Drug Screens: What, When, Who, and Why

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Goals and Objectives

- Understand the different types of drug screens
- Understand the limitations and uses of drug screens
- Understand how to interpret drug screens

Speaker disclaimer:

- None that I can think of

LEGAL disclaimer!

- KEEP IN MIND – this lecture does not cover legal procedure, chain of evidence etc
- I defer that to a different expert!

First of all. Why test?

- Most common reasons to confirm or exclude a toxic exposure
- Used to increase diagnostic certainty
- Intensity of exposure (quantitative)

Toxicological assays

- Large variety of screens with remarkable variability
- Many of the vary in the sensitivity and specificity
- Quantitative – usually require serum
- Qualitative – most urine tests (present or not)

Quantitative tests

- Acetaminophen
- Carbamazepine
- Co-oximetry (methemoglobin, carboxyhemoglobin etc)
- Digoxin
- Salicylate
- Several others

Qualitative tests

- Amphetamines
- Barbiturates
- Cocaine
- Opiates
  - Methadone, oxycodone etc
- Propoxyphene
- PCP
- TCAs

Our focus - the "UDS"

- We are looks most specifically at drugs of abuse screens
- Too large a topic to cover everything
- Will not include alcohol (serum v whole blood)
- Will not include other mediums (spit, hair etc)

Relative Comparison of Drug tests

Method	Sensitivity	Specificity	Quant?	Range of analytes	Speed	Cost
Spot test	+	+/-	No	Few	Fast	$
Spectochemical	+	+	Yes	Few	Med	$
Immunoassay	++	++	Yes	Mod	Med	$$
TLC	+	++	No	Broad	Slow	$$
HPLC	++	++	Yes	Broad	Med	$$
GC	++	++	Yes	Broad	Med	$$
GC/MS	+++	+++	Yes	Broad	Slow	$$$
LC/MS/MS	+++	+++	Yes	Broad	Med	$$$$

Spot test

- Not as widely used any more
- Simple
- Rapid reaction of xenobiotic with a colored reagent

Spectochemical

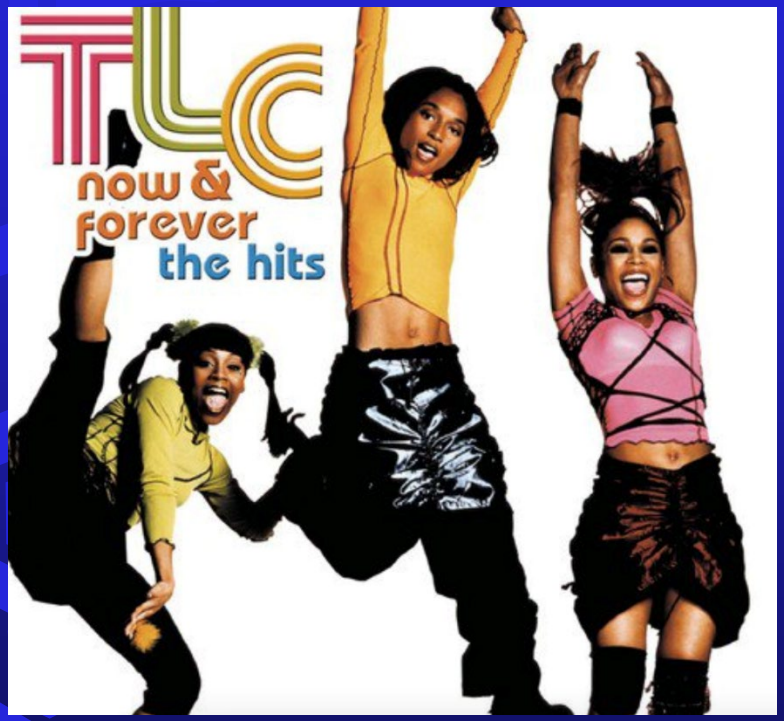
- Complex spot test
  - Rely on chemical reaction to form light absorbing substance
- Co-oximetry is a good example

TLC and HPLC

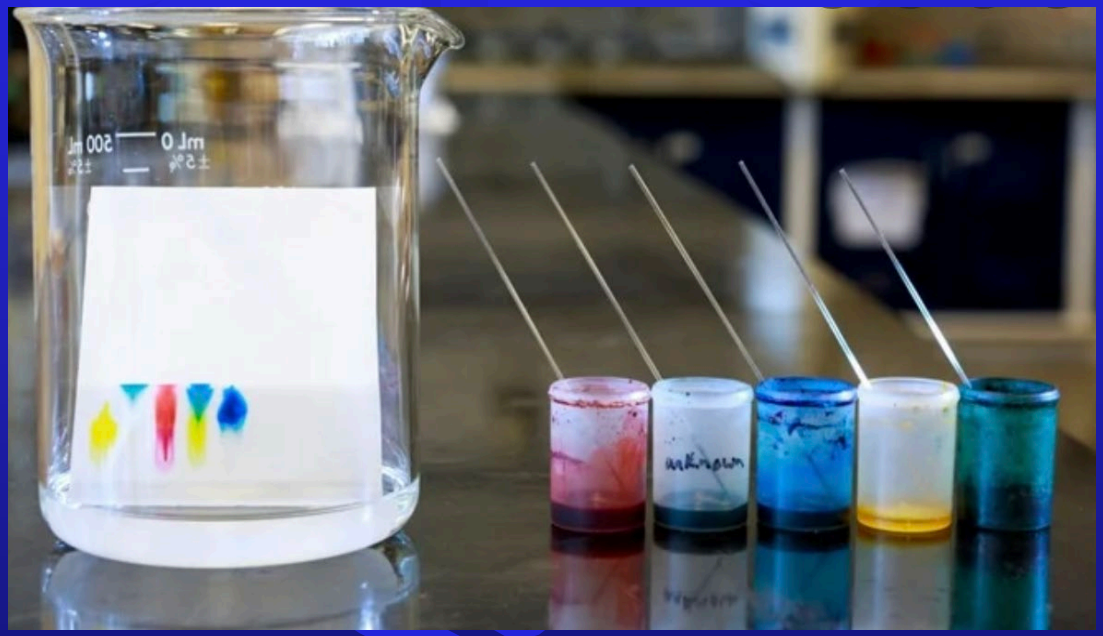
- Thin layer chromatography
- High performance liquid chromatography

TLC

- Not this one



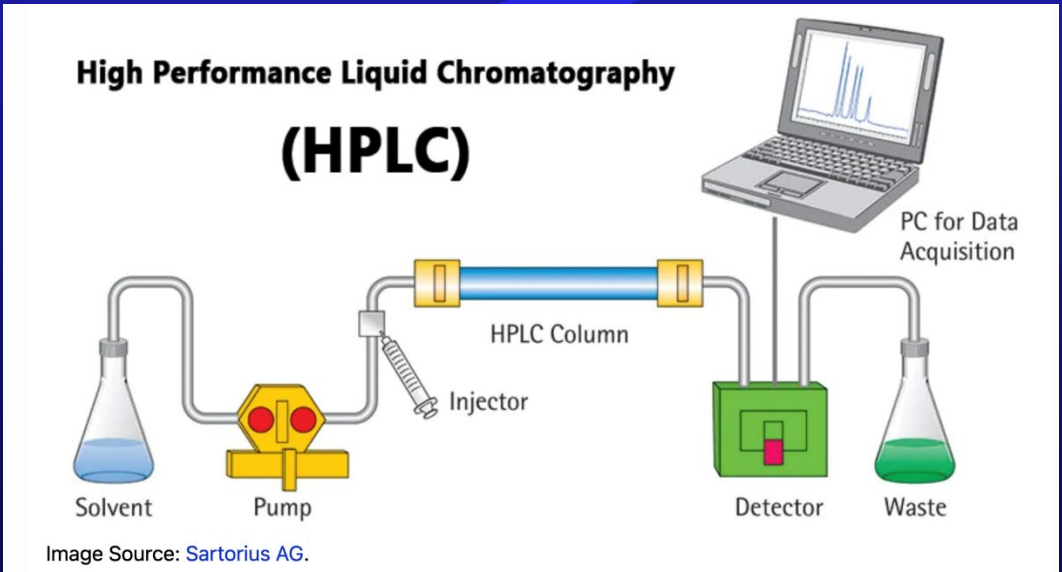
Didn't we all do this as kids?



- This one
- Takes many steps
- Substances move at different rates
- Can identify substance based on time/location of standard

HPLC

- Same idea
- Detect xenobiotic after the exit the column
- Identified by retention time



GC/GCMS/LCMSMS

- Gas chromatography
- Gas chromatography mass spectroscopy
- Liquid chromatography mass spec
- Similar except in gas states

GC-MS

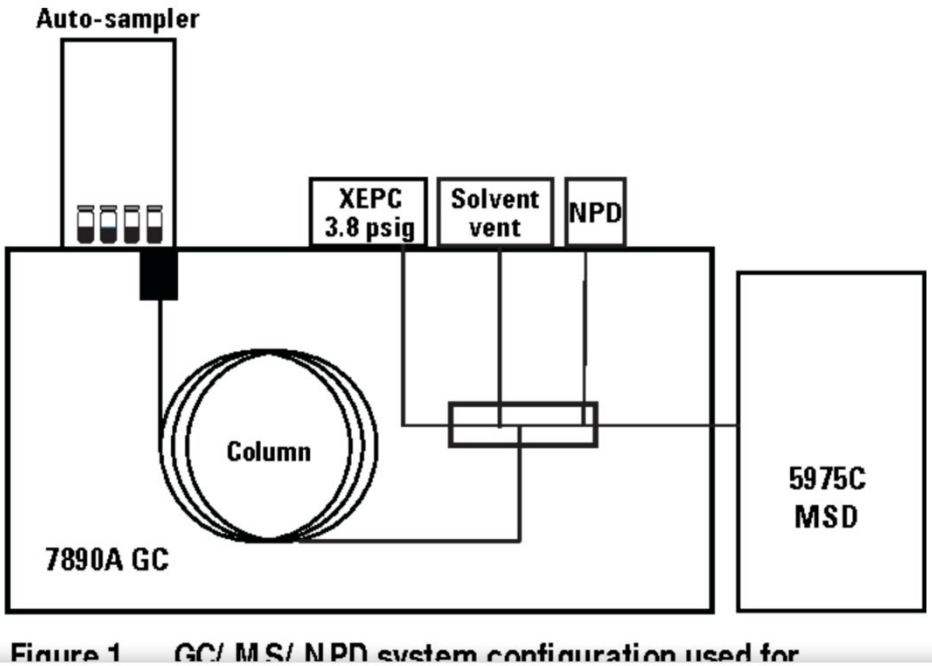


Figure 1 GC/ MS/ NPD system configuration used for

GC/MS/NPD system configuration used for screening blood extracts.

n 2008

d Forensic Toxicology Screening Using A GC / MS / NPD System with a 725-Compound DRS Database

Get something like this:

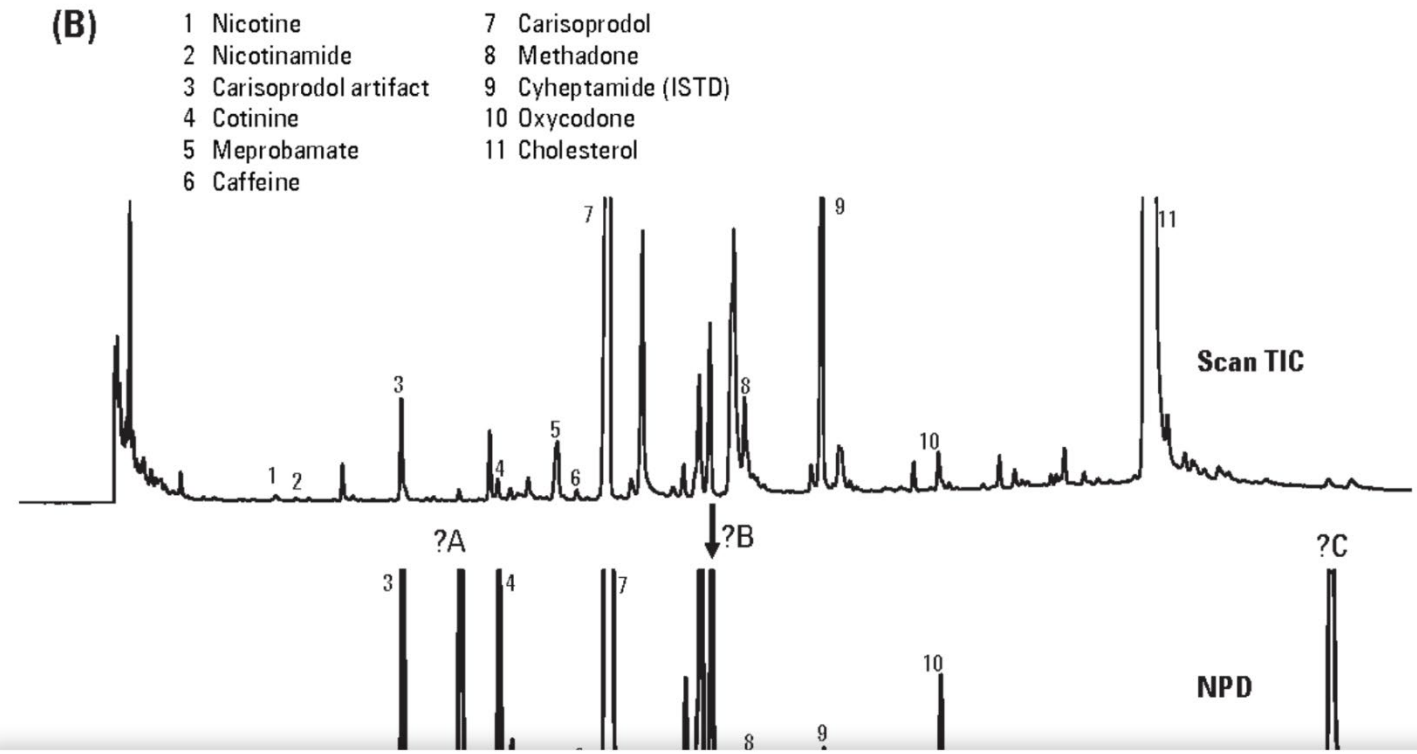
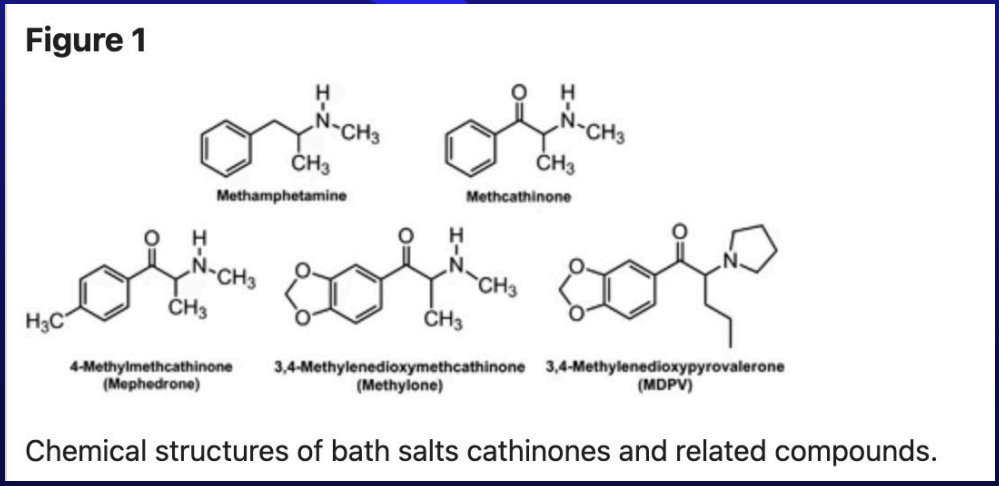


Figure 2B. Expanded scale chromatograms of scan TIC and NPD signals from analysis of blood extract. (continued)

Limitations:

- Have to have a library to compare
- So when ”new drugs” come along
- Eg. bath salts – have to identify one, test and create a standard that can be uploaded into a library



So what is the gold standard?

- GCMS, LCMS etc are considered the "gold standard"
- Sometimes called "comprehensive" drug screens
- Send out for most of us

Immunoassay – most applicable and common

- Drug screening immunoassays were developed for workplace drug screening
- But they are cheap, widely available and easy
- Hence they are what is most commonly used when we say “drug screen”

NIDA-5 – the most common

- 5 drugs recommended for screening of federal employees in 1988
  - Amphetamine
  - Cannabinoids
  - Cocaine
  - Opiates
  - Phencyclidine

- Other common screens
- Barbiturates, benzos, methadone, meperidine, propoxyphene, TCAs

There are many more depending on the type of test

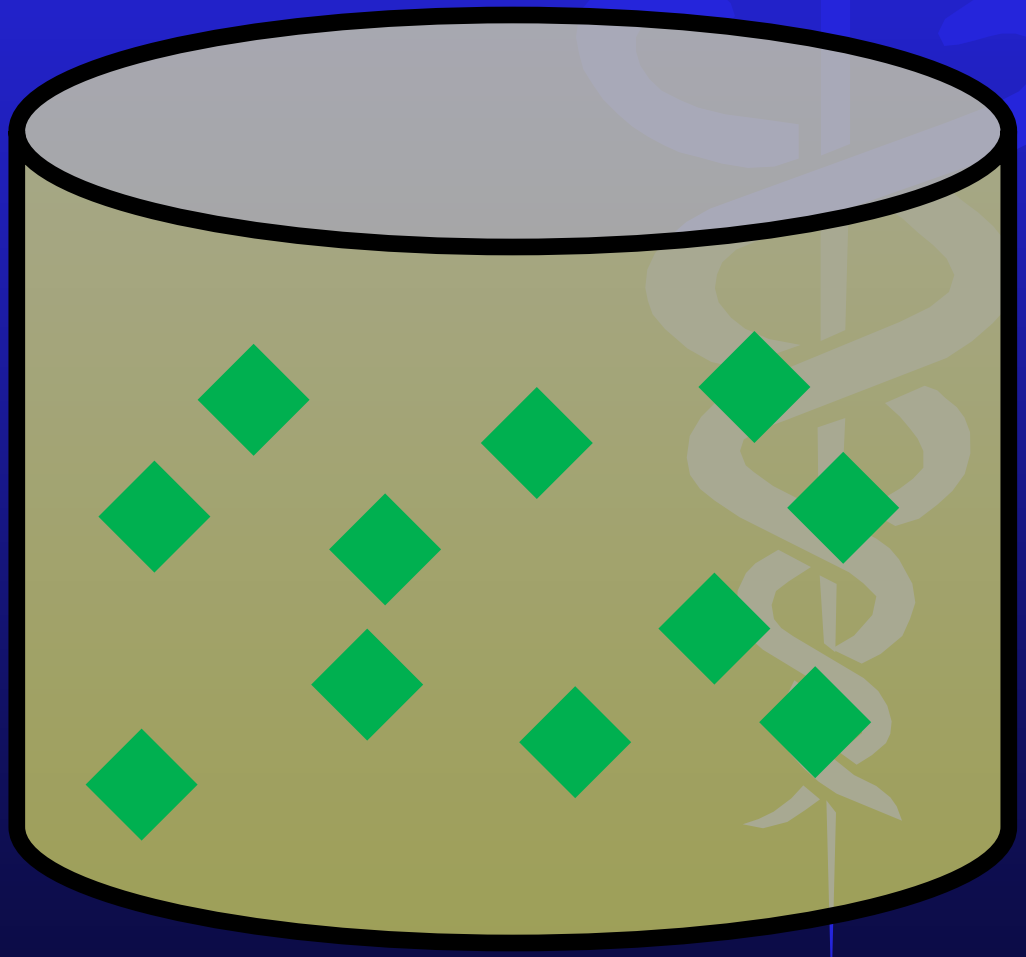
Test Results

- Are positive when they meet a predetermined cutoff
- Ideally high enough to minimize false positives from analytic variability or cross reactively
- Low enough to get a positive in someone using the drug
- May be a cause of confusion

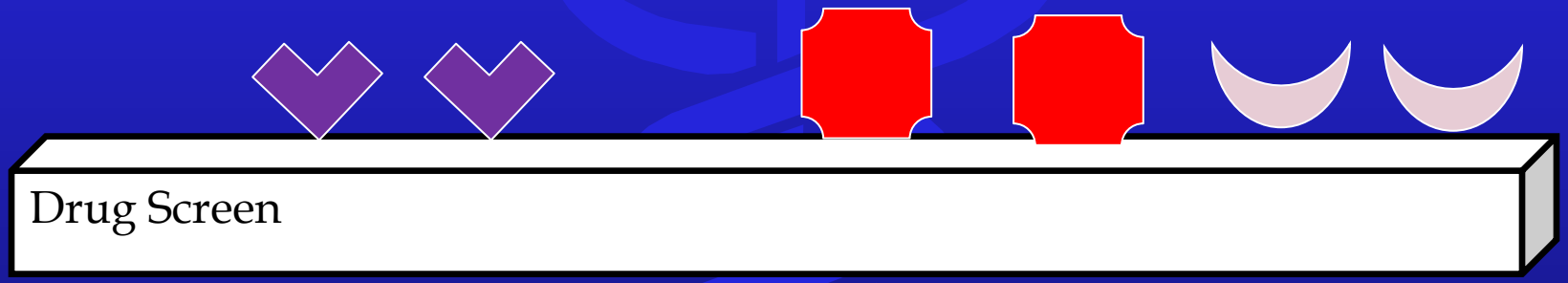
"I saw them take the drug and the screen is negative"

- Taken but the concentration is below the cutoff value
- Taken but not yet metabolized to the appropriate metabolite
- Taken but the particular drug in the class isn't picked up (benzos)

How they work



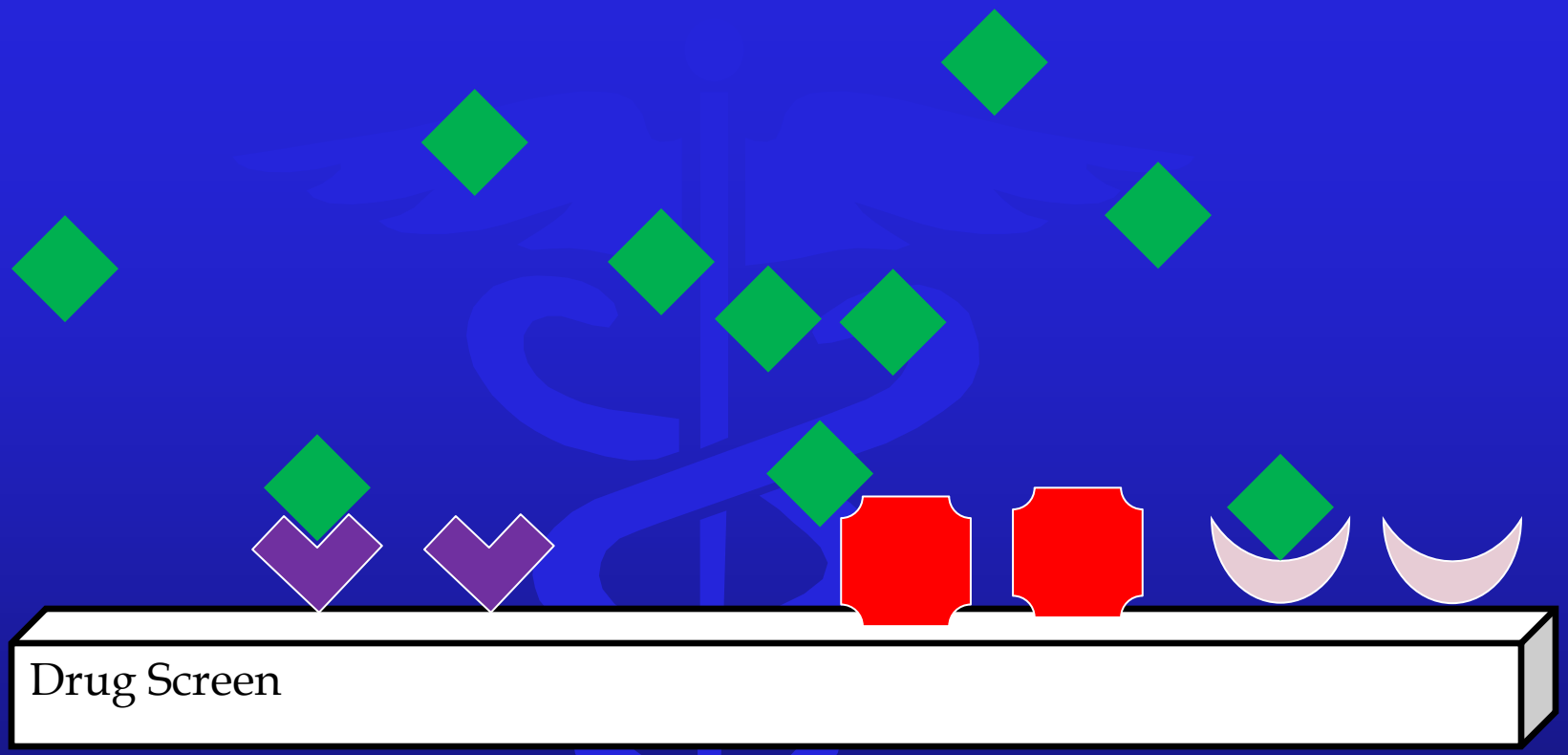
Drug or drug metabolite



Opioid

Amphetamines

Benzo


Drug Screen

- Some of these check for the drug
- Others for inactive metabolites (cannabis)

Confirmatory testing

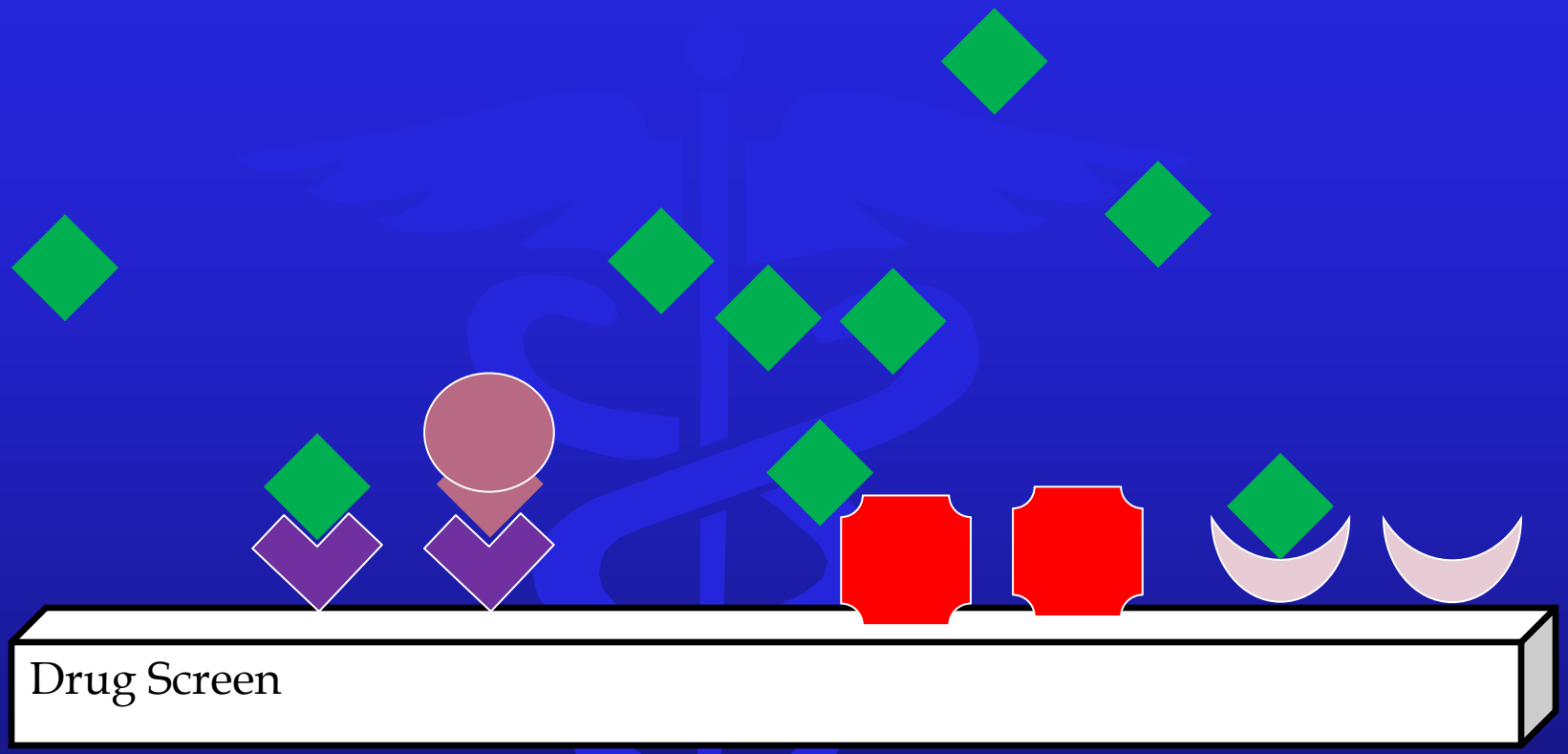
- If a screening test has sensitivity/specificity of 98%
- 2/100 may be a false positive

How to ensure best results?

- Two different types of testing
- GC/MS most common (less likely false positive and much more sensitive)

Cross reactivity

- Most common issue is methamphetamine
- Many similar structures and can have significant cross reactivity → false positive
- Eg. decongestants such as pseudoephedrine, herbal preparations containing l-ephedrine


Drug Screen

Incomplete list of common cross reactivities/errors

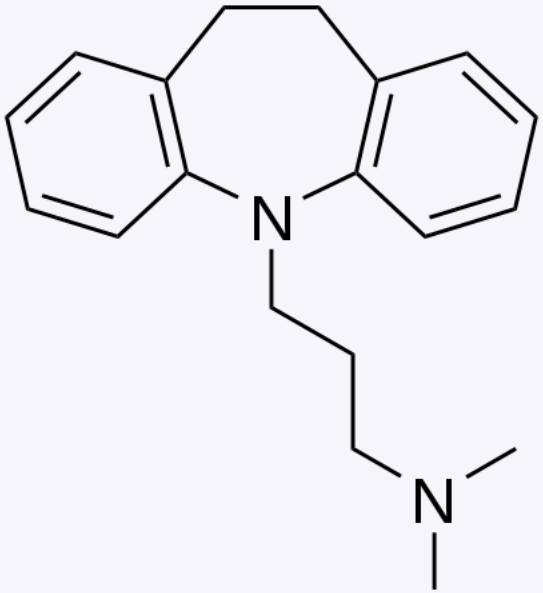
- Recommend looking at the package insert for the specific brand you use

Drug/class	Common false positive
Amphetamine	Decongestants, ephedrine, selegilene, bupropion
Benzos	Oxaprozin, may not detect all benzos
Cannabinoids	Detects inactive metabolites
Cocaine	Fairly specific, probably one of the better ones
Opiates	Minimal cross reactivity between classes - semisynthetic and synthetic. Quinolones may cross react
Methadone	Doxylamine
PCP	Dextromethorphan, DPH, ketamine, venlafaxine
TCA	SO MANY THINGS

Some examples..

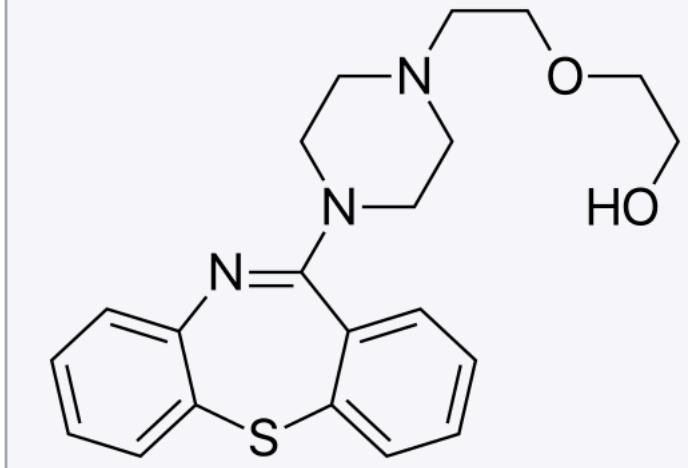
Tricyclic antidepressant

Drug class



Chemical structure of the prototypical and first marketed tricyclic antidepressant imipramine. Notice its three rings.

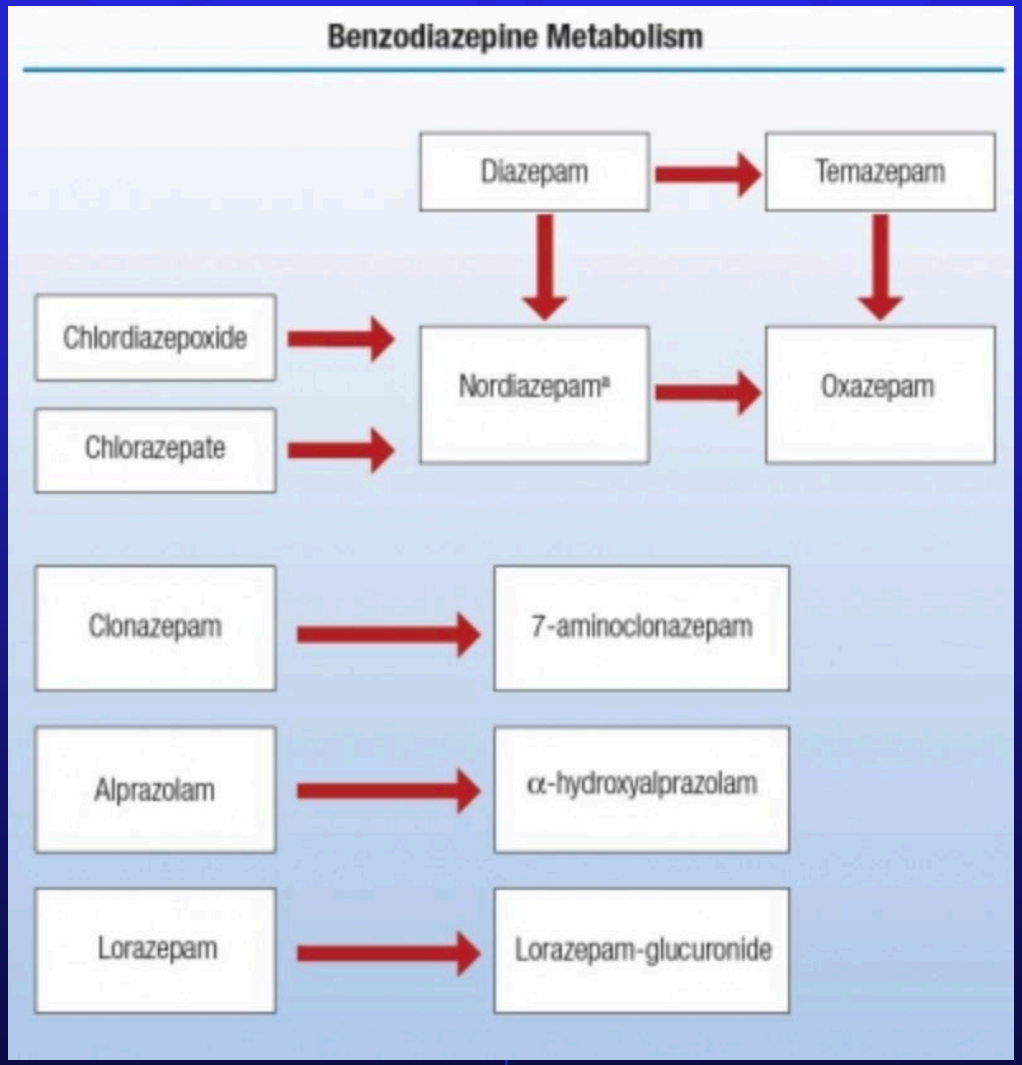
Quetiapine



Benzos – special beasts

- Variability
- Many assays screen for the metabolize oxazepam
- Oxazepam is a metabolite of many, but not ALL benzos
- False negative (lorazepam)

Benzo metabolism



In summary

- UDS we use is a great screening test
- But they are screening tests
- Recognize the limitations and fallibility
- If it is THAT important, get confirmatory testing
- If using in workplace or legal setting, make sure you know the process for screening vs confirmatory testing

References:

- Nelson et al. *Goldfrank's Toxicologic Emergencies*. 9th ed. Laboratory Principals
- Dept. Health and Human services, Substance Abuse and Mental Health Services Administration: *Fed Reg*. 2004; 69:19644-19673
- Lehner K et al. Psychoactive "bath Salts: compounds, mechanisms and toxicities. " *Neuropsych.* 2013. 38(234-244)
- Warner A. Setting Standards of practice in therapeuatic drug monitoring and clinical toxicology. A North American View. *Ther. Drug. Mon.*2000;22(93-97)