

Pediatric Toxicology

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Objectives

- Describe poisoning statistics in the United States
- Differentiate between common toxidromes in poisoned patients
- Describe the toxicology of THC/edible products in pediatric patients
- Review common pediatric drug & toxicant exposures
- Discuss the advantages and disadvantages of urine drug screens

2022 Annual Report: National Poison Data System (NPDS)



- Report published by America's Poison Centers
- Poison centers have managed an average of 3.3 million encounters annually since the year 2000
- One human exposure reported every 15.2 seconds
- Nearly half of all poison exposures occur in children under the age of six

CLINICAL TOXICOLOGY
2023, VOL. 61, NO. 10, 717-939
<https://doi.org/10.1080/15563650.2023.2268981>



NPDS REPORT 2022



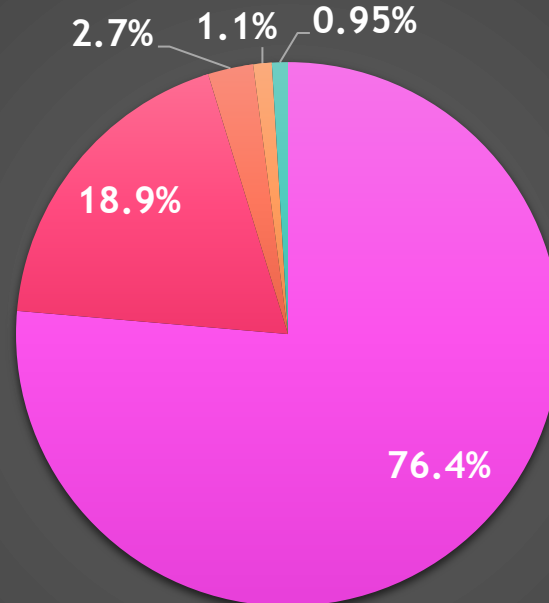
**2022 Annual Report of the National Poison Data System® (NPDS) from
America's Poison Centers®: 40th Annual Report**

David D. Gummin, James B. Mowry, Michael C. Beuhler, Daniel A. Spyker, Laura J. Rivers, Ryan Feldman,
Kaitlyn Brown, Nathaniel P.T. Pham, Alvin C. Bronstein and Carol DesLauriers

2022 Annual Report: National Poison Data System (NPDS)



Reason for Exposure (N = 2,064,875)

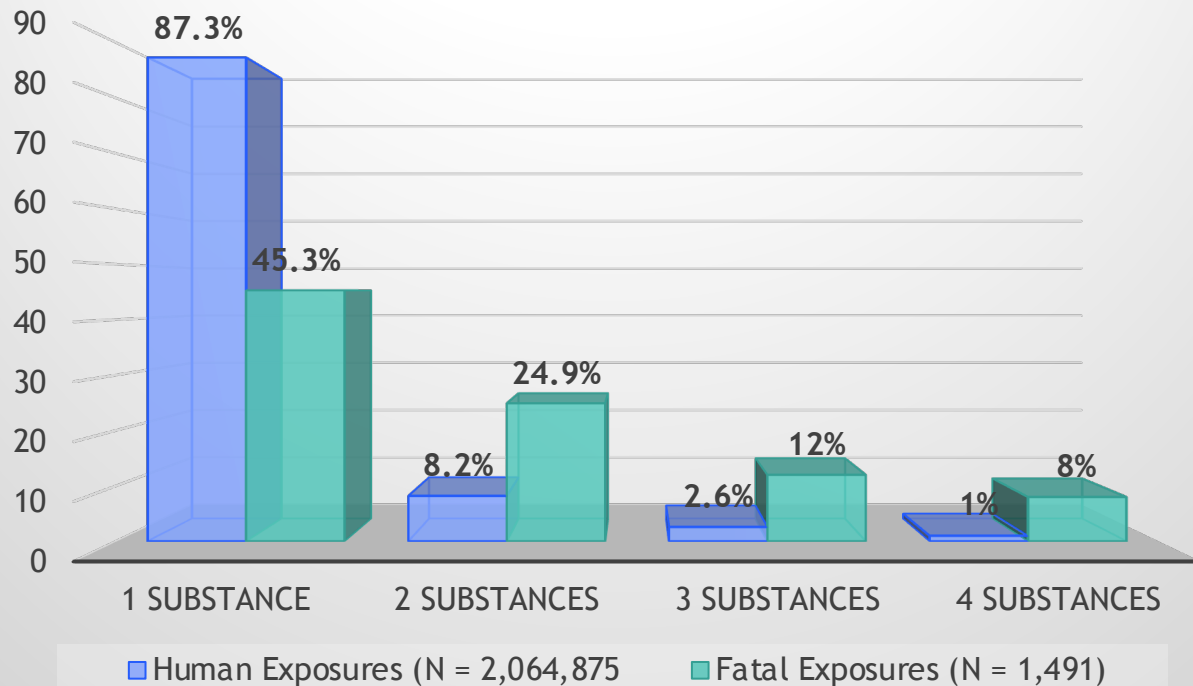


■ Unintentional ■ Intentional ■ Adverse Reaction ■ Unknown ■ Other

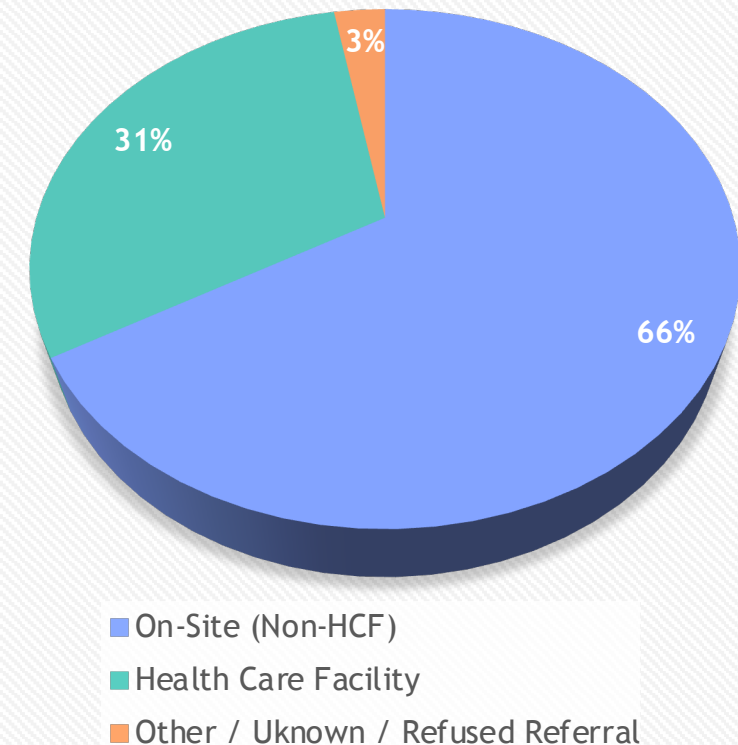
2022 Annual Report: National Poison Data System (NPDS)



Substances Involved in Human Exposure Cases



Management Site



2022 Annual Report: National Poison Data System (NPDS)



Pediatric (<5 Years)

- Household Cleaning Substances (10.3%)
- Analgesics (9.5%)
- Cosmetics / Personal Care (9.5%)
- Dietary Supplements /Herbals / Homeopathic (6.7%)
- Foreign Bodies / Toys (6.6%)
- Antihistamines (5%)
- Vitamins (4.9%)
- Topical Preparations (4%)
- Pesticides (3.4%)
- Plants (3.3%)

Adults (> 20 Years)

- Analgesics (11%)
- Sedative / Hypnotics / Antipsychotics (7.4%)
- Antidepressants (7.3%)
- Cardiovascular Drugs (7%)
- Household Cleaning Substances (6.2%)
- Alcohols (4.4%)
- Anticonvulsants (3.8%)
- Antihistamines (3.6%)
- Stimulants & Street Drugs (3.1%)
- Hormones & Hormone Antagonists (3%)

Top 5 Overall

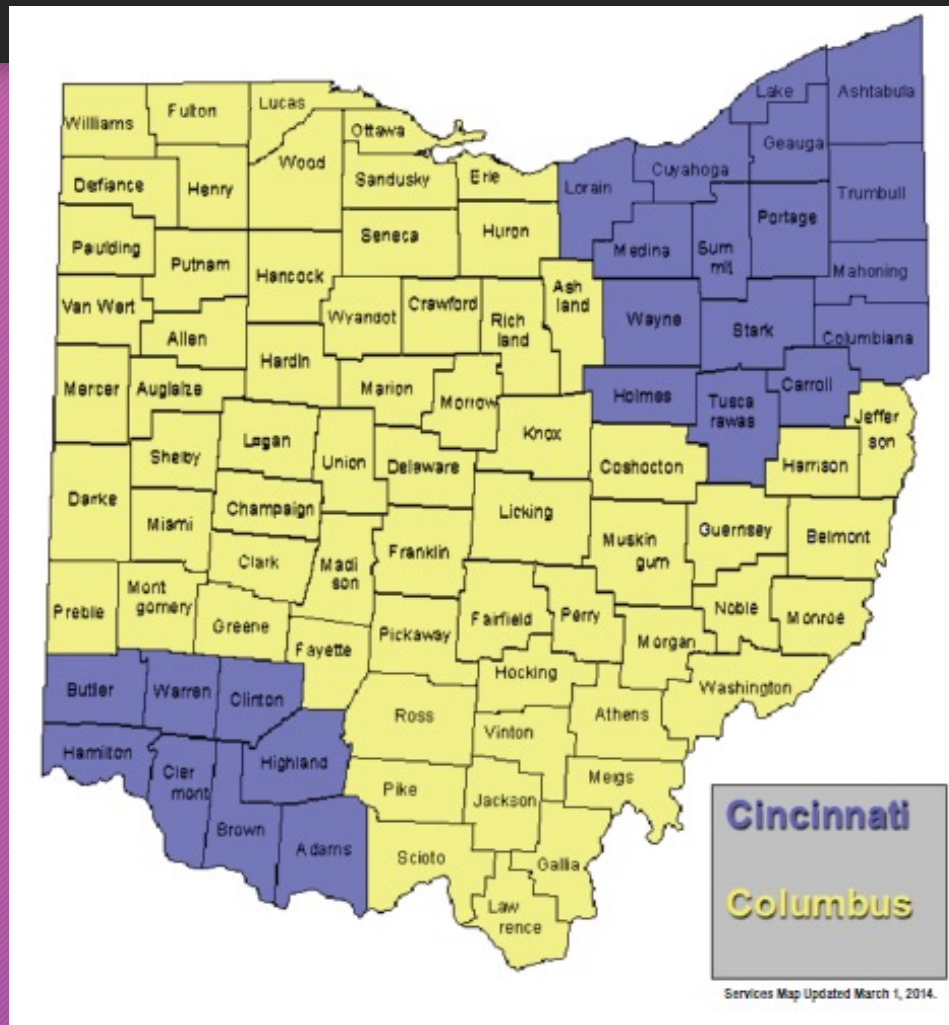
- Analgesics (11.5%)
- Household Cleaning Substances (7.2%)
- Antidepressants (5.6%)
- Cosmetics / Personal Care (5.2%)
- Antihistamines (4.8%)

Central Ohio Poison Center



- ~43,000 exposures / year
- Specially trained nurses & pharmacists
- Staffed 24/7/365
- Professional callers: consultation with board-certified medical toxicologist
- National phone number - routed by caller's location / area code / cell phone tower information

Central Ohio Poison Center



The Poisoned Child

Consider child abuse

- Especially in patients < 1 year old

Consider suicide if > 5 years

Poisoning: Therapeutics

- Mainstay of therapy: supportive care measures
- Decontamination
 - Eyes / skin: Yes!
 - GI Tract:
 - Charcoal / Whole Bowel Irrigation → Maybe...
 - Ipecac → NO! Never!
 - Lavage → NO! Never!
- Antidotes: somewhat rarely
- Chelators: rarely



Toxidromes

Anticholinergic

Cholinergic

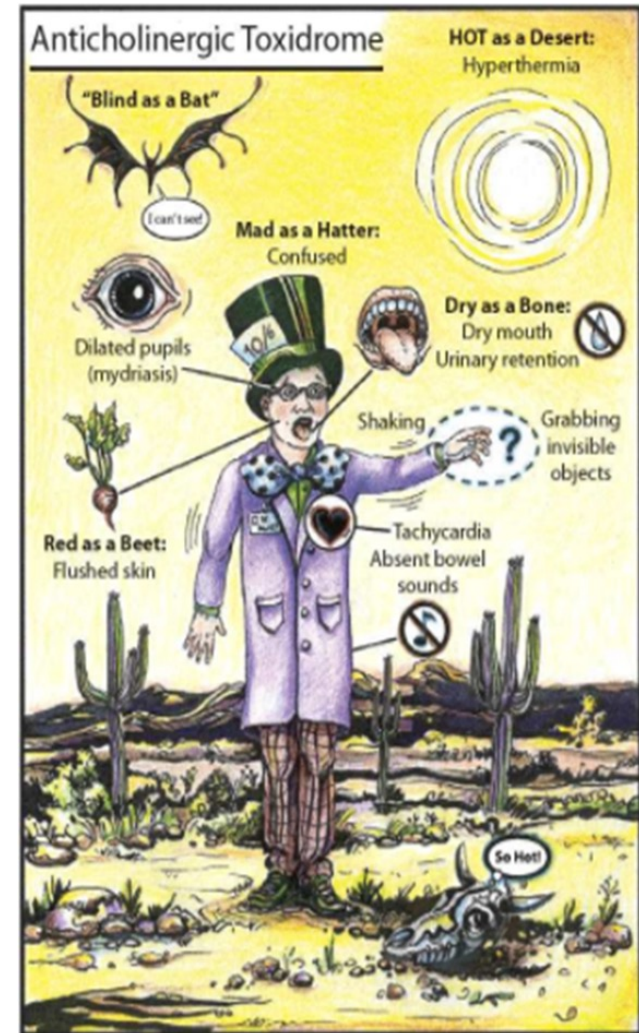
Sympathomimetic

Opiate

Serotonin
Syndrome

Anticholinergic Toxidrome

- DRY as a bone
- RED as beet
- HOT as a hare
- MAD as a hatter
- BLIND as a bat
- DUMB as a post
- TACHY like a leisure suit
- SEIZING like a squirrel
- FULL as a flask
- BLOATED as a toad



Anticholinergic Toxidrome - Sources

- Antihistamines
- Belladonna alkaloids (atropine)
- Jimson weed
- Tricyclic antidepressants
- Scopolamine
- Antispasmodic / anti-motility agents



Isidre Blanc at nl.wikipedia



Anticholinergics: Treatment

- Supportive care
- Benzos (and more benzos)
- Rare: physostigmine
 - Risk bradycardia, increases mortality of TCA OD
 - Can consider: **rivastigmine**

October 31, 2023: Temporary Importation available for Physostigmine Injection

[f Share](#) [X Post](#) [in LinkedIn](#) [✉ Email](#) [🖨 Print](#)

Physostigmine Salicylate Injection
Dr. Franz Köhler Chemie GmbH
Company Contact Information:
Provepharm: 833-727-6556

Presentation	Availability	Related Information
2 mg/5 mL (0.4 mg/mL), ampules (NDC 81284-831-05)	Available	Dear Healthcare Professional Letter (PDF - 505 KB)

Call Tox !

Cholinergic Toxidrome

- DUMBBELLS
- Diarrhea
- Urination
- *Miosis
- **B**radycardia
- **B**ronchorrhea / **B**ronchospasm
- Emesis
- Lacrimation
- Lethargy
- Salivation

Cholinergic Toxidrome



Cholinergic Toxidrome

Muscarinic Effects	
S	Salivation
L	Lacrimation
U	Urination
D	Defecation
G	Gastrointestinal Distress
E	Emesis
B	Bradycardia
B	Bronchorrhea
B	Bronchospasm

Nicotinic Effects

Fasciculations

Muscle weakness

Paralysis

*Mydriasis

CNS Effects

Respiratory depression

Lethargy

Coma

Seizures

Cholinergic Toxidrome - Sources

- Organophosphate & carbamate insecticides
- Nerve agents
 - Sarin (GB), soman (GD), tabun (GA)
 - NOT sulfur mustard, phosgene
- Some species of mushrooms
 - *Clitocybe* spp, *Inocybe* spp



A

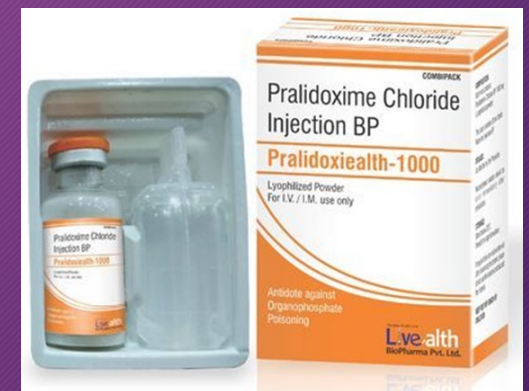


B

FIGURE 117-5. Group III: Muscarine-containing mushrooms. (A) *Clitocybe dealbata*. (B) *Omphalotus olearius*. (Used with permission from John Plischke III.)

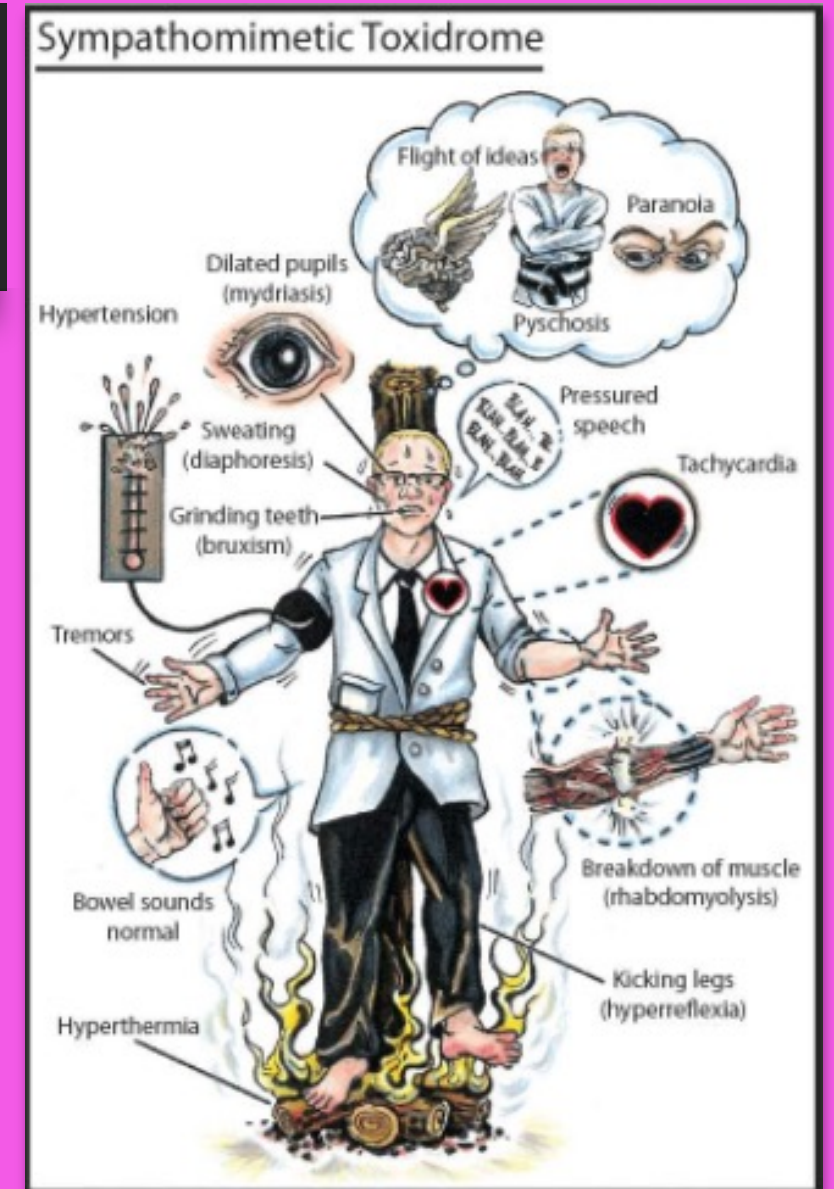
Cholinergic Toxidrome - Treatment

- Decontamination
 - Avoid secondary victims
- Atropine
 - May require high doses / continuous infusion
- For organophosphates:
 - Pralidoxime (2-PAM)
- Benzodiazepines for seizures, fasciculations



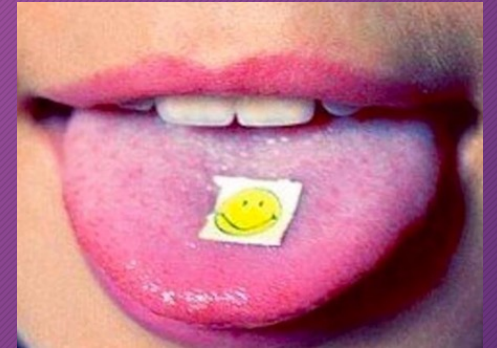
Sympathomimetic Toxidrome

- Anxiety
- Diaphoresis
- Hypertension
- Hyperthermia
- Mydriasis
- Seizures
- Tachycardia



Sympathomimetic Toxidrome - Sources

- Cocaine
- Amphetamines
 - Methamphetamine
 - LSD
- Phencyclidine
- Ephedrine
- Theophylline
- Caffeine
- Bath salts & other NPS (novel psychoactive substances)



What physical exam feature helps to distinguish between the sympathomimetic and anticholinergic toxidrome?



Anticholinergic vs Sympathomimetic

Sympathomimetic

- Diaphoresis
- Normal bowel sounds

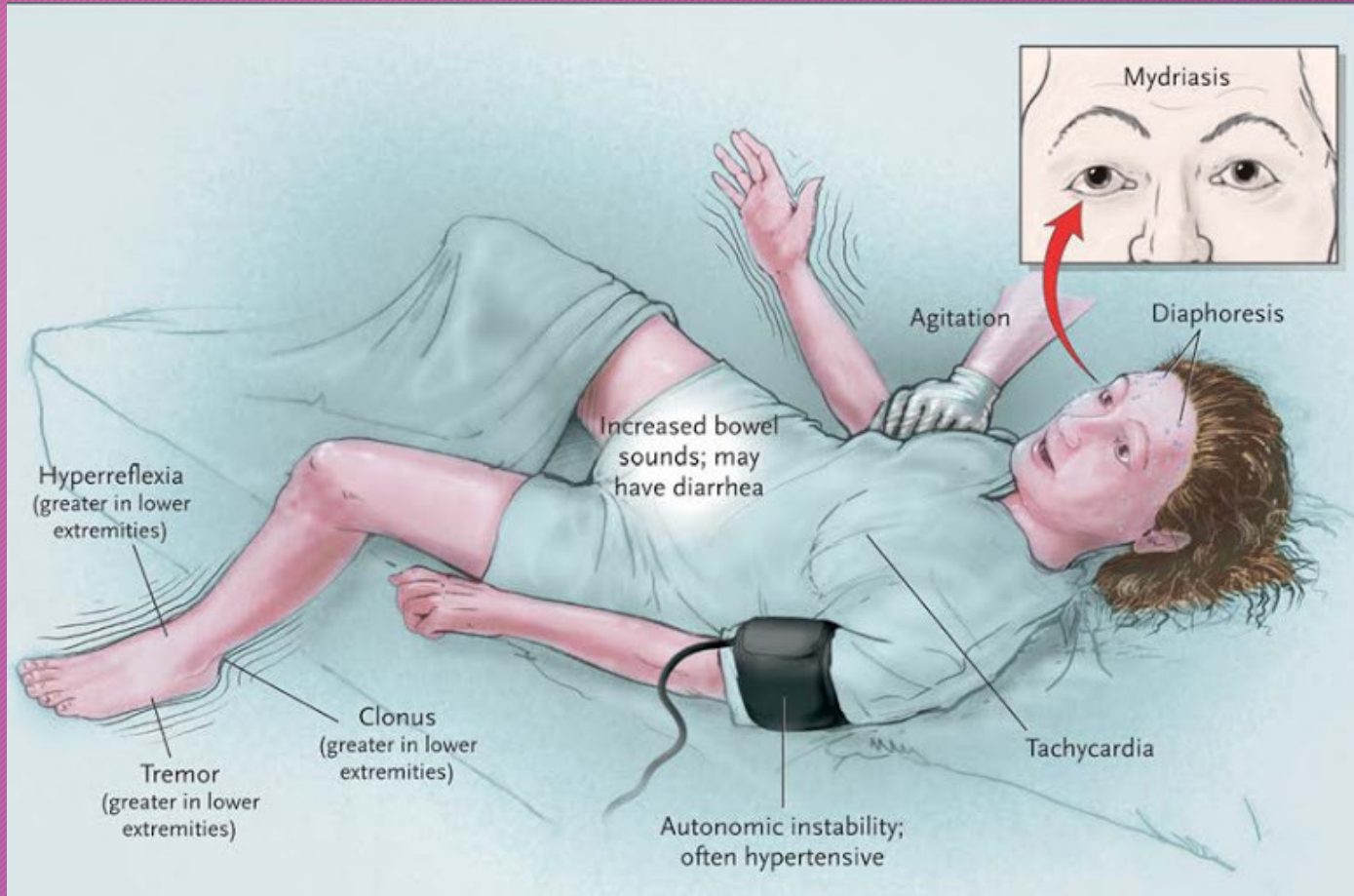
Anticholinergic

- Dry skin
- Hypoactive or absent bowel sounds

Opiate Toxidrome



Serotonin Syndrome



Serotonin Syndrome - Sources

- Many medications aside from SSRIs & SNRIs can be associated with serotonin syndrome!

Table 1. Drugs and Drug Interactions Associated with the Serotonin Syndrome.

Drugs associated with the serotonin syndrome

Selective serotonin-reuptake inhibitors: sertraline, fluoxetine, fluvoxamine, paroxetine, and citalopram

Antidepressant drugs: trazodone, nefazodone, buspirone, clomipramine, and venlafaxine

Monoamine oxidase inhibitors: phenelzine, moclobemide, dorgiline, and isocarboxazid

Anticonvulsants: valproate

Analgesics: meperidine, fentanyl, tramadol, and pentazocine

Antiemetic agents: ondansetron, granisetron, and metoclopramide

Antimigraine drugs: sumatriptan

Bariatric medications: sibutramine

Antibiotics: linezolid (a monoamine oxidase inhibitor) and ritonavir (through inhibition of cytochrome P-450 enzyme isoform 3A4)

Over-the-counter cough and cold remedies: dextromethorphan

Drugs of abuse: methylenedioxymethamphetamine (MDMA, or "ecstasy"), lysergic acid diethylamide (LSD), 5-methoxydiisopropyltryptamine ("foxy methoxy"), Syrian rue (contains harmine and harmaline, both monoamine oxidase inhibitors)

Dietary supplements and herbal products: tryptophan, *Hypericum perforatum* (St. John's wort), Panax ginseng (ginseng)

Other: lithium

Drug interactions associated with severe serotonin syndrome

Zoloft, Prozac, Sarafem, Luvox, Paxil, Celexa, Desyrel, Serzone, Buspar, Anaf-ranil, Effexor, Nardil, Manerix, Marplan, Depakote, Demerol, Duragesic, Sublimaze, Ultram, Talwin, Zofran, Kytril, Reglan, Imitrex, Meridia, Redux, Pondimin, Zyvox, Norvir, Parnate, Tofranil, Remeron

Phenelzine and meperidine

Tranylcypromine and imipramine

Phenelzine and selective serotonin-reuptake inhibitors

Paroxetine and buspirone

Linezolid and citalopram

Moclobemide and selective serotonin-reuptake inhibitors

Tramadol, venlafaxine, and mirtazapine

How to Diagnose Serotonin Syndrome

- First step: exclude differential diagnosis
 - Sedative / hypnotic drug or EtOH withdrawal
 - Exertional / environmental heat stroke
 - Thyrotoxicosis
 - Meningitis or encephalitis
 - Other serious infections
 - Malignant hyperthermia
 - Neuroleptic Malignant Syndrome (NMS)

Serotonin Syndrome: Sternbach's Criteria

Serotonergic agent and any 3 of the following:

Mental status changes
Agitation
Myoclonus
Hyperreflexia
Diaphoresis
Shivering
Tremor
Diarrhea
Incoordination
Fever

Serotonin Syndrome: Hunter Criteria

Serotonergic agent and any 1 of the following:



- 1) Spontaneous clonus
- 2) Inducible clonus **AND** (agitation **OR** diaphoresis)
- 3) Ocular clonus **AND** (agitation **OR** diaphoresis)
- 4) Tremor **AND** hyperreflexia
- 5) Hypertonia **AND** T > 38 degrees C **AND** (ocular clonus **OR** inducible clonus)

Serotonin Syndrome: Treatment

- Supportive care, safety
- Stop serotonergic & related drugs
- Benzos
- Watch CPK and treat rhabdo
- +/- cyproheptadine
 - Adverse effects:
 - Anticholinergic symptoms
 - Orthostatic hypotension



Common Pediatric Toxicants / Exposures



Cannabis: 2019

- Medical marijuana: 33 states, 4 territories & DC
- Recreational marijuana: 11 states

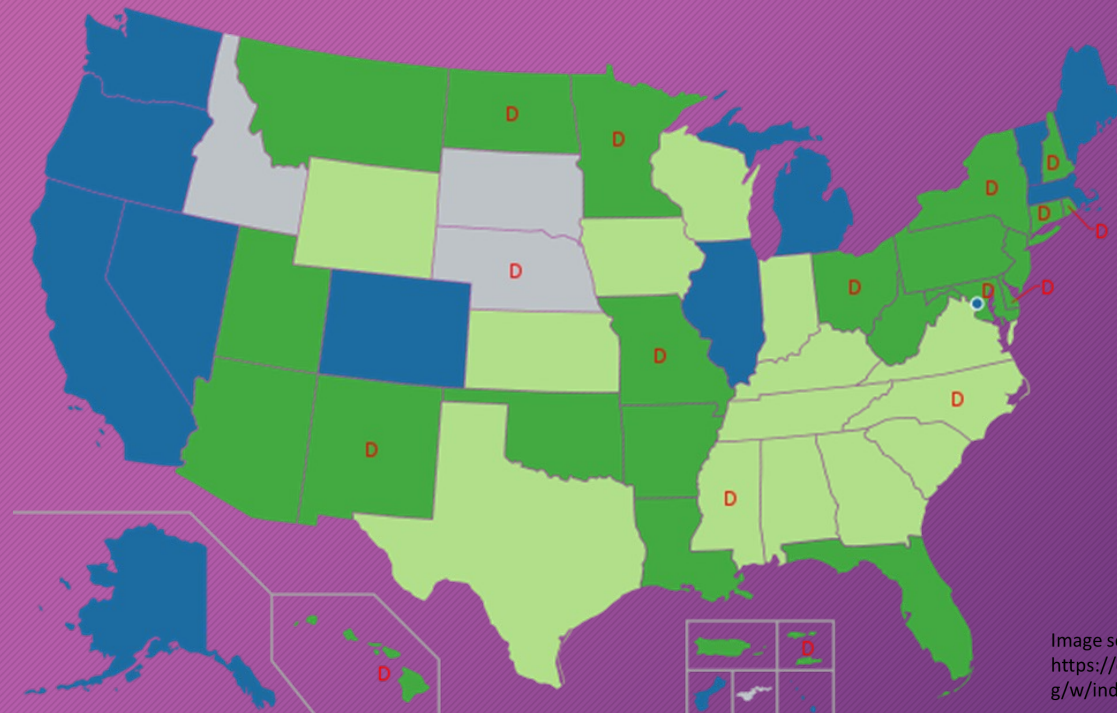
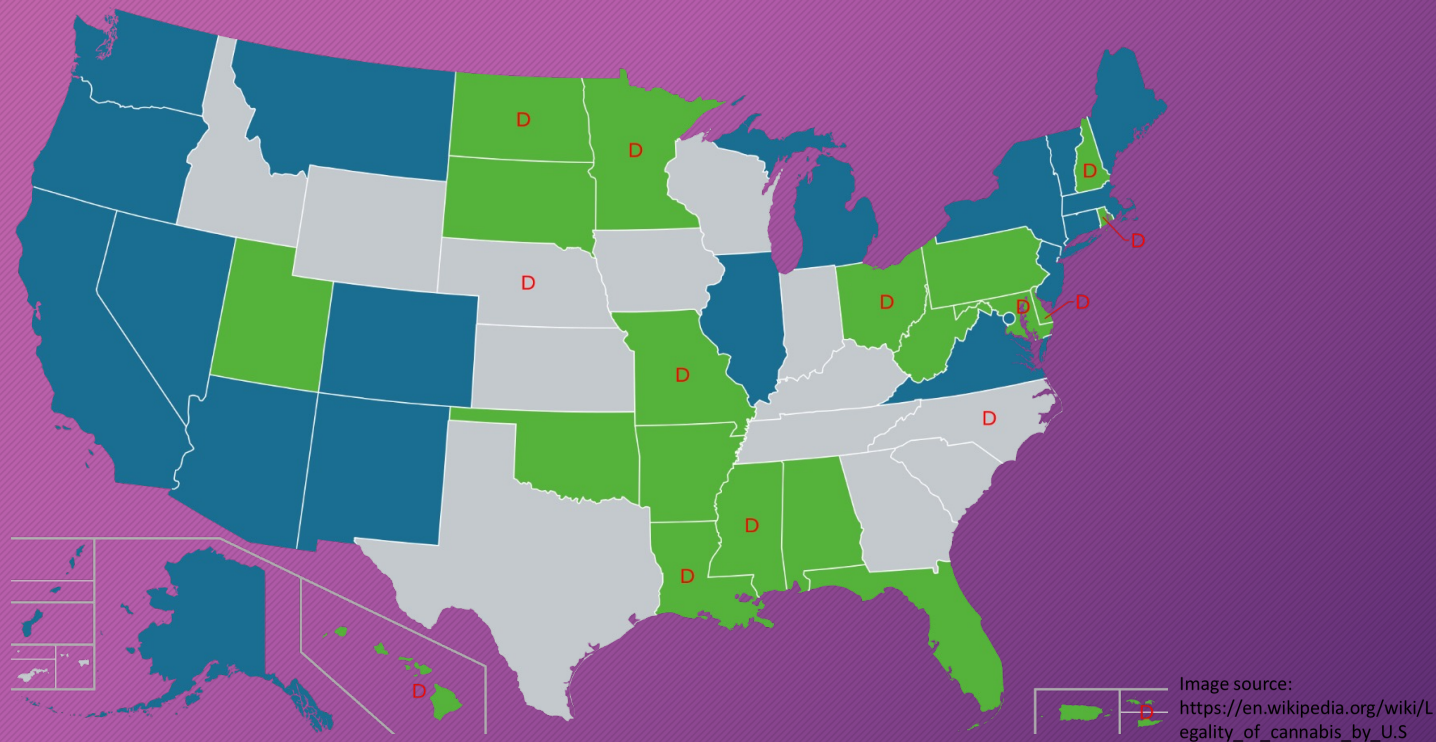


Image source:
<https://commons.wikimedia.org/w/index.php?curid=2370050>

Cannabis: February 2022

- Medical marijuana: 37 states, 4 territories
- Recreational marijuana: 18 states, DC, 2 territories



Cannabis: November - December 2023

Ohio Issue 2 Election Results: Legalize Marijuana

< See all Ohio state results


The possession and use of marijuana would become legal for people 21 and older, and its sale would be authorized.



PASSES ✓

Ohio has voted to legalize the possession and sale of marijuana.

Race called by The Associated Press.

Latest results from Dec. 5

>95% OF VOTES IN 

Answer	Votes	Pct.
✓ Yes	2,183,735	57.0% 
No	1,649,385	43.0 
Total reported	3,833,120	

 Dayton Daily News

[Changes to Issue 2 Ohio marijuana law stall in House](#)

The Ohio legislature's effort to reform Issue 2 has hit a temporary standstill as the House – which is content enough with the...

3 hours ago

 WKYC

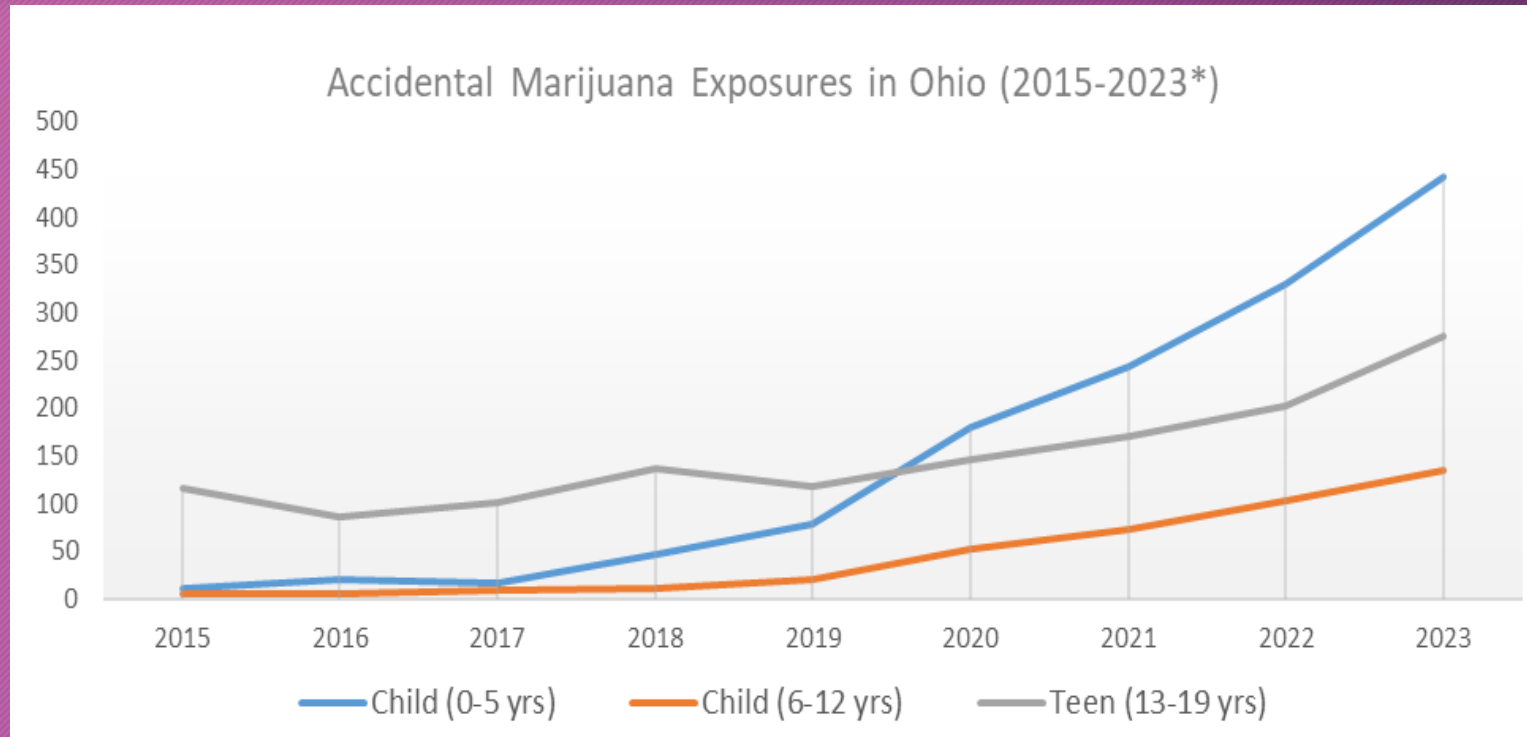
[Adults can now legally possess and grow marijuana in Ohio as Issue 2 becomes law – but there's nowhere to buy it](#)

COLUMBUS, Ohio – Ohioans woke up Thursday in a land of recreational marijuana limbo, in which adults can legally grow and possess cannabis...

5 days ago



Accidental Cannabis Exposures in Ohio



*Medical marijuana legalized 2019

THC Edibles

- Usual dose: 5-20mg
 - Tolerance
- Signs and symptoms
 - Tachycardia
 - Xerostomia
 - Sedation → → → → Coma
 - Respiratory depression



Ohio AG Dave Yost is warning about illegal cannabis products impersonating major snack brands. (Ohio Attorney General's Office)

By FOX19 Digital Staff

Published: Oct. 26, 2021 at 6:40 PM EDT

THC Edibles

- Emerging literature: 1.7 mg/kg of THC may be a useful threshold to guide medical management

[Pediatrics](#). 2023 Sep 1;152(3):e2023061374. doi: 10.1542/peds.2023-061374.

Toxic Tetrahydrocannabinol (THC) Dose in Pediatric Cannabis Edible Ingestions

Lesley C Pepin¹, Mark W Simon¹, Shireen Banerji¹, Jan Leonard², Christopher O Hoyte^{1 3}, George S Wang^{1 4}

Affiliations + expand

PMID: 37635689 DOI: 10.1542/peds.2023-061374

THC Edibles

- Exploratory ingestions becoming more common
- Tend to occur late in the day
- Peak absorption can be delayed (up to 4.5hr)
- COPC: refer in all children
 - Monitor for coma and respiratory depression
 - Social services

Buprenorphine

- Most common exploratory opioid ingestion in children < 6 years
- Approved in 2000 as a methadone alternative
- Often combined with naloxone
 - Brand names: *Suboxone*, *Zubsolv*

Buprenorphine - Pharmacodynamics

- Partial μ -receptor agonist
- Suppresses opioid withdrawal and cravings
- Less potential re-enforcing effects
- Better safety profile than methadone
 - Less respiratory depression
 - No risk of QT prolongation

Buprenorphine - Pharmacology

- Therapeutic doses → near complete occupancy of μ -receptor
 - Very high affinity
 - Slow dissociation
- Partial agonist-antagonist?
 - Agonist: at μ -receptors
 - Binds tight
 - Antagonist: at kappa receptors
 - May help prevent opioid-related dysphoria/psychosis

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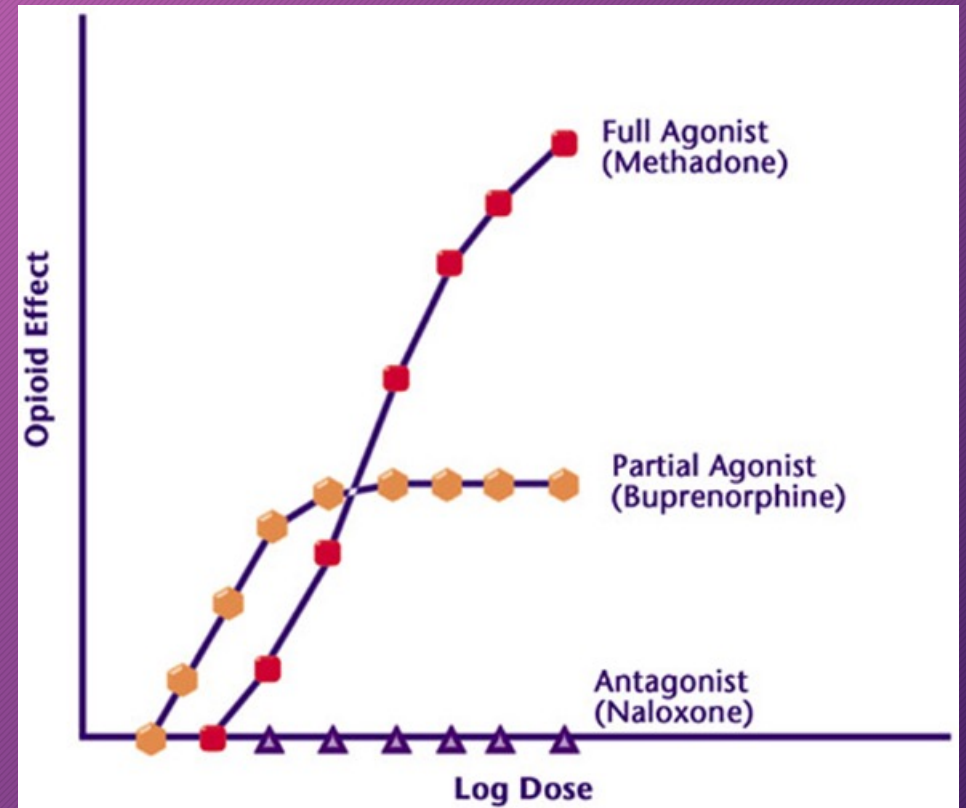
**NOT THE
NALOXONE!**

Buprenorphine - Abuse Complications

- Naloxone added to prevent diversion
- IV abuse leads to acute withdrawal

Buprenorphine

- Clinical Implications of “Partial Agonist”
- Buprenorphine is generally considered to have a ‘ceiling effect on respiratory depression’



Buprenorphine - Pediatric Exposures

- Different response in pediatric patients
 - Small doses have large impact
 - Fatal respiratory depression possible
 - Symptom onset can be delayed

Buprenorphine - Pediatric Exposures

- Hurdles to diagnosing exposure
- Most urine drug screens will be negative
- Symptom onset can be delayed up to 18 hours
- Some providers and parents believe the naloxone is protective

Buprenorphine - Other Complications

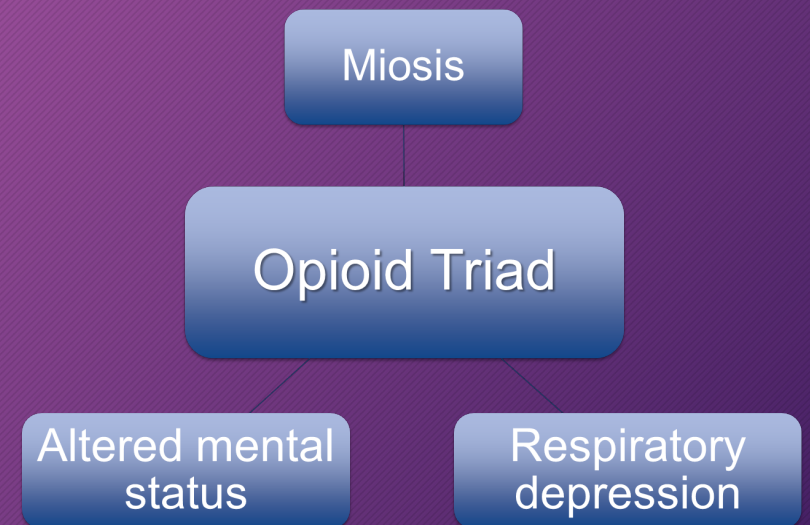
- Unique pediatric complication is often left out of buprenorphine waiver training
- Parents think it is a 'safer drug'
 - Studies show low rate of parental education

Buprenorphine - Summary

- Children can have delayed onset, fatal respiratory depression
- Minimum 24 hours observation
- Not on routine drug testing

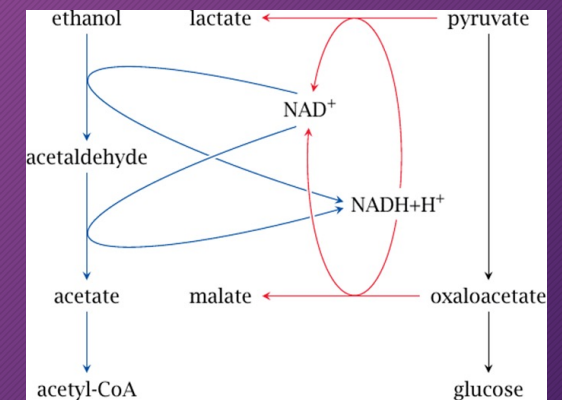
Clonidine

- More uses than blood pressure control
 - ADHD, opiate withdrawal
- Symptoms: hypotension, bradycardia, hypothermia, *bradypnea*, *miosis*, *AMS*
- Consider high-dose naloxone
 - Unclear efficacy



Ethanol

- Symptoms: inebriation, CNS/respiratory depression
 - For pediatric patients: hypoglycemia
- May delay or mask effects of methanol, ethylene glycol
- Treatment: supportive care
 - Watch blood glucose closely, especially in fasted toddlers



Hydrocarbons

- Sources:
 - Lamp oil, gasoline, Goo Gone, lighter fluid
- Risk: aspiration
 - Avoid GI decontamination
- Can expect to see fever from tissue damage not infection
 - No role for early steroids or antibiotics

Hydrocarbons

- Aspiration Risk Factors
- Low Viscosity
 - Thin, runny
- High Volatility
 - Evaporate → Burp → Inhale Vapors
- Low Surface Tension
 - High 'creep'
 - Spreads easily

Pop Quiz!

- 16-year-old admitted after intentional lorazepam overdose
- Drugs of abuse screen “negative” in ED
- Why?

Urine Drug Screen

Immunoassay

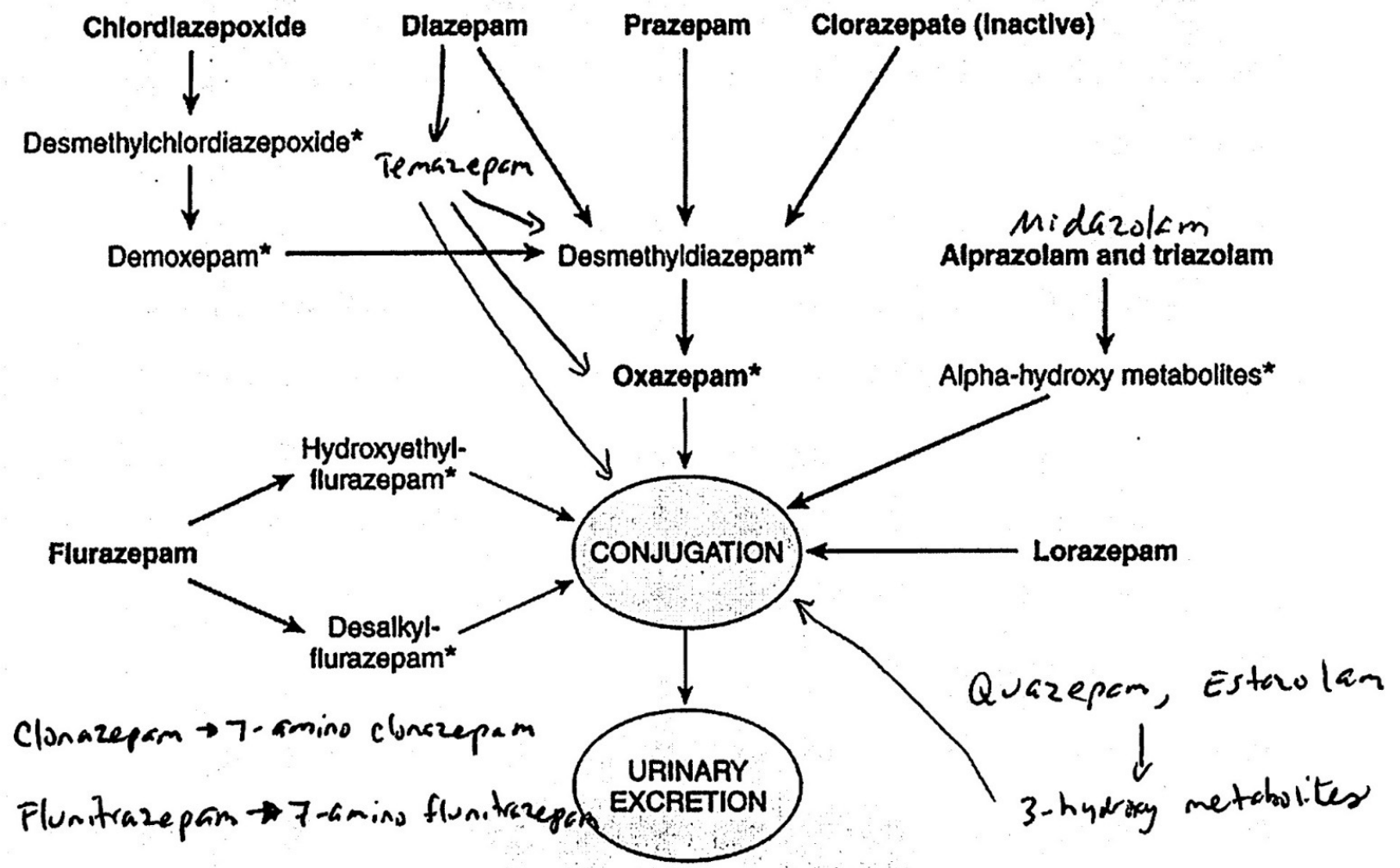
- Substances detected may vary by institution

Limitations

- Positive result does not imply intoxication
- False positives and negatives are common
- Many drugs of abuse are not detectable
- Opiates screen can create confusion

Urine Drug Screen - Detection Times

Compound	Occasional use	Chronic use
Amphetamines	2 days	4 days
Cannabinoids	1-3 days	> 1 month
Opiates	2 days	4 days
Barbiturates	2-4 days	
Benzodiazepines	1-30 days	
Cocaine	2 days	1 week
Methadone	1-4 days	
Phencyclidine	4-7 days	> 1 month
Propoxyphene	3-10 days	



- <https://www.medcentral.com/pain/chronic/demystifying-benzodiazepine-urine-drug>

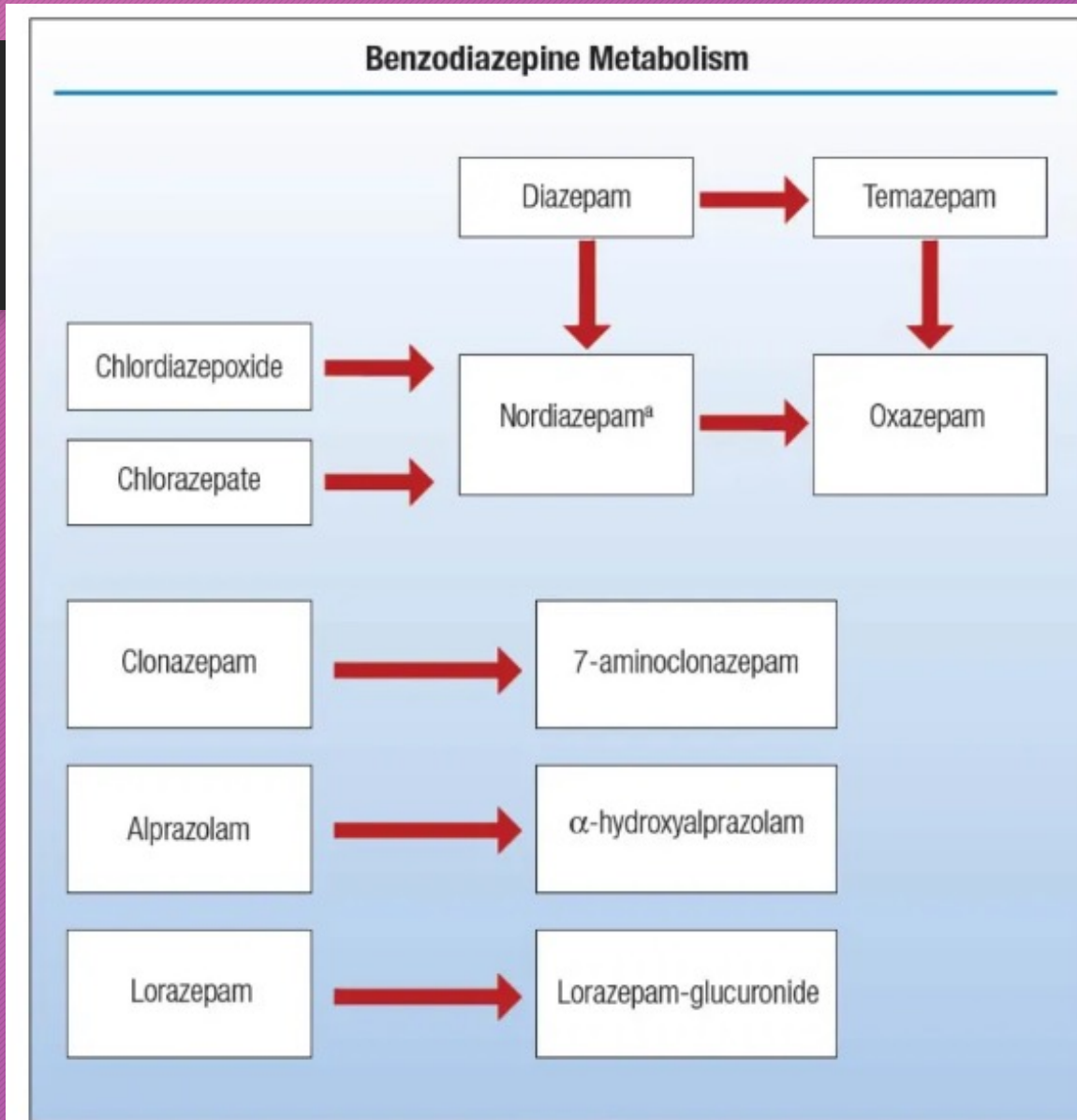


Figure 1: Illustrations of benzodiazepine metabolism.

Arrows indicate metabolic pathways

^aNordiazepam is also a metabolite of halazepam, medazepam, prazepam, and tetrazepam

Natural	Semi-synthetic	Synthetic
Morphine	Heroin	Fentanyl
Codeine	Oxycodone	Methadone
	Buprenorphine	Meperidine
Thebaine	Dextromethorphan	Propoxyphene
	Hydrocodone	Tramadol
Paregoric	Hydromorphone Oxymorphone	

NCH UDS

- How should this result be handled?

<input checked="" type="checkbox"/> AMPHETAMINE	Negative, presumptive	Negative, presumptive
Comment: Cutoff value of 1000 ng/mL for Amph/Methamphetamine		
<input checked="" type="checkbox"/> BARBITURATES	Negative, presumptive	Negative, presumptive
Comment: Cutoff value of 200 ng/mL for Barbiturates		
<input checked="" type="checkbox"/> BENZODIAZEPINE	Negative, presumptive	Negative, presumptive
Comment: Cutoff value of 200 ng/mL for Benzodiazepines		
<input checked="" type="checkbox"/> COCAINE METABOLITE LEVEL	Negative, presumptive	!
Screening results are not conclusive, confirmation testing to follow. See additional report. Estimated turnaround time for confirmation is three to four days. For additional information, please consider discussing results with the medical toxicology service.		
Comment: Cutoff value of 300 ng/mL for Cocaine Metabolite		

Call Tox !

Summary - Pediatric Toxicology



- History, history, history!
- Serotonin syndrome
 - Check for clonus
 - Stop offending agent
- Buprenorphine - different effects in children
- THC - monitor for delayed respiratory depression & coma
- Clonidine - may present like an opiate exposure
- UDS - error prone, easy to misinterpret and rarely change medical management
- Don't forget to utilize the poison center!



Questions?

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