Michigan Regional Poison Control Center at Children's Hospital of Michigan Health Alert:

Movement 2017: Detroit's Electronic Music Festival

May 27-29, 2017

The 11th annual Movement Electronic Music Festival is scheduled Memorial Day weekend, May 27th through 29th, at Hart Plaza. Over 100,000 participants from around the globe attended last year and a similar number are expected to attend the "Rave" or "Techno" gathering this year. The Chevrolet Belle Island Grand Prix will be June 2-4 on Belle Island. Other festivals include the Lakes of Fire (Rothbury) June 14-18, Electric Forest in Rothbury June 22-25 and June 29-July 2, Detroit River Days June 23-25, Common Ground in Lansing July 6-9, Faster Horses, and Mo Pop in July and the Hoedown in Detroit June 30 and others I did not include. All these festivals bring thousands of visitors to Michigan with emphasis on the big cities. This update highlights the drugs-of-abuse most likely to be encountered by pre-hospital or hospital providers. The discussion includes keys to the recognition and management of toxicity resulting from these substances.

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

As observed in previous years, these events provide a Michigan foothold for the less frequently observed and more regionally esoteric compounds including: gammahydroxybutyrate (GHB), gammabutyrolactone (GBL), butanediol (BD), ketamine, sympathomimetics and hallucinogenic sympathomimetics (methamphetamine, MDMA, MDEA, PMA, PMMA, ephedrine), piperazines, nitrous oxide, inhalants, and other hallucinogens, such as mushrooms or LSD. 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 iteration of agents seem to be much more potent and capable of causing significant toxicity with associated agitation and delirium. In contrast, cathinone derivatives—AKA "bath salts" (mephedrone, methylone, 3,4-methylenedioxypyrovalerone, alpha-PVP [Flakka] or MDPV) are losing popularity. Surprisingly, we have also noted 3-methoxyphencyclidine, a PCP analog recently.

Over the past 18 months, synthetic opioids have appeared in Michigan and have rapidly gained notoriety. These are agents that are highly potent and have been responsible for confirmed deaths in unsuspecting users. Agents such as carfentanil, acetyl fentanyl, acrylfentanyl, furanylfentanyl, and the W class opioids (U-477000 aka "u-4") are either cut into heroin or are being combined into tablets and

http://www .dea.gov/p r/microgra ms/2006/m g0106.pdf







U-477000 "oxycodone" tablets 16-225 BUL-SA NEORFC FSAB U-47700.pdf

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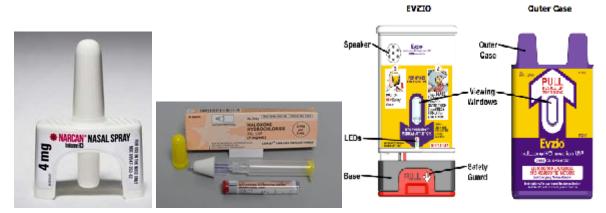
800-222-1222

substituted for oxycodone and hydrocodone tablets complete with appropriate imprint codes. Xanax™ tablets (alprazolam) have also been found to contain fentanyls. Heroin and the other usual opioids are always popular so expect to see opioid-related respiratory depression and death reflecting the increased purity of heroin or adulterated heroin. Cocaine and opioid combinations should be considered if patients do not have a clearcut toxidrome. Additionally, cocaine and heroin continue to be cut with **levamisole**, a veterinary antihelminth. 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, ears and fingers. This may be an autoimmune vasculitis and can lead to devastating disfiguration and amputations.



Levamisole vasculitisvasculitis N Engl J Med 2011; 364:e52June

Expect to see more naloxone readily available on the street. Naloxone kits are now prescribed to people at high risk for opioid overdose. You may see partial reversals if people are mixing their opioids with other agents. The naloxone kits come in 3 forms: a syringe with a nasal atomizer (2 mg/2ml), a voice actuated needle autoinjector (2 mg/0.4 ml) or a preloaded commercial nasal atomizer (4 mg/0.1 ml).



Etizolam, a benzodiazepine not US approved, has been found in some counterfeit alprazolam tablets ("bars"). Etizolam is a very potent benzodiazepine and has led to cases of respiratory depression



https://www.linkedin.co m/pulse/counterfeitstreet-drugs-up-datebruce-talbot

Both LSD and PCP have been recently confirmed in the Detroit area.



"Sizzurp" or Purple Drank (Phenergan <u>+</u> codeine mixed with lemon-lime soda, sometimes with a Jolly Rancher candy) may be present.

With the advent of "energy drinks", products specifically designed to de-energize (Slowtivate, Un'ergy, and Lazy Cakes) have emerged.

Ethanol-related issues remain at a high level and are frequently mixed with other medications.

PRE-HOSPITAL CONCERNS:

The principal pre-hospital concerns with these agents are:

- 1. Airway
 - a. Anticipate vomiting and aspiration before and during transport
 - b. This is especially common with naloxone administration
- 2. Respiratory depression and coma
- 3. Hyperthermia and heatstroke; initiate cooling as soon as possible
- 4. Rhabdomyolysis and acidosis
- 5. Dehydration and electrolyte abnormalities
- 6. Sequelae of behaviors which lead to trauma, sexual assault and other issues

Transport to the hospital should be considered in those with:

- 1. Incomplete reversal with naloxone
- 2. Tachycardia
- 3. Hypotension or poorly controlled hypertension
- 4. Hyperthermia
- 5. CNS depression
- 6. Delirium, agitation, or seizures
- 7. Persistent hallucinations
- 8. Persistent vomiting

Hospital Concerns

- 1. Patients who arrive unresponsive and apneic should be initially ventilated with a bag-valve-mask Even if they failed on scene intranasal naloxone, they may still respond to small doses of IV naloxone. The pre-hospital administration of IN naloxone does not guarantee adequate absorption especially if several doses were administered in rapid succession. Volumes over 1 ml (as found in the naloxone intranasal) given more frequently than every 5-10 minutes leads to nasopharyngeal overflow into the posterior pharynx followed by swallowing. Swallowed naloxone has no activity in reversing an opioid.
- 2. Incomplete reversal or no effect from naloxone suggests a polypharmacy overdose suggesting an opioid and another agent were administered. In this case, naloxone may actually enhance aspiration as the patient withdraws without gaining awareness and ability to protect the airway. The other major reason for patients not reversing with naloxone is anoxic encephalopathy. These patient 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. This goes for all drug classes.
- 4. Regardless of popular literature, most of the fentanyl analogs (fentalogs) including carfentanil, will respond to 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 are seeing severe rhabdomyolysis and compartment syndromes with these overdoses. Initial CKs may be negative but rise later over time. Compartment syndromes have occurred in the buttocks, flanks and abdominal compartments depending upon patient position. We have also seen peripheral neuropraxias especially from pressure effects



7. We highly suggest getting lactates, ABG/VBG, and core temperatures on these patients. A number of these chemicals have multifactorial effects on mitochondria and create high levels of lactate (Type A and B) with or without associated hyperthermia.

REVERSAL AGENTS:

1. Flumazenil

- a. There are a number of benzodiazepines used and abused by the public including etiozolam, clonazepam, flunitrazepam/nitrazepam, and alprazolam.
 - i. Pure benzodiazepine ingestion rarely cause apnea. Polypharmacy ingestions including ethanol however, are a different situation and can lead to apnea.
 - ii. We do not recommend the use of flumazenil in these patients unless the person is known to be benzodiazepine-naïve such a child without a seizure disorder. Patients who are benzodiazepine-dependent are at high risk for benzodiazepine withdrawal with seizures and status epilepticus
 - iii. If you do use flumazenil, dose it in small increments (0.05-0.1 mg IV) while supporting respirations with at least 2 minutes between doses
 - If seizures or status epilepticus do occur, since flumazenil is a competitive antagonist, it can be overridden with large doses of benzodiazepines such as 2-4 mg lorazepam or 10 mg diazepam. Intubation will be necessary in this situation

2. Naloxone

- a. Naloxone dosing is subject to great discussion and strong opinions. Naloxone is a competitive mu receptor antagonist and reverses respiratory depression. Its affinity for the receptor is extremely high and it preferentially binds the mu receptor displacing other opioids. Opioid displacement is not simple and multiple factors are involved including pharmacokinetics, pharmacodynamics, dose, genetics, and other factors. It will displace fentanyl and buprenorphine but buprenorphine may require higher doses and there is a bell shaped curve whereas additional naloxone (>4-6 mg) is counterproductive.
- b. Sudden reversal without oxygenation especially in the face of high endogenous catecholamines, significantly increases the risk of non-cardiogenic pulmonary edema. Or, it may be that naloxone uncovers the non-cardiogenic pulmonary edema that was there while the patient was breathing against a closed glottis. The etiology of pulmonary edema remains unclear. Patients should be oxygenated and ventilated initially before reversal
- c. Dosing is dependent upon route:
 - i. Intravenous dosing should always start with small titratable doses such as 0.01-0.4 mg even if designer drugs are suspected. Intravenous dosing can be repeated every 1-2 minutes until desired effect while providing ventilation with a BVM. Ventilation is improved by the use of airway adjuncts including nasopharyngeal and oral devices.
 - ii. There is no rationale for mg/kg naloxone dosing for pediatric patients. The naloxone dose is based on number of occupied receptors which has nothing to do with weight.
 - iii. Intranasal dosing is subject to the dose in the delivery system. These range from 2 mg/2 ml (naloxone intranasal) and 2-4 mg/0.1 ml (Narcan™ intranasal). Ideally, each nasal vestibule only holds 0.1 ml and any extra volume spills into the nasopharynx leading to swallowing the additional naloxone. So unless the Narcan™ intranasal system is used, the full 1-2 mg of naloxone is not being absorbed. Because of this, there is the perception that the patient required much more naloxone to have an effect (and presumption that it is a fentalog) when in reality, the patient is getting very little of the original dose. Nonresponse to intranasal naloxone should not preclude starting with small intravenous naloxone doses once an IV line is established



- iv. IM naloxone is well absorbed but peak effect is delayed.
- v. Failure to respond to IV naloxone suggests either anoxic encephalopathy or polypharmacy.

Specific Agents

THC and Homologs (Designer Marijuana or cannabinoid receptor agonists/homologs)

Herbal blends containing cannabinoid receptor agonists are extremely popular. They are sold over the Internet, in gas stations or groceries and in community "head shops". Trade names include "Spice Silver", "Spice Gold", "Spice Diamond", "Spice Arctic Synergy", "Spice Tropical Synergy", "Spice Egypt", "Smoke", "Sence", "Skunk", "Yucatan Fire", "Genie", "ChillX", "Highdi's Almdrohner", "Earth Impact", "Gorillaz", "Galaxy Gold", "Space Truckin", "Solar Flare", "Moon Rocks", "Blue Lotus", "Aroma", "Scope", "Serenity Now", "Bliss", "Blaze", "Black Mamba", "Zohai", "JWH-018, 073, and -250", and K2, K3, and K4. Labeled ingredients include blends of herbs designed to cause relaxation, such as *Leonotis leonurus* (Wild Dagga), *Pedicularis densiflor* (Indian Warrior), or *Nymphaea nouchali var caerulea* (Blue Lotus).

The newer cannabinoid homologs: AB-FUBINACA, AMB-FUBINACA, ADB-PINACA, MAB-CHMINACA, MDMB-CHMICA and AB-CHMINACA and others are responsible for a recent large spike in ED visits. Some brand names include: "Bob Marley", "Jeffrey", "Green Giant", "Blue Caution", "White Tiger Kush", "Caution", "Ah", "WTF", "AK-47", "AK-47 24 Karat Gold", "Hulk Purple Chronic", "Hulk Ultimate", "Black Diamond", "Scoobie Snax Potpourri", "Next Generation Herba", "Cloud 9 Mad Hatter Incense", "Platium Caution Super Strong Incense 3rd Generation", "Down 2 Earth Climaxxx Fragrant Potpourri", "Out of this World", "Skunk 101", "Happy Start", "Pretty Woman", "Camp Climbing Chalk", "Bon Air", and "Little Secrets Fresh Scents."

You may remember the "Zombie" outbreak in New York in July 2016. The subsequent paper found in the New England Journal described the clinical effects of one of the 33 people taken to local hospitals:

"The clinical features in this outbreak were typified by the index patient, a man who was 28 years of age and described by EMS providers as being slow to respond to questioning and having a 'blank stare.' He had intermittent periods of 'zombielike' groaning and slow mechanical movements of the arms and legs."

E-cigarette devices originally designed to deliver nicotine, are effective delivery devices 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.

THC is widely available mixed into various foods and candies and are indistinguishable from non-adulterated foods. Children and pets appear to have an exaggerated response to eating these items and may present with altered mental status, ataxia, confusion, tremors and akinetic mutism.

Butane Hash Oil: Also known as "Dabs" 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 60-90% THC (average 52% according to the DEA) and a drop or two 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.

A brief handout for health care workers on these agents is available on the www.mitoxic.org website under Physicians and Health Professionals then listed as Synthetic marijuana fact sheet



(http://www.childrensdmc.org/upload/docs/Drug%20Abuse/03-19-12%20Updated Synthetic%20Marijuana HCPFactSheet.pdf.

A separate handout for the lay public is found at:

http://www.michigan.gov/documents/mdch/K2 Spice - General Fact Sheet 4.30.12 384319 7.pdf

- 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.
- Powder or liquid formulations may be used in combination with an E-cigarette device.

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 persisted for six hours with mild after-effects lingering through the following day.

Toxicity:

- Symptoms included 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:

- These 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). If you need to test for these compounds, the labs below can pick up some of them:
 - Beaumont-Royal Oak. The samples should be sent to Michael Smith in their Toxicology Lab 248-551-8058. Please call them with notification before sending
 - NMS Labs (866-522-2216) has several synthetic cannabinoid panels which detect many
 of the synthetic cannabinoids. The lab runs active surveillance on these compounds

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)
- Treat seizures with benzodiazepines or propofol
- Non-GABA acting anticonvulsants are ineffective (phenytoin, levetriacetam)
- 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
- Withdrawal should be treated with high-dose benzodiazepines or barbiturates

Cannabis Hyperemesis Syndrome (CHS)

People who have chronically used cannabis for years may develop this syndrome whose pathophysiology is poorly understood. Patients have nausea and vomiting with or without abdominal pain. Many will self-treat with more cannabis which worsens the situation. Patients feel better if they take hot showers or baths but the symptoms recur. Definitive treatment involves stopping cannabis



use completely. Symptomatic relief may be obtained from IV fluids, antiemetics (which may not work well), haloperidol, and capsaicin cream applied to the abdomen.

STIMULANTS

I. Phenylethylamines: The phenylethylamine structure is the backbone of epinephrine, norepinephrine, and dopamine as well as a variety of abused substances including all amphetamines, "bath salts", the 2C series, and most "designer" drugs. In general, phenylethylamines increase norepinephrine, dopamine, and serotonin levels. Clinical effects and treatment are similar.

A. Amphetamines:

1. MDMA (methylenedioxymethamphetamine):

Slang terms include: E, Ecstasy, XTC, Adam, Clarity, Essence, Lover's Speed, M&M, bean, roll, love-hearts, doves, icebergs, strawberries, yellow kellys, hug drug, whizz

- combined with LSD= "rolling and trolling", "candy-flipping"
- combined with heroin = "rolling"
- combined with Viagra = "hammerhead", "Sextasy"
- combined with Methamphetamine = "MethX"
- These agents are both stimulants (enables users to dance for extended periods) and entactogens (promotes empathy, increase the need to touch, removes fear)
- "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 is generally taken orally as a white/off-white/tan tablet, embossed with one of many possible logos (four-leaf clover, the Mitsubishi logo, TNT, omega, bird, butterfly symbol to name only a few; numbers are generally absent from the tablets)
 - The typical dose is 75-100 mg and multiple doses
 - Doses are stacked on each other every 30-60 minutes
 - Onset of action is 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
- N-bomb: 251-NBOMe, 25C-NBOMe, 25b-NBOMe. aka "Legal acid", "Smiles", "Mr. Happy" or 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
- 6. The stimulant effect enable 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
 - Laboratory:
 Urine drug screens may be positive for amphetamines
- B. 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.
 - These agents are stimulants with hallucinogenic properties
 - They 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"
 - The typical dose is 10-60 mg
 - Onset of action is 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 amphetamine

C. 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 not intended for use in bathwater and are ingested, inhaled, or injected.
 - None of these chemicals are covered by the federal Controlled Substance Act, although mephedrone, methylone, and MDPV are scheduled drugs in Michigan with legislation proposed to include others as Schedule I controlled substances.
 - These chemicals 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.

- Slang terms include:
 - "meow-meow", "bounce", "bubble", "bubble love", "plant food", "drone", "MCAT", "miaow miaow", and "Neo Doves" = [mephedrone (4-methylmethcathinone)]
 - o "sonic" = [methylenedioxypyrovalerone (MDPV)]
 - o (MPBP)[40394]
 - "woof-woof" = 5,6-Methylenedioxy-2-aminoindane (MDAI)
 - o "rave", "NRG-1" = [naphyrone (Naphthylpyrovalerone)]
 - o "Gravel", "Flakka", "Smokin Slurries Scrubba" = alpha PVP
 - There have been a number of cases in Florida
 - A man stood with a handgun on an apartment building roof yelling "I feel delusional and I'm hallucinating"
 - A man thought he was being chased by an automobile so he kicked in the front door of a local police station
 - A man impaled himself on a spiked fence during a hallucination



800-222-1222

- White Rush, Cloud Nine, Ivory Wave, Ocean Snow, Charge Plus, White Lightning, Scarface, Hurricane Charlie, Red Dove, White Dove, and Sextasy
- 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 cannabinoid and designer stimulant 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
 - o Rhabdomyolysis, hyperthermia, metabolic acidosis, and liver failure may occur
 - o Some like Sonic, have a prolonged duration of 3-8 hours
 - o Interestingly, MDPV does not typically cause seizures
 - o MDPV may cause false positive PCP screen

Phenylethylamine 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 or ziprasidone but check ECG for prolonged QTc
- Consider intracranial bleed or electrolyte disturbance if the mental status is altered or seizures occur
- Laboratory testing: these agents WILL NOT BE detected by standard drugs of abuse screening.
 Testing (send out) can be done by:
 - Beaumont-Royal Oak. Please contact Michael Smith in their 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.
 - 1. Expanded designer stimulant panel
 - 2. MDVP and mephedrone

800-255-2159

- NMS Labs can determine mephedrone and MDPV and has an expanded cathinone panel (866-522-2216) in blood (serum/plasma) and urine
- **II. 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
- III. **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 sinesis, 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
- **IV.** <u>Cocaine</u>: Detroit cocaine is often contaminated with unusual drugs such as levamisole (veterinary worming agent. 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 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

OPIOIDS

- <u>I. Oxymorphone ("stop signs", "octagon")</u>: red octagonal tablets which can be swallowed or snorted. Treatment is as for other opioids (see section IX. Fentanyl below).
- II. 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.



- **III. Heroin:** The purity of Detroit-area heroin is high. The increased demand is believed to be driven by opioid users and abusers who switch to heroin because it is cheaper and more available. Newer formulations make some opioids (e.g. OxyContin™) more difficult to abuse. Adulterants include quetiapine (Seroquel™), quinine, caffeine, or lidocaine, or fentanyl/fentalogs. Heroin may also be sold in capsules. Capsules are red/white or blue/white. These capsules have heroin contaminated with quinine, procaine, cocaine, and diphenhydramine.
- **IV. W class synthetic opioids** such as U-47700 and AH-7921. These agents are both mu and kappa agonists and the kappa agonism may lead to dysphoria. First synthesized by the UpJohn company in the 1970s, **U-47700** is about 7.5X as potent as morphine. As stated above, these agents are being pressed into tablets and stamped with imprint codes referable to oxycodone. There are also reports of counterfeit Norco containing fentanyl and U-47700. They are ultra-potent agents with onset within 30-90 minutes and duration is dependent upon route of administration. Orally, they tend to last several hours but inhaled through a vaporizer, can have extremely rapid onset and short duration. There is no data on reversal with naloxone although the blogs (Reddit and Bluelight) state that Suboxone doesn't have much effect with U-4. This suggests that there isn't much competition at the receptor. Naloxone is a mu receptor antagonist only and will have no effect on the kappa response.
- **V. Tramadol:** Prescriptions for tramadol have been on the rise over the past 5 years. According to the DEA, in 2011, more than 2.5 million people used tramadol recreationally.
 - 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
 - In overdose, in addition to the usual opioid effects, tramadol can cause seizures including status epilepticus
 - It can cause serotonin syndrome especially when combined with other serotoninergic drugs.
 Patients may present with autonomic instability, altered mental status, fever, and 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
- **VI. Methadone**: Methadone is used to treat opioid addiction and chronic pain. Street prices for methadone range from 0.50 \$1 per mg. Methadone has a long duration of action and recurrent toxicity should be anticipated after reversal with naloxone. A continuous naloxone infusion may be required and the patient admitted.
- VII. 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. Buprenorphine is sold under the trade names Subutex[™], Suboxone[™], Zubsolv[™]. Temgesic[™], Buprenex[™]. Pediatric ingestions are particularly lethal with delayed respiratory failure 16-24 hours after ingestion.
- **VIII. 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.
- IX. Fentanyl: Fentanyl is an analgesic with a potency of about 80 times that of morphine and is available under the trade names of Sublimaze®, Duragesic® (transdermal patch), Fentora® (effervescent buccal patch) and Actiq® (a lollipop). Related drugs include alfentanil (Alfenta®), an ultrashort acting analgesic, and sufentanil (Sufenta®), an exceptionally potent analgesic, 5 to 10 times more potent than fentanyl. Carfentanil (Wildnil®) is an analogue of fentanyl with an analgesic potency 10,000 times that of morphine and is used in veterinary practice to immobilize large animals. Over 12 different analogues of fentanyl (fentalogs) have been produced in clandestine laboratories in the US.

Acetylfentanyl, acrylfentanyl, and furanylfentanyl have all been reported in this region. The Wayne and Washtenaw Medical Examiners have reported an increasing number of deaths associated with confirmed carfentanil.

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. Recently, a batch of equal parts heroin and fentanyl was responsible for over 100 deaths along the East Coast and Pennsylvania. It has been referred to as "Bud Ice", "Theraflu", and "Income Tax".

- **X. Kratom**: Kratom 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". It can be chewed or made into a tea. The active ingredients are mitagynine and 7-hydroxymitagynine which have weak opioid and serotoninergic activity leading to the substance described as both a stimulant AND and opioid. Kratom may be combined with tramadolpublished recent publication reported that commercial kratom was spiked with much higher levels of the potent 7-hydroxymitagynine alkaloid (17X more potent than morphine). Treatment is generally supportive with titrating doses of naloxone for respiratory depression.
- **XI. Loperamide**. Loperamide has become a popular drug of abuse. It 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 keeps it in check, is overwhelmed and loperamide can pass through the blood-brain-barrier to the brain 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. SWidened QRS > 110 msec is a sodium channel issue and is treated with sodium bicarbonate serum alkalinization and long QTc reflects K channel effects. It is treated with with IV magnesium and keeping potassium normal. Serum alkalinization will cause hypokalemia and worsen the QTc prolongation so patients should be empirically treated with potassium in this case. Patients may have prolonged periods of toxicity lasting 5-7 days. Amiodarone is not recommended because of its potassium blocking effect.
- XII. Carfentanil: Carfentanil was originally developed as a large mammal immobilizer and tranquilizer. It made headlines in 2002 when Russian authorities used an aerosolized spray to subdue Chechen rebels who had taken hostages in a Moscow theatre. Currently it is used as a highly potent heroin substitute. Its relative strength is approximately 10,000x equivalent doses of morphine and can result in respiratory arrest even in experienced users. Carfentanil has been identified locally both as a single substance or substituted for heroin. While potency is high, duration of effect is relatively short. Treatment is primarily supportive, but may require larger doses of naloxone. Careful titration of naloxone based on respiratory status is recommended and you may be surprised very large doses may not be required. The. The enhanced potency has led to a concern that contact with this agent during resuscitation can be deadly. Universal precautions and avoidance of powder inhalation should be adequate.
- XIII. Grey Death: In the last 4 weeks, headlines have described the arrival of another potent opioid product. Grey death, so named because of its color and similarity of appearance to concrete, is a highly potent mixture of various opioid compounds including U-47700, fentanyl analogues, and heroin. Contrary to sensationalist media reports, death through unintentional contact is highly unlikely. Traditional universal precautions are sufficient. Treatment is supportive, and should be focused on maintenance of respiratory status and mitigation of potential secondary effects. of naloxone ultra-potent

GABA-B Agonists:

I. Gammahydroxybutyrate (GHB): Schedule I, clandestine manufacture



- Slang: GHB, GBH, Grievous Bodily Harm, Easy Lay, Georgia Home Boy, Liquid Ecstasy, Liquid X, Liquid E, Soap, Scoop, Salty water, G-Riffick, Cherry Meth, Organic Quaalude, Natural Sleep-500, Oxy-Sleep, Somatomax, Somsanit, Gamma OH, Gamma hydrate, 4-hydroxybutyrate, Alcover, Anetamin, and Zonked, GHB+ketamine+alcohol = Special K-lude
- 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.
- · May be used in drug-facilitated sexual assault
- · Taste is described as salty or soapy
- Very short half-life
- Symptoms begin 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
- Laboratory: GHB levels will not be useful in OD setting
- Drug screens may reveal co-ingestants
- Contact the Poison Center for a listing of laboratories that will analyze GHB in cases of date rape or sexual assault

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
 - -patient may need intubation if benzodiazepines are used
- -Current evidence does not support the use of physostigmine

II. GHB-Like Agents: These products are sold in health food stores, sports nutrition stores and on the Internet, as "registered chemicals."

- GBL (gammabutyrolactone). Slang and trade names: Renewtrient, Regenerize, Invigorate, Revivarant 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.

Clinically, the presentation and management are identical to GHB.

NMDA Antagonists:

I. Ketamine: Schedule III

This is an 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. Ketamine was not seen in the Michigan area until recently. There are now confirmed ketamine cases.

Slang terms include: K, Special K, Green, Jet, Kay, Mauve, Purple, Special LA Coke, Super acid, Super C, Cat Valiums)

- The onset of symptoms is 1-10 minutes after use. The effects last 2 to 3 hours.
- Symptoms include
 - 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
 - Dissociated patients may not be aware of severe injuries such as fractures or lacerations
 - Akinetic mutism has been observed in children.
- **II. Methoxetamine**: this a "research chemical product" and has been identified in the Detroit area. It is sold under the names "MXE", "M-Ket", "Kmax", "Minx", "Jipper", "Roflcoptr", 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
- III. Dextromethorphan: non-scheduled

Slang terms include: DXM, Dex, Robo, Tussin, CCC, Red Devils, High C, Coricidin HBP Cough & Cold™, skittles, blue velvet (combined with nitrous)

- 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)
- Effects: LSD-like high, dissociation, hallucinations, vivid dreams, tachycardia, hypertension, vomiting, choreoathetosis
- Possibly synergistic with MDMA



- Note: Coricidin HBP Cold & Flu[™] contains acetaminophen and laboratory evaluation for APAP is required in the dosages used for abuse.
 - Coricidin formulations also contain chlorpheniramine so patients will present with anticholinergic signs (agitation; tachycardia; hypertension; hyperthermia; dilated pupils; dry mouth, dry, warm, flushed skin; diminished bowel sounds; urinary retention)
- 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

IV. Methoxphenidine (MXP)

- Designed 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

I. Nitrous Oxide:

- Slang: Laughing gas, buzz bomb, shoot the breeze, N20, N0X
- Nitrous oxide abuse poses unique ability to oxidize cobalt in the B12 molecule and can lead to functional B12 deficiency.
- Typically sold as balloons or as whippets

II. 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"
- 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 is important
 - -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

I. 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)
- 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
- II. Amanita muscaria (mushroom): non-scheduled, not truly a hallucinogen



- This bright orange colored mushroom is purchased freeze-dried from the Internet and is available as either intact mushroom caps or concentrated extract that contains 25 grams per gram of extract.
- 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.
- Usually ingested as a cold tea
- Onset of action is 30-90 minutes; peak 2-3 hours; duration 12 hours
- Laboratory:
 - Not detected on routine urine drug screens
- Treatment:
 - o -ABC's
 - o -Benzodiazepines may be useful to control agitation and myoclonus

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III. "Shrooms": these are Schedule I psychedelic mushrooms which contain psilocybin and psilocin. They are generally dried but may be fresh. The trip is dependent upon the set and setting. Many people will vomit initially then proceed onto their trip. Treatment is supportive and mostly these people just need a "trip sitter" in a quiet room with minimal stimulation

BENZODIAZEPINES

Xanax (alprazolam):

Slang:

- 2-mg white rectangle-shaped tablets: Xanax 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)
- Abuse of Xanax (alprazolam) is on the rise in children and young adults, often in combination with alcohol or other depressants. Older adults use it as a "downer" after binging on cocaine or other stimulants. "Trinity" is the combination of Xanax (alprazolam), Vicodin or other opioid (hydrocodone), and Soma (carisoprodol).
- Xanax is ingested or crushed and snorted
- Symptom onset is rapid. The half-life is approximately 12 hours.
- Urine drug screens may not be positive for benzodiazepines given the low concentrations of the metabolite typically found in the urine
- Treatment:
 - -Stabilization: ABC's
 - -Anticipate vomiting
 - -Naloxone, thiamine, glucose
 - -Avoid flumazenil given the potential for use in combination with other drugs or drug tolerance with rapid precipitated withdrawal (seizures) and dysrhythmias (see above)
 - -No need for GI decontamination

Etizolam: As discussed above, etizolam is a non-US approved benzodiazepine found in some counterfeit alprazolam tablets ("bars"). Etizolam is a very potent benzodiazepine and has led to cases of respiratory depression. Treatment is supportive.

MISCELLANEOUS:

I. <u>Sizzurp</u>: 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 know as "drank", "barre", "purple jelly", "Texas Tea", or "Tsikuni". Toxicity is predominantly respiratory and CNS depression.

- II. <u>Slowtivate, Un'Ergy, Lazy Cakes, Marley's Mellow Mood, Sippin Syrup, Mary Jane Relaxation Soda, Unwind:</u> (relaxation drinks and 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
- **III. Lemon Drop**: created by mixing painter's solvent with over-the-counter medications containing dextromethorphan. The mixture is heated to extract the DXM and then mixed with lemon juice or powdered lemonade.
- **IV. 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.
- **V. 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.

For further information or to report a case, please contact the
Regional Poison Center.*

Many of these agents are now reportable.

The Poison Center is the designated provider of surveillance for the Michigan
Department of Community Health.

Thank You

Children's Hospital of Michigan Regional Poison Control Center

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

*Alternatively, cases may be reported as a list with patient name, age and outcome and faxed to the Poison Center at 313-745-5493

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