mu receptor antagonist only and will have no effect on the kappa response.

Tramadol

ED visits for tramadol abuse were on the rise until 2009 and has since leveled off. According to the DEA, in 2011, more than 2.5 million people used tramadol recreationally.

- In overdose, in addition to the usual opioid effects, tramadol can cause seizures including status epilepticus.
- Respiratory depression can be reversed with small incremental doses of naloxone. There is some literature to suggest that naloxone reversal may make the patient more likely to seize.
- Serotonin syndrome may be seen especially when combined with other serotonergic drugs. Patients may present with autonomic instability, altered mental status, fever, myoclonus or hyperreflexia.
- Benzodiazepines and good supportive care are first line treatment for serotonin syndrome.
- Aggressive seizure control with benzodiazepines, barbiturates, or propofol (with airway control) is recommended

Methadone

Methadone is used to treat opioid addiction and chronic pain. It has a long duration of action and recurrent toxicity should be anticipated after reversal with naloxone. A continuous naloxone infusion may be required. Methadone is a potassium channel blocker and can cause significant QTc prolongation.

Buprenorphine

Buprenorphine is a partial opioid agonist and is manufactured in a number of formulations including soluble sublingual films or tablets, pills, and injectable solutions +/- naloxone. It is primarily used to treat opioid addiction but is gaining use as an opioid analgesic. Buprenorphine can induce withdrawal in people with recent use of a full opioid agonist. Naloxone can reverse respiratory depression but onset of reversal is slower and higher doses may be needed. Buprenorphine is sold under the trade names Subutex™, Suboxone™, Zubsolv™, Temgesic™, Buprenex™, Belbuca™, or as a transdermal patch. Pediatric ingestions are particularly lethal with delayed respiratory failure 16-24 hours after ingestion.

Fentanyl

Fentanyl is an analgesic with a potency of about 80 times that of morphine. Related drugs include alfentanil (Alfenta®), an ultra-short acting analgesic, and sufentanil (Sufenta®), an exceptionally potent analgesic, 5 to 10 times more potent than fentanyl. Over 12 different analogs of fentanyl (fentalogs) have been produced in clandestine laboratories in the US. Acetylfentanyl, acrylfentanyl, and furanylfentanyl are some of the fentalogs seen in Michigan.

Fentanyl can be injected, snorted or smoked, absorbed transdermally or transbuccally. The liquid form of the transdermal patch can be chewed. The matrix form of the transdermal patch can be cut into squares and chewed or inserted into body cavities (rectal "Chicklets"). The transdermal patch liquid can be extracted and injected IV or boiled, dried and smoked. It has been referred to as "Bud Ice", "Theraflu", and "Income Tax".

Carfentanil

Carfentanil was originally used as a large mammal tranquilizer. It is a highly potent heroin substitute or replacement. Its relative strength is approximately 10,000x equivalent doses of morphine and can result in respiratory arrest, even in experienced users. It was prevalent in 2016, but has since been replaced by fentanyl and other analog. The enhanced potency had led to a concern that contact with this agent during resuscitation can be deadly but unlikely unless inhaled. Universal precautions and avoidance of powder inhalation should be adequate to protect first responders.

Kratom

This is a "natural substance" and comes from a tree native to southeast Asia. It goes by the names "herbal Speedball", "biak-biak", "ketum", "Kahuam", "Ithang", and "Thom". The leaves can be chewed or made into a tea. It can also be found in a powder form. The active ingredients are mitragynine and 7-hydroxymitragynine which have weak opioid and serotonergic activity leading to the substance described as both a stimulant AND an opioid. A 2016 publication reported that commercial kratom was spiked with much higher levels of the potent 7-hydroxymitragynine alkaloid (17X more potent than morphine). Treatment is generally supportive with titrating doses of naloxone for respiratory depression. Currently, kratom is legal in Michigan and sold without restrictions to anyone over 18 years old in many smoke shops so it is considered easily accessible.

Loperamide

The over-the-counter antidiarrheal, loperamide is being used in two ways, either as self-treatment for opioid withdrawal and as a drug of abuse itself. Loperamide normally does not pass the gut and is locally metabolized. However, at very large doses, the p-glycoprotein system which normally keeps it in check, is overwhelmed and loperamide can pass through the blood-brain-barrier to the central reward centers. Doses of 100-200 mg/day are commonly reported. At these doses, loperamide is extremely cardiotoxic. Both QRS, QTc prolongation have been noted with subsequent ventricular dysrhythmias and Torsades de Pointes. Treatment is supportive. While appropriate history may not be obtainable, patients may show both widened QRS requiring sodium bicarbonate and widened QTc requiring magnesium and potassium optimization at the same time. A number of patients have required repeat cardioversion over days. Patients may have prolonged periods of toxicity lasting 5-7 days. Overdrive pacing or isoproterenol have been the most effective therapies in case series. Amiodarone is not recommended because of its potassium blocking effect.

Krokodil

Desomorphine is a morphine derivative that is popular in Russia but has never been confirmed in the U.S.A. It is synthesized from codeine using hydrocarbons, iodine, HCl, alcohol, and red phosphorus. The included solvents and by-products of synthesis remain in the extract and are injected causing local tissue damage. The resulting disfigurement has led to Krokodil's nickname as the "flesh-eating drug." It is reportedly up to 10X more potent than morphine.

Treatment of opioid toxicity

Unique characteristics and treatment are covered under the specific agents.

- Opioid toxicity classically presents with CNS depression, respiratory depression and miosis
- Incremental small repeated doses of naloxone are preferred to single large doses
 - **In cases of severe respiratory depression or apnea, patients should first be well ventilated by BVM before reversal**
 - Rapid reversal from severe respiratory depression may lead to agitation, vomiting, aspiration, with prolonged ICU stay
- Higher doses of naloxone may be required with the ultrapotent designer opioids BUT ALL SUSPECTED OPIOID TOXIC PATIENTS SHOULD BE STARTED WITH LOWER DOSES OF NALOXONE. Naloxone is only indicated for respiratory depression.
 - Longer-acting opioids may require a naloxone infusion (e.g. methadone) or intubation
 - Patients who are intubated do not require a naloxone infusion
 - **Patients who overdose on buprenorphine may take longer to respond to naloxone**
- Incomplete responses to naloxone may indicate co-ingestion of a non-opioid drug or anoxic encephalopathy. Airway protection and intubation may be the preferred way to proceed
 - Most of these patients will vomit after naloxone
- Many of the synthetic opioids are not detected on routine drug screens and thus diagnosis will be clinical
- Co-ingestions are common and should be identified and treated accordingly (e.g. APAP toxicity)

GABA-B AGONISTS

Gammahydroxybutyrate (GHB)

GHB is a Schedule I drug, likely to be sold as a clear solution in small shampoo, hand lotion, or mouth wash bottles (typically one ounce) or carried in mineral water bottles. It may be used in drug-facilitated sexual assault. The taste is described as salty or soapy. It has a very short half-life.

- Symptom onset within 15 minutes of ingestion
 - Initially the patient may exhibit aggression (especially in response to direct gaze) and impaired judgment
 - Dizziness, lightheadedness, "high feeling", hallucinations, confusion, ataxia, loss of peripheral vision
 - Nausea & vomiting, possibly excessive salivation
 - Abrupt unconsciousness with intermittent respiratory depression and apnea
 - Random clonic movements of face and extremities
 - Pupils may be constricted or dilated, hypothermia or bradycardia are seen with severe cases

Slang terms for GHB	
GBH	Soap
Grievous Bodily Harm	Scoop
Easy Lay	Salty water
Georgia Home Boy	G-Riffick
Oxy-Sleep	Gamma-OH
Somatomax	Gamma hydrate
Somasanit	4-hydroxybutyrate
Alcover	Anetamin
Zonked	Special K lude
Liquid Ecstasy	Cherry Meth
Liquid X	Organic Quaalude
Liquid E	Natural Sleep-500

- Laboratory: GHB levels will not be useful in OD settings and require specialized lab testing
 - Drug screens may reveal co-ingestants
- Treatment:
 - Stabilization: ABC's
 - Anticipate vomiting
 - Naloxone, thiamine, glucose
 - Flumazenil does not effectively reverse effects from GHB

- No need for GI decontamination
- Atropine for bradycardia if hemodynamically significant
- Very cautious administration of benzodiazepines for severe agitation or seizure-like activity but the respiratory depressant effects are additive
- Patients may require intubation but frequently self-extubate within 6 hours

GHB-Like Agents

These products are sold in health food stores, sports nutrition stores and on the Internet, as “registered chemicals.” Clinically, the presentation and management are identical to GHB.

GBL (gammabutyrolactone)

- Slang and trade names: Renewtrient, Regenerize, Invigorate, Revivarent G, Blue Nitro, Blue Nitro Vitality, GH Revitalizer, Gamma G, Remforce, Firewater, ReActive, Rest-Eze, Beta-Tech, Thunder, Jolt, Verve. Recently being sold as CleanStar 24” Wheel Cleaner

BD (1,4-butanediol)

- Slang terms and trade names: Pine Needle Oil, Natural Borametz Extract, Biocopia, Zen, Serenity, SomatoPro, Inner G, NRG3, Enliven, Growth Hormone Release Extract, Thunder Nectar, Weight Belt Cleaner, Rest-Q, X-12, Dormir, Amino Flex, Orange fX, Rush, Lemon fX Drop, Cherry fX Bomb, Promusol, BVM.

NMDA ANTAGONISTS

Ketamine

This is a Schedule III anesthetic agent (Ketalar® and other products) that is diverted from legitimate human or veterinary use. It is available as clear liquid that is usually dried and then sold in small Ziploc bags, paper folds, foils, vials or capsules. The powder is then snorted, put into drinks, injected or smoked. Slang terms include: K, Special K, Green, Jet, Kay, Mauve, Purple, Special LA Coke, Super acid, Super C, Cat Valiums

- Onset of symptoms is 1-10 minutes after use. Effects last 2 to 3 hours.
 - Transiently increased blood pressure and heart rate
 - Dose dependent respiratory depression
 - Nystagmus
 - Cataleptic state
 - Hypertonicity, vocalizations, dystonic reactions
 - Increased secretions and salivation
 - State of dissociation: loss of awareness of environment
 - Mellow, colorful hallucinations, sense of immobility and being transported through space = “K-land”
 - Near-death experience, paralysis = “K-hole”
 - Seizures, respiratory arrest, cardiac arrest following high doses
 - Amnesia for 1-2 hours after use
 - Akinetic mutism has been observed in children
- Dissociated patients may not be aware of severe injuries such as fractures or lacerations
- Treatment is supportive
 - Place in quiet room with trip sitter
 - Excessive salivation can be treated with glycopyrrolate
 - High doses of sedating medications may be required
 - We recommend benzodiazepines but patients may require the addition of a neuroleptic agent if severely out of control

Esketamine

This was recently approved as nasal spray for depression (Spravato) but is only supposed to be used under very restricted conditions. There is no overdose data available but would treat it as ketamine.

Methoxetamine

This a “research chemical product”. It is sold under the names “MXE”, “M-Ket”, “Kmax”, “Minx”, “Jipper”, “Roflcopter”, or “Mexxy.” Similar to bath salts and synthetic cannabinoids, packaging is labeled as “not for

human consumption". It is sold as a white powder and either ingested as a capsule or snorted. It is currently unscheduled. Effects are first noted 10-15 minutes but can be delayed up to 60-90 minutes after use. This delay may cause the user to "double-dose" and increases the chance of toxicity. Severe reversible cerebellar ataxia was described in one case series.

- Laboratory: Ketamine is not detected on routine drug screening and will not cross-react with PCP
- Treatment:
 - ABC's with drooling
 - Anticipate vomiting
 - Benzodiazepines for panic reactions or severe agitation
 - Diphenhydramine has reversed dystonia
 - No role for GI decontamination
 - Placement in a quiet location, the presence of "trip sitter" may be helpful
 - External cooling may be needed
 - Evaluate for associated injuries

Dextromethorphan

Non-scheduled and commonly found in many over-the-counter cold and cough preparations. Effects are LSD-like and include dissociation, hallucinations, vivid dreams, tachycardia, hypertension, vomiting and choreoathetosis. There is possibly synergy with MDMA. Slang terms include: DXM, Dex, Robo, Tussin, CCC, Red Devils, High C, TM, skittles, blue velvet (combined with nitrous)

- Coricidin HBP Cough & Cold
 - Dosing: 300 mg to 900 mg (8 to 24 Coricidin tablets); half-life 2- 4 hours
 - Users dose to reach a "plateau". There are 5 plateaus and there are apps online to tell users how many pills they need to reach each level (www.dextroverse.org)
 - NOTE: Coricidin HBP Cold & FluTM contains acetaminophen and laboratory evaluation for APAP is required in the dosages used for abuse.
 - Coricidin formulations also contain chlorpheniramine so patients can present with anticholinergic signs.
- Laboratory: DXM may cross-react with phencyclidine (PCP) on some urine screens
- Treatment:
 - Airway and supportive care
 - Naloxone reversal of DXM effect is variable
 - Cooling and benzodiazepines for agitation related to chlorpheniramine

Methoxphenidine (MXP)

This is a designer stimulant similar to PCP, MXE, DXM and ketamine sold as a "research chemical" and "not for human consumption". Presenting symptoms may include: confusion, echolalia, hypertension, tachycardia, nystagmus, miosis.

INHALANTS

Nitrous Oxide

Nitrous oxide abuse poses a unique ability to oxidize cobalt in the B12 molecule and can lead to functional B12 deficiency. Typically sold as balloons or as whippets. Patients with long term abuse can present with gait disturbance and peripheral neuropathy. Slang: Laughing gas, buzz bomb, shoot the breeze, N2O, N2X

Other Inhalants (Dust Off and Axe Deodorant)

Rapid CNS effects occur with use: initial disinhibition followed by inebriation, dizziness, vertigo, drowsiness or in severe cases, coma. Hypoxemia may result in uncontrolled twitching while unconscious, coined by users as "going fishing". Lip and upper airway injuries may be seen as the gas rapidly expands, freezing local tissue. **Ventricular dysrhythmias** (classically while running or surprised) and respiratory depression may be seen

- Treatment:
 - ABC's

- 100% oxygen
- **Cardiac monitoring**
- Keep victim calm
- Anticipate coma, seizures, dysrhythmias
- Avoid epinephrine or other sympathomimetics if possible, unless cardiac arrest
- Consider esmolol or other beta blocker for tachydysrhythmias
- Consider bypass for intractable dysrhythmias

OTHER HALLUCINOGENS

Other Hallucinogenic Agents (mescaline, psilocybe mushrooms, or LSD)

Most commonly, abusers present with hallucinations and signs of catecholamine excess (tachycardia, hypertension, dilated pupils, sweating). Treatment is supportive (calm environment, reassurance) however benzodiazepines may be used in the agitated patient. A “trip sitter” may be all that is necessary to keep a person calm. There is no role for GI decontamination with LSD (minute quantities are typically involved). Charcoal may be administered for recent mescaline or mushroom ingestions.

Amanita muscaria (mushroom)

This bright orange or tan colored mushroom is non-scheduled and not truly hallucinogenic. It is purchased freeze-dried from the Internet and is available as either intact mushroom caps or concentrated extract. It is usually ingested as a cold tea. Patients often show a biphasic presentation with initial hallucinations, excitability, myoclonus, followed by CNS depression. Patients may not have respiratory depression. They can be bradycardic with large doses. Onset of action is 30-90 minutes; peak 2-3 hours; duration 12 hours. Not detected on routine urine drug screens. Treatment includes stabilization of ABCs and benzodiazepines to control agitation and myoclonus.

BENZODIAZEPINES

Xanax

Abuse of Xanax (alprazolam) is on the rise in children and young adults, often in combination with alcohol or other depressants. Admissions for benzodiazepine withdrawal treatment doubled from 2015-2016 in Wayne County. In 2016, it was the 4th most commonly seized drug in metro Detroit. Older adults use it as a “downer” after binging on cocaine or other stimulants. “Trinity” is the combination of Xanax (alprazolam), Vicodin/Norco or other opioid (hydrocodone), and Soma (carisoprodol). Xanax is ingested or crushed and snorted. Symptom onset is rapid with a half-life of approximately 12 hours. Urine drug screens may not be positive for benzodiazepines given the low concentrations of the metabolite typically found in the urine. Since 2015, some counterfeit “Xanax” bars have contained fentanyl so be on the alert for atypical presentations of so called benzodiazepines.

- Slang:
 - 2-mg white rectangle-shaped tablets: Xanax Bars, Xany Bars, Coffins, French Fries, Totem Poles, Candy Bars, Yellow Ladders
 - 1-mg lavender-colored tablets: Footballs or Blues
 - Xanax Blotter Paper (“Xanax” inside a tablet shape repeatedly printed on the paper)
- Treatment
 - Stabilization: ABC’s
 - Anticipate vomiting
 - Naloxone, thiamine, glucose potentially for coingestants
 - **Avoid flumazenil** given the potential for use in combination with other drugs or drug tolerance with rapid precipitated withdrawal (seizures) and dysrhythmias
 - No need for GI decontamination

Etizolam

Non-US approved benzodiazepine found in some counterfeit alprazolam tablets ("bars"). Cases of this have been on the rise. It is a very potent benzodiazepine and has led to cases of respiratory depression. Treatment is supportive.

MISCELLANEOUS**Sizzurp**

This is a liquid mixture of Phenergan (Promethazine) with or without codeine mixed into soda, usually a lemon-lime flavor and a Jolly Rancher is added for flavor. Dextromethorphan may be substituted if codeine is not available. It is also known as "Drank" or "Purple Drank" related to the color of the liquid. It is also known as "drank", "barre", "purple jelly", "Texas Tea", or "Tsikuni". Toxicity is predominantly respiratory and CNS depression.

Relaxation Drinks & Brownies

These are foods and drinks laced with up to 8 mg of melatonin and valerian root and are labeled as a "dietary supplement". They may contain *kava kava*. Toxicity primarily manifests as CNS depression and treatment is supportive.

Slang: Slowtivate, Un'Ergy, Lazy Cakes, Marley's Mellow Mood, Sippin Syrup, Mary Jane Relaxation Soda, Unwind

Lemon Drop

Created by mixing hydrocarbon-based solvents with over-the-counter medications containing dextromethorphan. The mixture is heated to extract the DXM and then mixed with lemon juice or powdered lemonade.

Tropane Alkaloids

Examples include Jimsonweed and Angel's trumpet. Toxicity is mainly antimuscarinic delirium and treatment is supportive with benzodiazepines and possibly physostigmine if conditions are appropriate.

Salvia Divinorum

Sold as "Sally D", "Salvinorin A", "Diviner's Sage", "Mystic Sage", "Purple Sticky", "Magic Mint", it is an herb in the mint family. It has been popularized in the media on Tosh.0 and YouTube, Salvia Divinorum is a potent kappa opioid agonist. It is mostly smoked but can be chewed as well and causes perceptual distortion, uncontrollable laughter, incoordination, hallucinations, and dysphoria. Effects are generally short-lived and treatment is supportive.

**Many of these agents are now reportable.
For further information or to report a case, please contact the
Michigan Regional Poison Control Center**

**The Poison Center is the designated provider of surveillance for the
Michigan Department of Health and Human Services**

Thank You

**313-745-5711
or
1-800-222-1222**