Toxicology Testing: Limitations and Complexities

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Disclosures

None

Learning Objectives

Describe the major differences between screening and confirmatory tests

List three major limitations of screening tests

Appreciate the importance of informed consent

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What can tox testing tell you?

A tox test MIGHT tell you if a patient was exposed to a substance or a class of substances
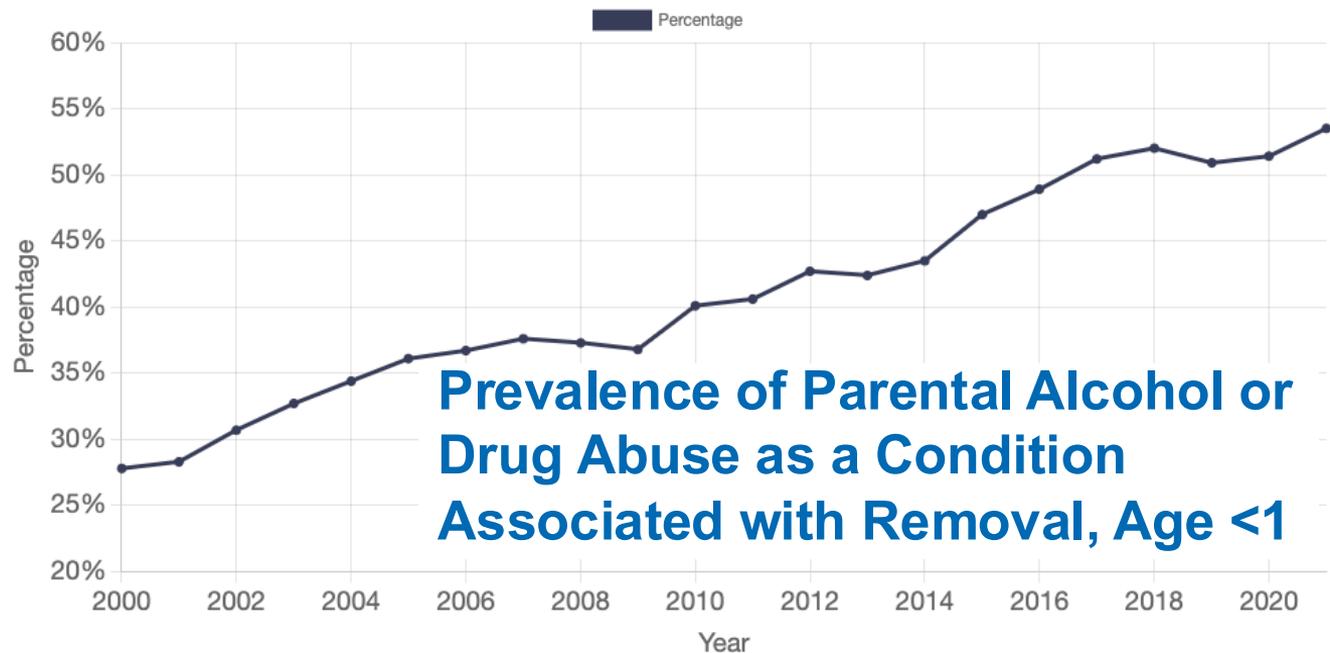
A tox test WILL NOT tell you:

- Who administered the drug
- The route of administration
- How much drug was administered
- When the exposure occurred
- Whether, and to what degree, a person was impaired/intoxicated
- **Whether a person was/is fit to parent or is a safe caregiver**
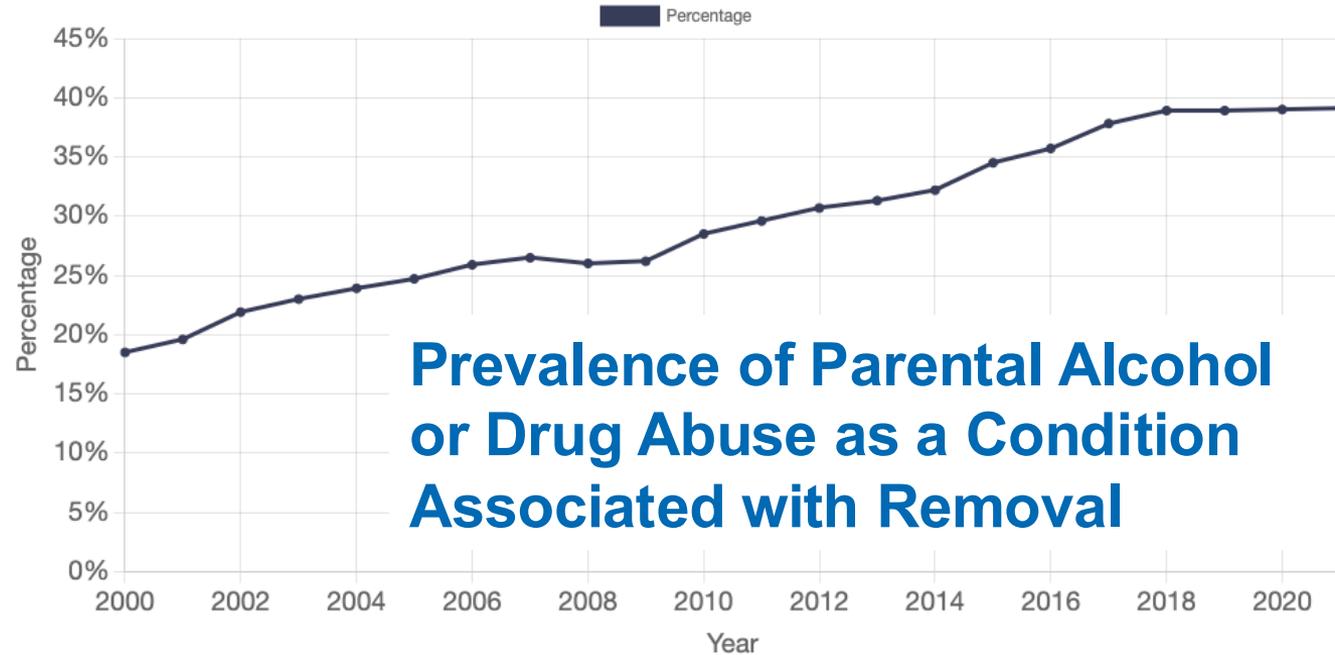
Prevalence of Parental Alcohol or Drug Abuse as a Condition Associated with Removal

The percentage of children in out-of-home care with parental alcohol or other drug (AOD) abuse as a condition associated with removal has steadily increased from 18.5% in 2000 to 39.1% in 2021.

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Prevalence of Parental Alcohol or Drug Abuse as a Condition Associated with Removal, Age <1

The percentage of children under age 1 who entered out-of-home care with parental alcohol or drug abuse as a condition associated with removal increased from 27.8% in 2000 to 53.5% in 2021.

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Confusing words

Screening:

- Process of gathering information from patient about substance use
- Use clinician-administered or self-administered validated tool
- ALL PREGNANT AND BIRTHING PEOPLE should be screened for substance use

Testing:

- Collection of a biological sample that assesses for the presence of a substance and/or its metabolite
- A positive SCREEN does not always necessitate a toxicology TEST

Screening Tests vs. Confirmatory Tests

Screening tests:
- Usually immunoassays
- Usually qualitative
- Riddled with false positives and false negatives
- Inexpensive
- Fast
- Readily available

Confirmatory tests:
- Usually HPLC, GC/MS or LC/MS (or similar)
- Quantitative
- Highly accurate and precise
- Expensive
- Slow
- Usually requires "sending out"

Nuances of urine drug screening tests

What you find depends on what you look for and where you look for it

Cross reactivity is a major problem for immunoassays

There is a "threshold" or minimum amount necessary to make the test read "positive"

What you find depends on what you look for

Hospital 1:
- Amphetamines
- Benzodiazepines
- Cocaine metabolites
- Methadone
- Opiates

Hospital 2:
- Amphetamines
- Barbiturates
- Benzodiazepines
- Cannabinoids
- Cocaine metabolites
- Ethanol
- Opiates
- Phencyclidine
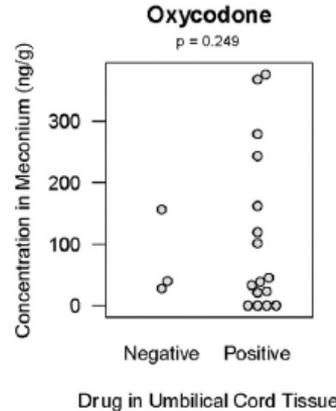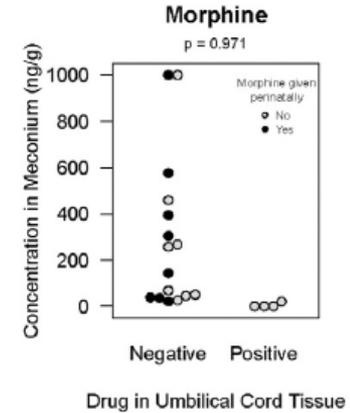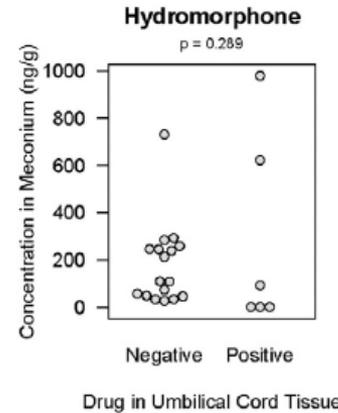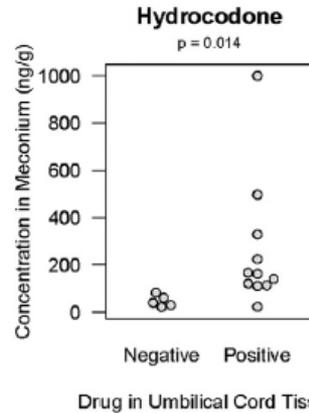
Hospital 3:
- Amphetamines
- Barbiturates
- Benzodiazepines
- Cannabinoids
- Cocaine metabolites
- Methadone
- Methamphetamine
- Opiates
- Oxycodone
- Phencyclidine
- Propoxyphene
- Tricyclic antidepressants
- Buprenorphine

Comparison of umbilical cord tissue and meconium for the confirmation of in utero drug exposure

Jennifer M. Colby

…and where you look for it

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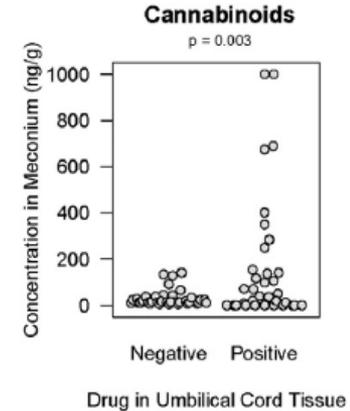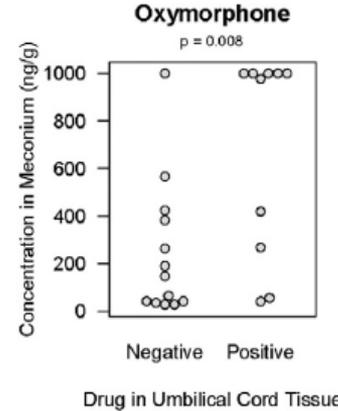
Evaluating a switch from meconium to umbilical cord tissue for newborn drug testing: A retrospective study at an academic medical center

Kendra L. Palmer [a], Kelly E. Wood [b], Matthew D. Krasowski [a,*]

Table 4
Concordance in umbilical cord tissue drug analysis between twins and triplets sorted by degree of separation.

	Di/di twins[a]	Mono/di twins[a]	Triplets (all three infants tested)
Umbilical cord negative for all multiples	18	4	1
Umbilical cord positive			
Complete agreement	6	1	0
Different in drugs detected[b]	2	0	0

[a] Di/di, dichorionic/diamniotic; mono/di, monochorionic/diamniotic. No monochorionic/monoamniotic twins were in dataset.

[b] One case of phentermine detected in one twin but not other; other case had THC metabolite detected in one twin but not other.

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Cross Reactivity (and lack thereof)
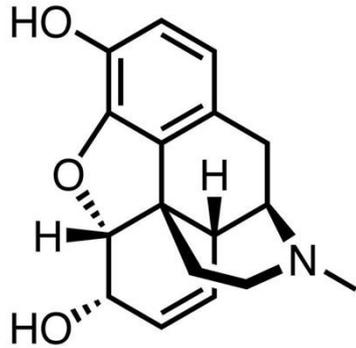
Morphine
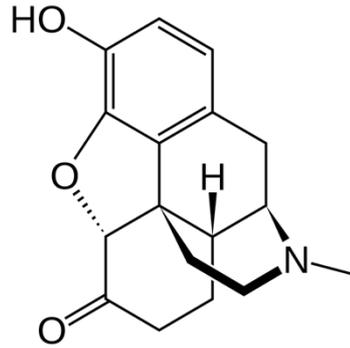
Hydromorphone
(Dilaudid)

Fentanyl

Cross Reactivity

Fentanyl
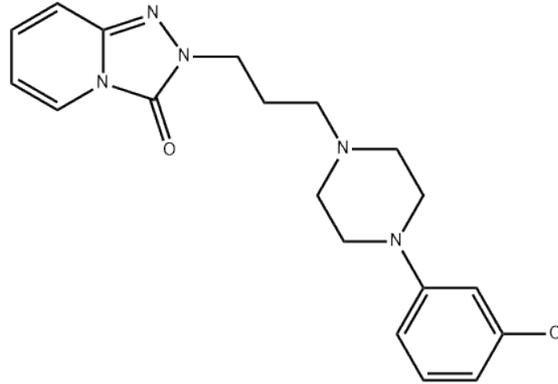
Trazodone
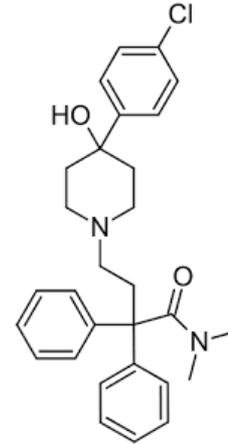
Loperamide

Documented causes of fentanyl false + UDS

Loperamide (Geno 2022)

Risperidone (Shroitman 2021)

Ziprasidone (Waters 2003)

Labetalol (Wanar 2022) **btw this pt was pregnant

Methamphetamine (Abbott 2022)

Haloperidol (Wang 2024)

Trazodone (Wang 2024)

Performance of Two Fentanyl Immunoassays against a Liquid Chromatography–Tandem Mass Spectrometry Method

Sheng Feng, Theodore J. Rutledge, Maureen Manzoni, Thuan Le, JoAnn Gardiner, Michael Milone, Leslie Shaw and Ping Wang*
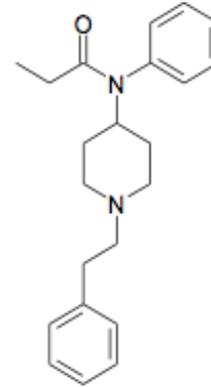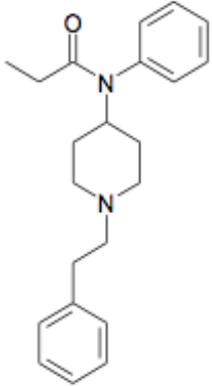
Performance of Fentanyl Immunoassays in an ED Patient Population

Catherine M. Mills,[a] Parker C. Dryja,[a,b] Elizabeth Champion-Lyons,[a] Charles Keppler,[a] and Nikolina Babic [a,*]

Immunoassay		LC–MS-MS	
		Positive	Negative
ARK	Positive	57	8
	Negative	0	217
SEFRIA	Positive	54	44[a]
	Negative	3	181

		Fentanyl present[a]	Fentanyl absent[b]	Total
ARK II	Detected	19	2	21
	Not detected	1	188	189
	Total	20	190	210
SEFRIA	Detected	19	5	24
	Not detected	1	185	186
	Total	20	190	210

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ARK: 8/65 positives were false + (12.3%)

ARK II: 2/21 positives were false + (9.5%)

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Journal of Analytical Toxicology, 2021;45:117–123

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	Not detected	1	185	186
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SEFRIA: 44/98 positives were false + (44.9%)

SEFRIA: 5/24 positives were false + (20.8%)

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SEFRIA	Detected	19	5	24
	Not detected	1	185	186
	Total	20	190	210

SEFRIA: 3/184 negatives were false - (1.6%)

SEFRIA: 1/186 negatives were false - (0.5%)

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Common causes of false positives

Drug Classification	Potential Interference
Amphetamines	ADHD medications Decongestants Bupropion Ephedrine (Ma Huang)
Methadone	Diphenhydramine Doxylamine Vortioxetine Quetiapine
Phencyclidine	Dextromethorphan Ketamine Diphenhydramine
TCA	Diphenhydramine Quetiapine Cyclobenzaprine

THIS IS <u>NOT</u> AN ALL INCLUSIVE LIST

Cross reactivity across brands

Drug	Company 1	Company 2	Company 3
l-Amphetamine	1	101	100
d.l-Amphetamine	88	58	100
Methamphetamine	100	100	100
d,l-Methamphetamine	77	65	100
MDA	116	2	100
MDMA	196	69	30
Ephedrine	1	1	50
Fenfluramine	1	1	10
Pseudoephedrine	1	1	100

Thresholds for positivity (aka cut offs)

Initial Test Analyte	Initial test cutoff	Confirmatory analyte	Confirmatory test cutoff concentration
Marijuana Metabolites (THCA)	50 ng/m	THCA	15 ng/mL
Cocaine Metabolite (Benzoylecgonine)	150 ng/mL	Benzoylecgonine	100 ng/mL
Phencyclidine (PCP)	25 ng/mL	Phencyclidine (PCP)	25 ng/mL
Amphetamine			
Amphetamine	500 ng/m	Amphetamine	250 ng/mL
Methamphetamine	500 ng/mL	Methamphetamine	250 ng/mL
MDMA/MDA	500 ng/mL	MDMA/MDA	250 ng/mL
Opioids			
Codeine/Morphine	2000 ng/mL	Codeine/Morphine	2000 ng/mL
6-Acetylmorphine (6AM or Heroin)	10 ng/mL	6-Acetylmorphine (6AM or Heroin)	10 ng/mL
Hydrocodone	300 ng/mL	Hydrocodone	100 ng/mL
Hydromorphone	300 ng/mL	Oxymorphone	100 ng/mL
Oxymorphone	100 ng/mL	Oxymorphone	100 ng/mL
Oxycodone	100 ng/mL	Oxycodone	100 ng/mL

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Tox testing can be harmful

Inappropriate interpretation

Racial/ethnic disparities in child welfare reporting specifically related to substance use

Damage to the therapeutic alliance during this and future healthcare encounters

Tox testing can be beneficial

Diagnostic tool to guide medical management

Demonstrate sobriety or compliance with therapy

Informed consent

Opportunity to build/enhance the therapeutic alliance

Necessary before testing a birthing person unless the patient lacks capacity

Best practice in most cases of newborn testing. If consent is not obtained, testing should only be sent if there is a compelling medical need

Many professional societies and governmental agencies (ACOG, ASAM, SAMHSA) clearly state that informed consent (usually a separate written consent) is best practice

Informed consent is poorly documented when obtaining toxicology testing at delivery in a Massachusetts cohort

Kathleen J. Koenigs MD; Joseph H. Chou MD PhD; Samuel Cohen MD; Moira Nolan BA; Gina Liu MSc; Mishka Terplan MD MPH; Brian M. Cummings MD; Timothy Nielsen MPH; Nicole A. Smith MD MPH; Joseph Distefano BS; Sarah N. Bernstein MD; Davida M. Schiff MD MSc

N=929 tested at a hospital with consent policy

341/929 = 36.7% with documented consent

588/929 = 63.3% no documented consent

Characteristics	Crude Odds Ratios*			Adjusted Odds Ratios**		
	OR	95% CI		OR	95% CI	
Hospital consent policy						
Yes	2.29	1.40	3.74	**2.10**	**1.01**	**4.37**
No	1.00	reference		1.00	reference	
Primary testing indication						
Recent non-prescribed use	1.00	reference		1.00	reference	
Opioid agonist therapy	1.37	0.87	2.16	1.23	0.77	1.97
Remote non-prescribed use	2.06	1.11	3.83	1.85	0.98	3.49
Cannabis use	**1.60**	**1.18**	**2.17**	**1.44**	**1.05**	**1.97**
Monitoring medicine	1.75	0.58	5.25	2.18	0.68	7.00
Maternal complication	**0.41**	**0.27**	**0.63**	**0.46**	**0.28**	**0.76**
Inadequate prenatal care	1.33	0.82	2.18	1.09	0.64	1.86
Other/unknown	0.97	0.52	1.83	0.78	0.40	1.53

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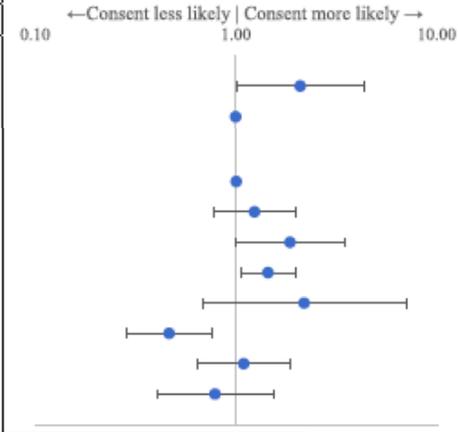
What if testing is declined?
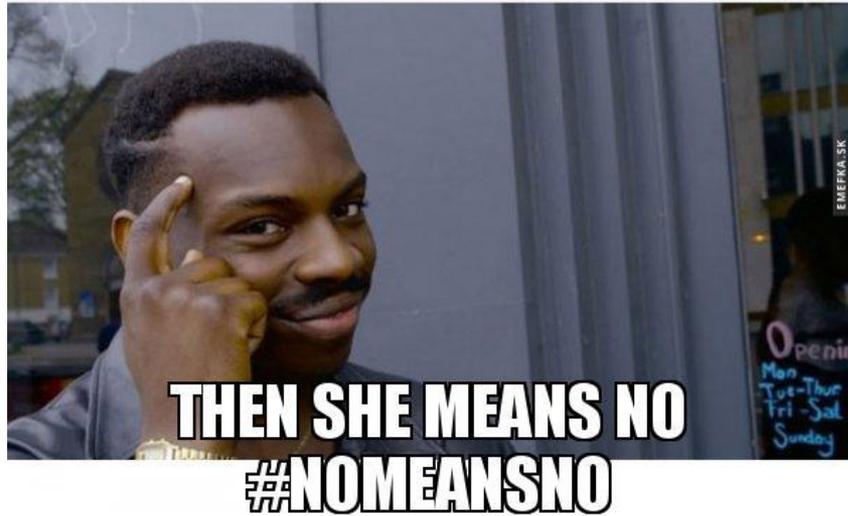
Her Parenting Time Was Restricted After a Positive Drug Test. By Federal Standards, It Would've Been Negative.

by Alice Hines, graphics by Lucas Waldron

January 6, 2026, 5:00 am

https://www.propublica.org/article/drug-testing-thresholds-child-welfare

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In summary

Tox testing is complicated

Tox testing can be harmful and can be beneficial

If you order a tox test, you should be able to articulate **precisely** how the results will change your **clinical** management

Thank you!

Questions? Comments? Rude remarks? Email me! Laurie.halmo@childrenscolorado.org

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