Drug Testing Pearls from the Adolescent Substance Use and Addiction Program

Miriam Schizer MD MPH

Medical Director, Adolescent Substance Use & Addiction Program

Division of Addiction Medicine, Boston Children's Hospital

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Opioid Response Network

Working with communities.

- The SAMHSA-funded *Opioid Response Network (ORN)* assists states, organizations and individuals by providing the resources and technical assistance they need locally to address the opioid crisis and stimulant use.
- Technical assistance is available to support the evidence-based prevention, harm reduction, treatment and recovery of opioid use disorders and stimulant use disorders.

Funding for this initiative was made possible (in part) by grant no. 1H79TI085588-02 from SAMHSA. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

Working with communities.

- The *Opioid Response Network (ORN)* provides local, experienced consultants in prevention, treatment and recovery to communities and organizations to help address this opioid crisis and stimulant use.
- *ORN* accepts requests for education and training.
- Each state/territory has a designated team, led by a regional Technology Transfer Specialist (TTS), who is an expert in implementing evidence-based practices.

Contact the Opioid Response Network

- To ask questions or submit a request for technical assistance:
  - Visit www.OpioidResponseNetwork.org
  - Email orn@aaap.org
  - Call 401-270-5900

Objectives

- This presentation will review the following:
  - Proper urine collection procedures
  - Interpretation of drug test results, including false negative and false positive results
  - Strategies to employ when the patient refuses to participate in drug testing
  - Recent challenges in urine toxicology, including detection of newer substances and designer drugs

Types of Drug Tests

- Breath
- Saliva
- Blood
- Sweat
- Hair

http://www.drugcheck.com/dc_salivascan.html
http://www.overdriveonline.com/random-drug-testing-of-truckers-to-continue-at-50-percent-rate/
http://aboutdrugtesting.org/cheat.html

Matrices for Drug Testing: Oral Fluid

Advantages

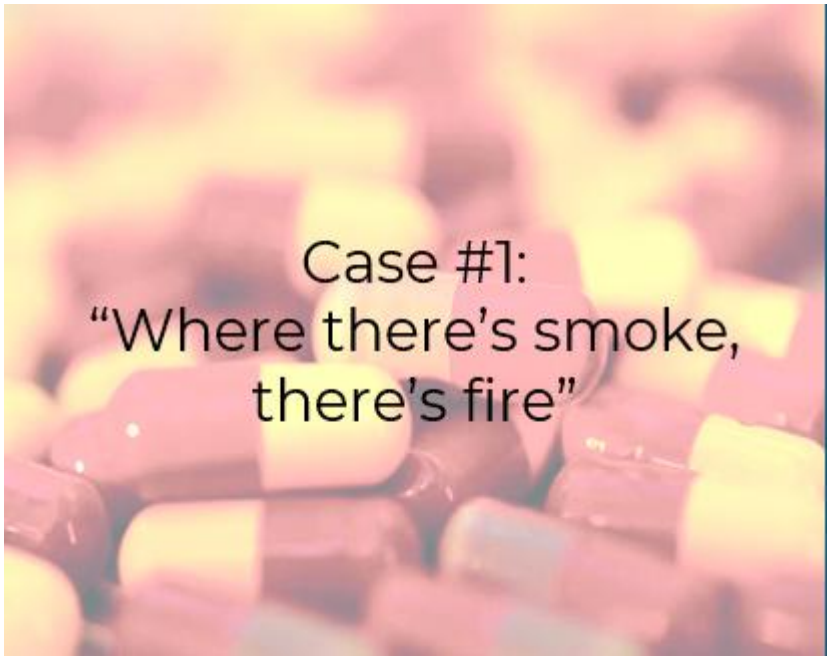
- Noninvasive specimen collection, can be directly observed
- Easy to collect
- Available for POCTs

Disadvantages

- Short window of detection (24-48 hours)
- Requires supervision of patient for 10-30 minutes before sampling
- Limited specimen volume

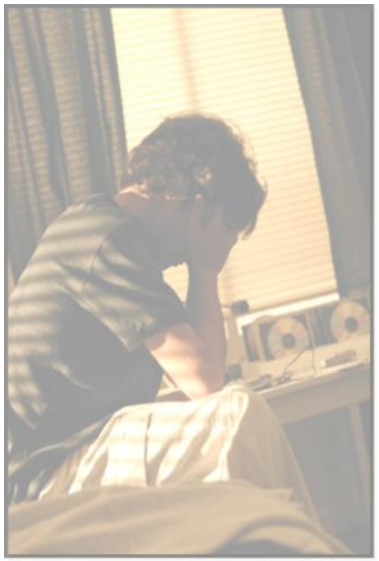
Types of Drug Tests

- Urine:
  - Well-studied, standardized, relatively non-invasive
  - Drug concentrations relatively high.
  - Relatively long window of excretion after acute intoxication


Case #1:
“Where there’s smoke,
there’s fire”

Billy

- 15-year-old boy
- Previous “problem use” of cannabis
- No use in the past 3 months
- Comes home from a school dance with red eyes and smelling of cannabis
- Parents request a drug test
- What would you do?



Billy

- Denies cannabis use
- Agrees to drug test
- Results:
  - Drug screen: positive for cannabis
  - Urine creatinine (random): 150 ug/dL; SG=1.008
  - GC/MS confirmation positive for cannabis

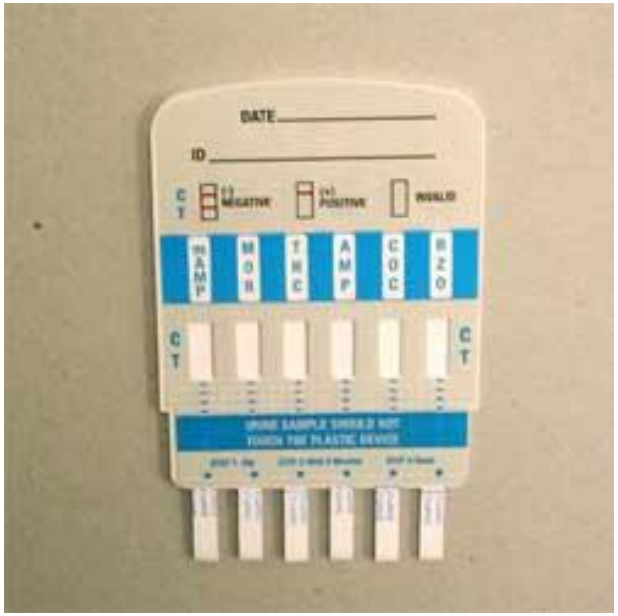
Billy

- Billy says he must have been exposed to “secondhand smoke”
- What do you do next?

Urine Panels

Immunoassays

- Quick, inexpensive
- Screen for multiple drugs at the same time
- Pre-determined "cut-off" value
  - **Marijuana cut-off = 50 ng/mL**
- Good sensitivity
- High rate of false positives



Confirmatory Testing

Gas chromatography/Mass spectrometry

- Gold standard in drug testing
- Highly specific
- Can give quantitative levels
- More expensive than screening

When you order a urine drug test:

- Know what you are ordering, i.e. know what is included in the lab's custom panel
- Order additional tests as needed based on the patient's history
- Decide in advance who will be getting the results (i.e. parents)

“Hot Boxing”

Some teens intentionally expose themselves to highly concentrated secondhand smoke in order to “get high without smoking,” a practice known as “hot boxing.”

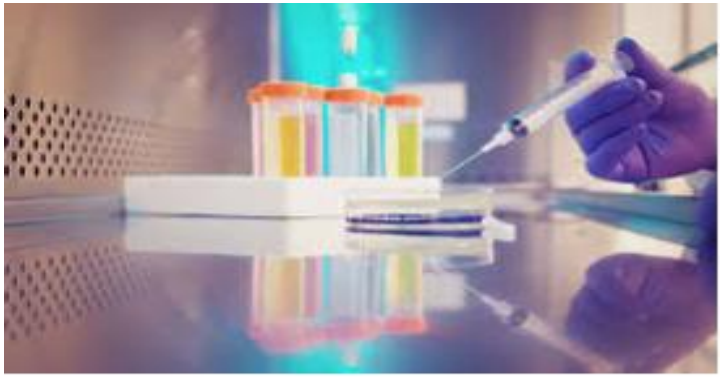
This should be considered cannabis use and treated the same as smoking.

Case #2:
“Big gulp”

Alex

- 16-year-old boy
- Caught with cannabis and suspended from school
- Denies cannabis use
- Agreed to drug test
- Results:
  - Drug screen: negative
  - Urine creatinine (random):
    - 6 ug/dL; SG=1.001
- What would you do next?

Interpretation of Urine Drug Test Results: *False Negative Test Results*



Common Sources of False Negative Drug Test Results:

- (1) Intentional *dilution* of urine sample
- (2) *Adulteration* of urine sample
- (3) *Substitution* of a different urine sample
- (4) Use of substance *not detected* by the drug test panel
- (5) Substance used, but *outside of the time frame* detectable by the test

Jaffee W.B., et al. Is this urine really negative? A systematic review of tampering methods in urine drug screening and testing. *Journal of Substance Abuse Treatment*, 2007 Jul;33(1):33-42.

False Negative Tests

Dilute Tests

- One of the most common methods for attempting to defeat a urine drug test
- Patient consumes a large amount of fluid in order to dilute the specimen and drive down drug concentrations below the screening threshold.
- Important to check "**random urine creatinine**" and **specific gravity** of each sample.

False Negative Dilute Tests

- Creatinine 20-50, SG < 1.010
  - Moderately dilute, repeat test
  - Limit water intake to less than 8 ounces in the 2 hours before the test
- Creatinine 5-20 mg/dL; SG < 1.005
  - very dilute, consider positive
- Creatinine <5
  - Substituted (not urine), consider positive

Result Date: 01/20/20 03:52 PM

Analyte	Result Value	Ref. Range	Units
NICOTINE, URINE	<2		ng/mL
COTININE, URINE	<2		ng/mL

Reference Range:

Nicotine, Urine
Smokers: 200-700 ng/mL
Nonsmokers: < or = 17 ng/mL

Cotinine, Urine
Smokers: 300-1300 ng/mL
Nonsmokers: < or = 20 ng/mL

Individuals exposed to second-hand or passive tobacco smoke may demonstrate concentrations of nicotine and cotinine greater than those indicated for non-smokers.

This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics Nichols Institute Chantilly, VA. It has not been cleared or approved by the U.S. Food and Drug Administration. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

STAND PNL + FENTANYL

Result Date: 01/20/20 03:52 PM

Analyte	Result Value	Ref. Range	Units
Alcohol Metabolites See Note 1 See Note 2	NEGATIVE	<500	ng/mL
Creatinine Verified by repeat analysis.	<1.0	> or = 20.0	mg/dL
Specific Gravity	1.003	> or = 1.003	
pH	6.5	4.5-9.0	
Oxidant	NEGATIVE	<200	mcg/mL
Fentanyl See Note 1	NEGATIVE	<0.5	ng/mL
Norfentanyl See Note 1 See Note 2	NEGATIVE	<0.5	ng/mL
Amphetamines	NEGATIVE	<500	ng/mL
Barbiturates	NEGATIVE	<300	ng/mL
Benzodiazepines	NEGATIVE	<100	ng/mL
Buprenorphine	NEGATIVE	<5	ng/mL
Cocaine Metabolite	NEGATIVE	<150	ng/mL
Heroin Metabolite	NEGATIVE	<10	ng/mL
Marijuana Metabolite 20	NEGATIVE	<20	ng/mL
MDMA/MDA	NEGATIVE	<500	ng/mL
Methadone Metabolite	NEGATIVE	<100	ng/mL
Opiates	NEGATIVE	<100	ng/mL
Oxycodone	NEGATIVE	<100	ng/mL
Phencyclidine	NEGATIVE	<25	ng/mL

False Negative Adulterated Tests

- Household products: bleach, salt, Visine, soap
- Gluteraldehyde
- Potassium nitrate
- Pyridinium chlorochromate
- Hydrogen peroxide

A Sample of Products

Synthetic Urine

Urine "detoxifier" (in vitro adulterant)

Real powdered urine

Urine Collection Procedures

Proper urine collection technique:

- Direct observation
- Department of Transportation protocol

Department of Transportation Protocol

Patient is required to:

- Show picture identification
- Empty pockets/wash hands

Facility:

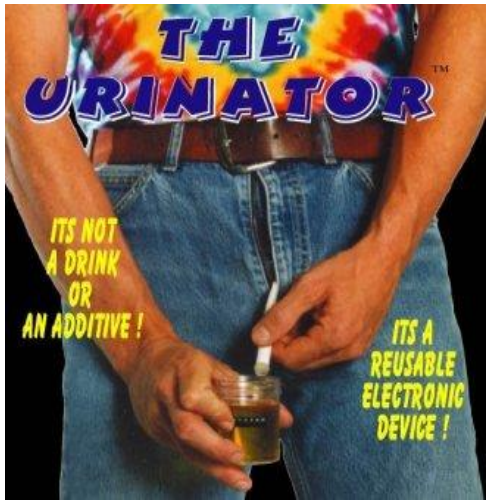
- No running water
- Toilet water is dyed blue
- Temperature is checked immediately

Commercial labs may offer this service but generally require a specific order.

Detecting Presence of Adulterants

- Importance of **Specimen Validity Testing**
- pH 4.5-9 (HHS cutoff)
- Creatinine greater than 20
- Specific gravity
- Specific testing for adulterants
  - Detect oxidants, nitrites etc.

False Negative Substituted Tests



… a one-of-a kind, state of the art, electronic urine testing device that will maintain testing temperature for a minimum of 4 hours with one set of batteries.

False Negative Tests

Substance not detected by panel

- Many of the drugs commonly used by teens are not reliably detected by immunoassay screens.
- Examples include inhalants, fentanyl, Ecstasy, dextromethorphan, and synthetic cannabinoids (K2, Spice).
- It is critical to know what the testing panel includes when ordering a drug test.
- Deciding which substance to test for should be based on the suspected substance being used, the substances of misuse in the patient population, and substances used locally (http://www.samhsa.gov/data/DAWN.aspx).

Most substances can be detected in a urine sample, but an appropriate assay must be specifically ordered. Inhalants are not excreted in urine and cannot be detected with urinalysis.

False Negatives:
Missed Window of Detection

Substance	Detection Window
THC	3-30 days
Amphetamines	2-3 days
Barbiturates	1-3 days
Benzodiazepines	1-7 days
Cocaine & metabolite	6 hours – 3 days
Methadone	7-9 days
PCP	8 days
Opiates	1-3 days

Case #3:
“Unexpected result”

Angela

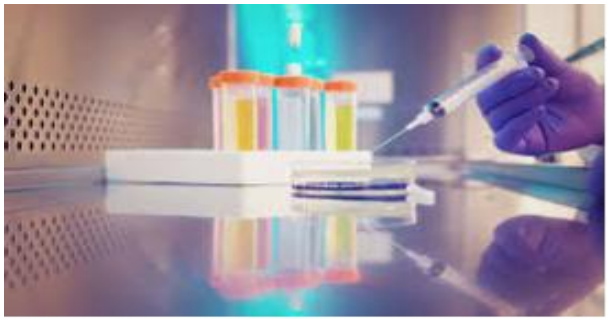
- 15-year-old girl
- Parents concerned about nicotine vaping, occasional cannabis use
- No known history of other substance use
- Prescribed sertraline for anxiety disorder
- Agrees to drug test

Results:

- Drug screen: positive for benzodiazepines and nicotine and cotinine
- Urine creatinine (random): 170 ug/dL; SG=1.010
- GC/MS confirmation positive for nicotine and cotinine

What would you do next?

Interpretation of Urine Drug Test Results: *False Positive Test Results*



False Positives Common Cross-Reactors**

Marijuana	•NSAIDs (Ibuprofen, Ketoprofen, Naproxen) • Vitamin B supplements (Promethazine)
Benzodiazepines	•Sertraline
Amphetamine	•Cold medications (ephedrine) •Diet aids (Phenylephrine) •Asthma medications (Afrin, Primatine)
PCP	•Dextromethorphan
Opiates	•Fluroquinilone antibiotics

**Confirmatory test will be negative

Cross-Reactivity with Amphetamine Immunoassay

Benzphetamine	Mexiletine	Pseudoephedrine
Buproprion	N-acetyl procainamide	Quinacrine
Chloroquine	Oxymetazoline (Afrin)	Ranitidine
Chlorpromazine	Phentermine	Selegiline
Ephedrine	Phenylephrine	Trazodone
Fenfluramine	Phenylpropanolamine	Tyramine
Fluoxetine	Propranolol	Vicks inhaler
Labetolol		

Clinical “False Positives”

- Food products or appropriate use of medications can result in a positive drug test result even in the context of a patient who is not using drugs.

http://fiestafarms.ca/12186/food/behold-the-magical-poppyseed

Clinical False Positives **

Marijuana	Prescription Marinol use (uncommon in teens)
Cocaine	De-cocanized teas, used common in South America.
Amphetamine	Prescription use of amphetamines (I.e. for ADHD).
Opiates	•Poppy seeds (in very large quantities). •Prescription use of opiates for pain.

**Confirmatory test will be positive

NICOTINE AND COTININE, URINE

Result Date: 01/17/20 11:41 PM

Analyte	Result Value	Ref. Range	Units
NICOTINE, URINE	2		ng/mL
COTININE, URINE	5		ng/mL

Reference Range:

Nicotine, Urine
Smokers: 200-700 ng/mL
Nonsmokers: < or = 17 ng/mL

Cotinine, Urine
Smokers: 300-1300 ng/mL
Nonsmokers: < or = 20 ng/mL

Individuals exposed to second-hand or passive tobacco smoke may demonstrate concentrations of nicotine and cotinine greater than those indicated for non-smokers.

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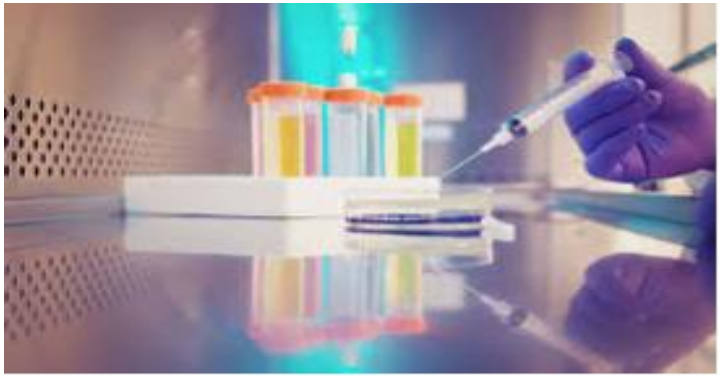
STAND PNL + FENTANYL

Result Date: 01/17/20 11:41 PM

Analyte	Result Value	Ref. Range	Units
Alcohol Metabolites See Note 1 See Note 2	NEGATIVE	<500	ng/mL
Creatinine	133.3	> or = 20.0	mg/dL
pH	7.2	4.5-9.0	
Oxidant	NEGATIVE	<200	mcg/mL
Fentanyl See Note 1	NEGATIVE	<0.5	ng/mL
Norfentanyl See Note 1 See Note 2	NEGATIVE	<0.5	ng/mL
Amphetamines	NEGATIVE	<500	ng/mL
Barbiturates	NEGATIVE	<300	ng/mL
Benzodiazepines	NEGATIVE	<100	ng/mL
Buprenorphine	NEGATIVE	<5	ng/mL
Cocaine Metabolite	NEGATIVE	<150	ng/mL
Heroin Metabolite	NEGATIVE	<10	ng/mL
Marijuana Metabolite 20	POSITIVE	<20	ng/mL
Marijuana Metabolite See Note 1	479	<5	ng/mL
MDMA/MDA	NEGATIVE	<500	ng/mL
Methadone Metabolite	NEGATIVE	<100	ng/mL
Opiates	POSITIVE	<100	ng/mL
Codeine See Note 1	NEGATIVE	<50	ng/mL
Hydrocodone See Note 1	NEGATIVE	<50	ng/mL
Hydromorphone See Note 1	NEGATIVE	<50	ng/mL
Morphine See Note 1	139	<50	ng/mL
Norhydrocodone See Note 1	NEGATIVE	<50	ng/mL
Oxycodone	NEGATIVE	<100	ng/mL
Phencyclidine	NEGATIVE	<25	ng/mL

Interpretation of Urine Drug Test Results: *Cannabis, Alcohol, Nicotine & Opioids*



Detecting Cannabis in a Urine Drug Test

- Generally cleared in 3-5 days in "occasional users"
- Lipid soluble and may be stored in adipose tissues in ***heavy, chronic*** users
  - Prolonged excretion may be up to 6 weeks in these cases

Detecting Alcohol in a Urine Drug Test

- Alcohol (ethanol) has a relatively short detection window in urine – about 12 hours after use
- Preferred method is to test for *alcohol metabolites* in the urine:
- **Ethyl glucuronide** and **Ethyl sulfate**
- These metabolites are detectable in the urine for up to 80 hours after use
- Many lab panels don't include alcohol but testing for these metabolites can be added upon request

Detecting Nicotine in a Urine Drug Test

- Usually test for **cotinine** in addition to **nicotine** because of its longer half-life in the body (cotinine 7-40 hours vs nicotine 1-4 hours)
- Cotinine generally detectable in the urine for about 3 days after use
- Many lab panels don’t include nicotine and cotinine but testing can be added upon request

Detecting Opioids in a Urine Drug Test

- **Opiate Screen**: Detects morphine and codeine
- Heroin is metabolized to morphine and codeine and will give a positive screen for opiates
- **Oxycodone Scree**n: Detects use of prescription opioids such as OxyContin**,** Percocet and Vicodin
- **Fentanyl Screen**: Detects the presence of fentanyl; must be added separately

Urine Drug Test (Quest Diagnostics)

Alcohol Metabolites	POSITIVE	<500	ng/mL
See Note 1			
Ethyl Glucuronide (ETG)	1204	<500	ng/mL
See Note 1			
Ethyl Sulfate (ETS)	662	<100	ng/mL
See Note 1			
See Note 2			
Creatinine	276.2	> or = 20.0	mg/dL
pH	6.1	4.5-9.0	
Oxidant	NEGATIVE	<200	mcg/mL
Fentanyl	219.0	<0.5	ng/mL
See Note 1			
Norfentanyl	>1000.0	<0.5	ng/mL
See Note 1			
See Note 2			
Amphetamines	NEGATIVE	<500	ng/mL
Barbiturates	NEGATIVE	<300	ng/mL
Benzodiazepines	NEGATIVE	<100	ng/mL
Buprenorphine	POSITIVE	<5	ng/mL
Buprenorphine	35	<5	ng/mL
See Note 1			
Norbuprenorphine	495	<5	ng/mL
See Note 1			
Cocaine Metabolite	POSITIVE	<150	ng/mL
Benzoylecgonine	237	<100	ng/mL
See Note 1			
Heroin Metabolite	NEGATIVE	<10	ng/mL
Marijuana Metabolite 20	NEGATIVE	<20	ng/mL
MDMA/MDA	NEGATIVE	<500	ng/mL
Methadone Metabolite	NEGATIVE	<100	ng/mL
Opiates	NEGATIVE	<100	ng/mL
Oxycodone	NEGATIVE	<100	ng/mL
Phencyclidine	NEGATIVE	<25	ng/mL

What to do When a Patient Refuses a Drug Test

- The explicit policy of the American Academy of Pediatrics is that physicians should not order a drug test without the adolescent patient's knowledge or consent.
- If a patient refuses an indicated drug test, parents should set limits using logical consequences.
- An example would be restriction of driving or other activities until the adolescent agrees to a drug test, and parents could ascertain the safety of these activities.

AAP Clinical Report:
Testing for Drugs of Abuse in Children and Adolescents
Levy, Siquirera & COMMITTEE ON SUBSTANCE ABUSE
June 2014

- "Many national organizations, including the AAP, have consistently cautioned against involuntary drug testing in adolescents. Adolescents should be engaged in their own care…**Drug testing of a competent adolescent without his or her consent is, at best, impractical and without his or her knowledge is unethical and illegal**. However, an adolescent's refusal to consent to a drug test should not prematurely conclude an evaluation of a substance use problem or disorder…"

American Academy of Pediatrics

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Recent Challenges in Urine Toxicology

- Development of designer drugs that can evade detection in standard urine drug tests
- Testing for fentanyl as part of routine drug screening: Why has it been such an uphill battle?
- Tyler’s Law, California

Novel Psychoactive Substances

- Also known as designer or synthetic drugs or “legal highs”
- Designed to have similar effects to illegal drugs; circumvent national and international drug scheduling laws
- Popularity began to rise in the mid 2000’s; >1000 different NPS reported worldwide
- Quest Diagnostics NPS test includes designer opioids, designer fentanyl analogues, designer benzodiazepines, designer stimulants, synthetic cannabinoids

NPS class	NPS analyte	Analyte cutoff (ng/m)[a]	Drug class cutoff (ng/mL)
Designer benzodiazepines	Aminoclonazolam	2	10
	Bromazolam	2	
	Clonazolam	1	
	Desalkylflurazepam	5	
	Deschloroetizolam	1	
	4Cl-Deschloroalprazolam	2	
	Etizolam	2	
	Flualprazolam	1	
	Flubromazepam	10	
	Flubromazolam	1	
	Fluetizolam	5	
	Hydroxy-Bromazolam	5	
	Hydroxy-Flualprazolam	10	
	Hydroxy-Flubromazolam	10	
	Phenazepam	10	

NPS class	NPS analyte	Analyte cutoff (ng/m)[a]	Drug class cutoff (ng/mL)
Designer fentanyl analogs	Acetyl Fentanyl	1	5
	Acryl Fentanyl	5	
	Alfentanil	1	
	Butyryl Fentanyl/Isobutyryl Fentanyl	5	
	Carfentanil	2	
	Chlorofentanyl (*o*- and *p*-)	1	
	Cyclopropyl Fentanyl	5	
	p-Fluorobutyryl Fentanyl	1	
	Fluorofentanyl (*o*-, *m*-, and *p*-)	5	
	Furanyl Fentanyl	2	
	Methoxyacetyl Fentanyl	1	
	Sufentanil	1	
	Tetrahydrofuranyl Fentanyl	2	
	Valeryl Fentanyl	1	

NPS class	NPS analyte	Analyte cutoff (ng/m)[a]	Drug class cutoff (ng/mL)
Designer opioids	5-Amino-Isotonitazene	5	10
	Brorphine	1	
	Desethyl Isotonitazene	5	
	Dipyanone	1	
	Etodesnitazene	2	
	Hydroxy-Nitazene	5	
	Isotonitazene	5	
	2-Methyl AP-237	1	
	5-Methyl-Etodesnitazene	5	
	Metonitazene	1	
	Piperidinyl Etonitazene	5	
	Piperidinyl Hydroxy-Nitazene	10	
	Protonitazene	5	
	Pyrrolidino Etonitazene	2	
	Pyrrolidino Hydroxy-Nitazene	10	
	Pyrrolidino Metonitazene	5	
	Pyrrolidino Protonitazene	2	

NPS class	NPS analyte	Analyte cutoff (ng/m)[a]	Drug class cutoff (ng/mL)
Designer stimulants	Cyclohexyl Butylone	2	10
	Cyclohexyl Methylone	1	
	2F-Deschloroketamine	1	
	Dimethyl Pentylone	5	
	Eutylone	2	
	Fluorexetamine	2	
	Hydroxy-PCP	1	
	Methylmethcathinone (2-, 3-, and 4-)	1	
	Pentylone	5	
	α-PHP/α-PiHP	5	
	Propyl Butylone	1	
	α-PVP	10	

Synthetic cannabinoids	ADB-BINACA	2	10
	ADB-5Br-BINACA	2	
	ADB-5Br-PINACA	2	
	ADB-BUTINACA	2	
	ADB-BUTINACA N-butanoic acid (NBA) metabolite	10	
	ADB-BUTINACA N-(4-hydroxy-butyl) (NHB) metabolite	5	
	ADB-FUBIATA	2	
	ADB-FUBIATA dimethyl butanoic acid (DBA) metabolite	5	
	BZO-CHMOXIZID	2	
	BZO-4en-POXIZID	2	
	CH-FUBIATA	2	
	CH-PIATA	2	
	4F-MDMB-BUTICA	2	
	4F-MDMB-BUTICA butanoic acid (BA) metabolite	2	
	4F-MDMB-BUTINACA	2	
	4F-MDMB-BUTINACA carboxy indazole (CI) metabolite	10	
	5F-MDMB-PICA	2	
	5F-MDMB-PICA metabolite 7 (M7)	2	
	MDMB-4en-PINACA	2	
	MDMB-4en-PINACA butanoic acid (BA) metabolite	2	
Other illicit additives	Hydroxy-Xylazine	10	10
	Tianeptine	2	
	Xylazine	1	

“Decade long struggle for a POC fentanyl test”

- Dec 2022: FDA approved a qualitative POC instrument for testing urine for fentanyl
- Categorized under CLIA as moderate complexity, precludes use in many health care settings
- Urine fentanyl test strips represent a viable alternative
- The FDA could expand access to POC fentanyl testing by classifying urine test strips and similar test options as CLIA waivered.

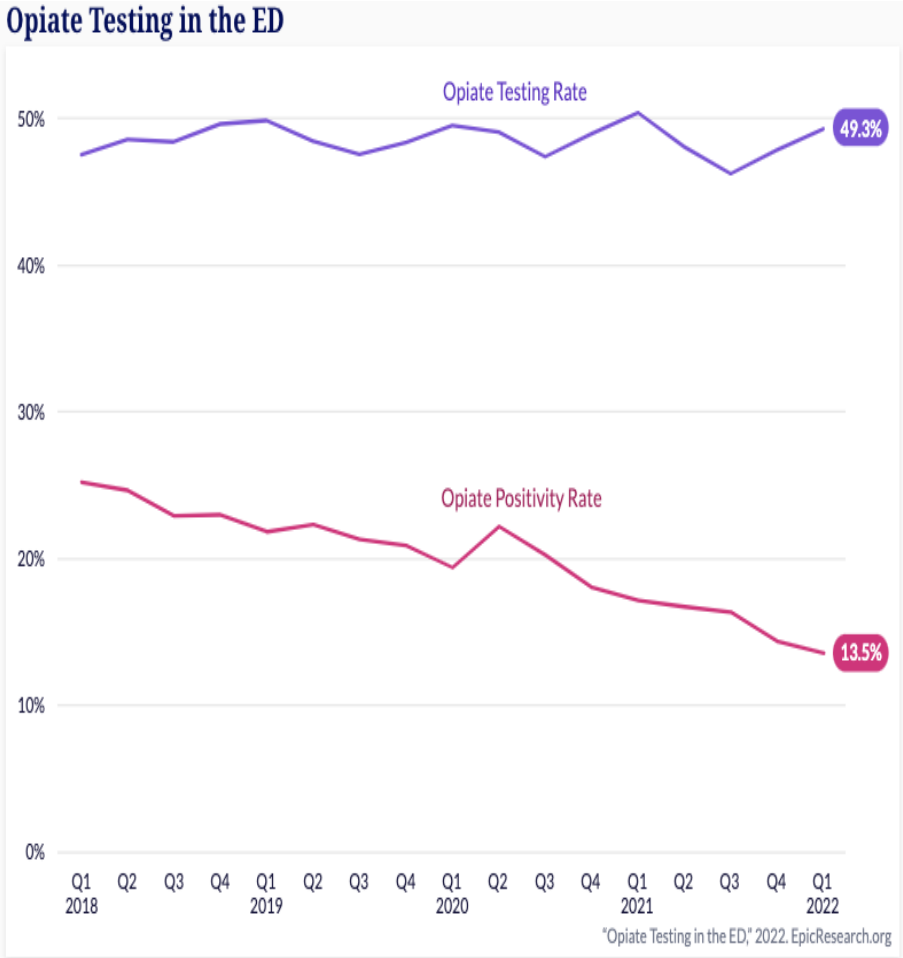
The NEW ENGLAND JOURNAL of MEDICINE

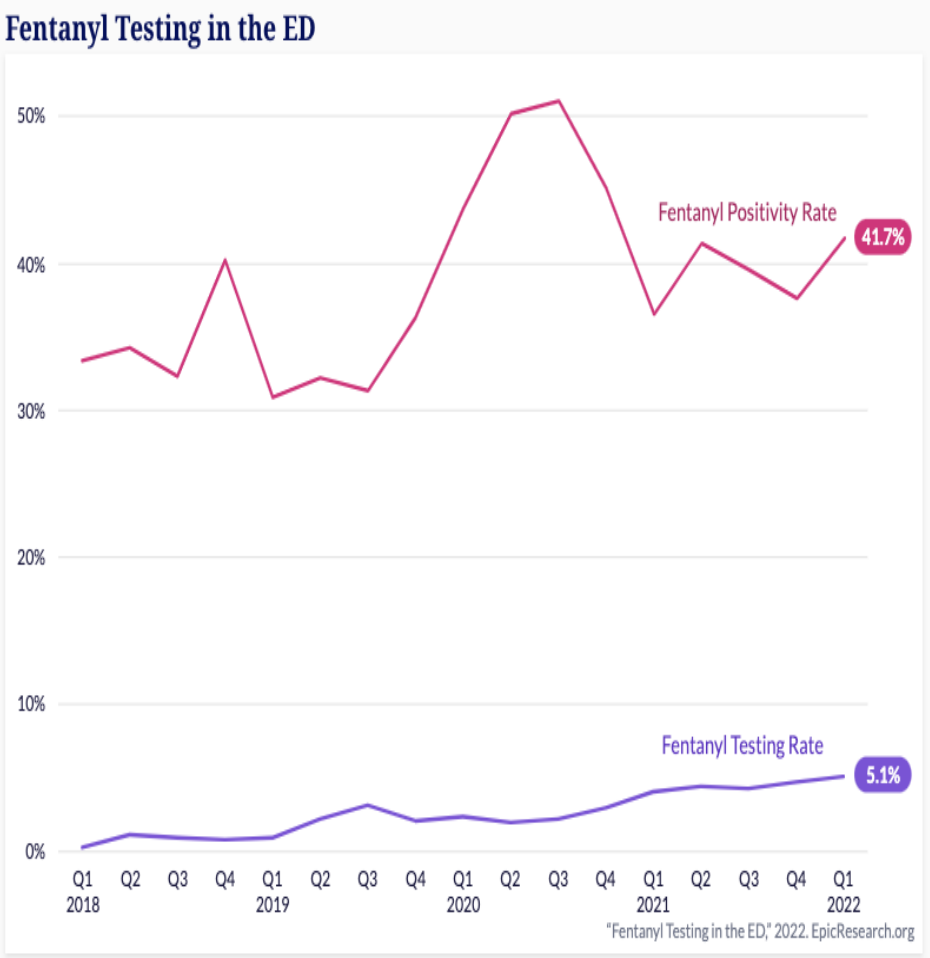
Perspective

Scaling Up Point-of-Care Fentanyl Testing — A Step Forward

Brian S. Barnett, M.D., Peter R. Chai, M.D., M.M.S., and Joji Suzuki, M.D.

Testing in ED Overdose Encounters, 2017-2022 (315,467 visits)





Epic Research D Little et al, August 23, 2022, Only 5% of overdose patients tested for fentanyl, #1 killer of Americans 18-45.

Tyler’s Law in California Passed in 2023

Fentanyl accounts for a majority of fatal overdoses. But ERs aren’t testing for it.

After her son's death in 2018, Juli Shamash began advocating for legislation that would require hospitals to test for fentanyl. Tyler’s Law took effect in California this year.

NBC News, March 17, 2023

Summary

Urine drug testing is a complex procedure!

- Use proper collection procedures.
- Check for dilution.
- Confirm all positive tests.
- Use extended panels if indicated by history.
- Use caution in interpreting tests.

References

- Clinical Drug Testing in Primary Care. SAHMSA Technical Assistance Publication Series, TAP 32
- Review: Clinical Interpretation of Urine Drug Tests: What Clinicians Need to Know about Urine Drug Screens. Moeller K et al, *Mayo Clinic Proceedings*, May 2017, pp 774-796.

Questions?

ORN Evaluation Survey Link

Please scan the below QR code or use the link below to access a very brief survey.

Link to survey:
https://orn.qualtrics.com/jfe/form/SV_3FdzXtRH7gogcHI?RequestID=5826&ActivityType=2&Intensity=2&Training=1&Date=4/10/24&Name=DrMimiSchizer

The survey will ask about your satisfaction with the training program you just completed as well as some basic demographic information. Your responses will help the Opioid Response Network improve the services they provide.

Thank you in advance for completing this survey!