ASAM REVIEW COURSE 2025

Pharmacology and Toxicology: Principles, Applications, and Limitations

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Financial Disclosure

Lewis S. Nelson, MD, MBA, FASAM

- No relevant disclosures

Learning Objectives

1

Explain the differences between and clinical relevance of tolerance, dependence, and hyperalgesia.

2

Describe the pharmacologic principles of pharmacokinetics and pharmacodynamics and how each impacts addiction risk and addiction treatment.

3

Discuss the interpretation pitfalls of screening and confirmatory urine drug tests in the management of patients with substance use.

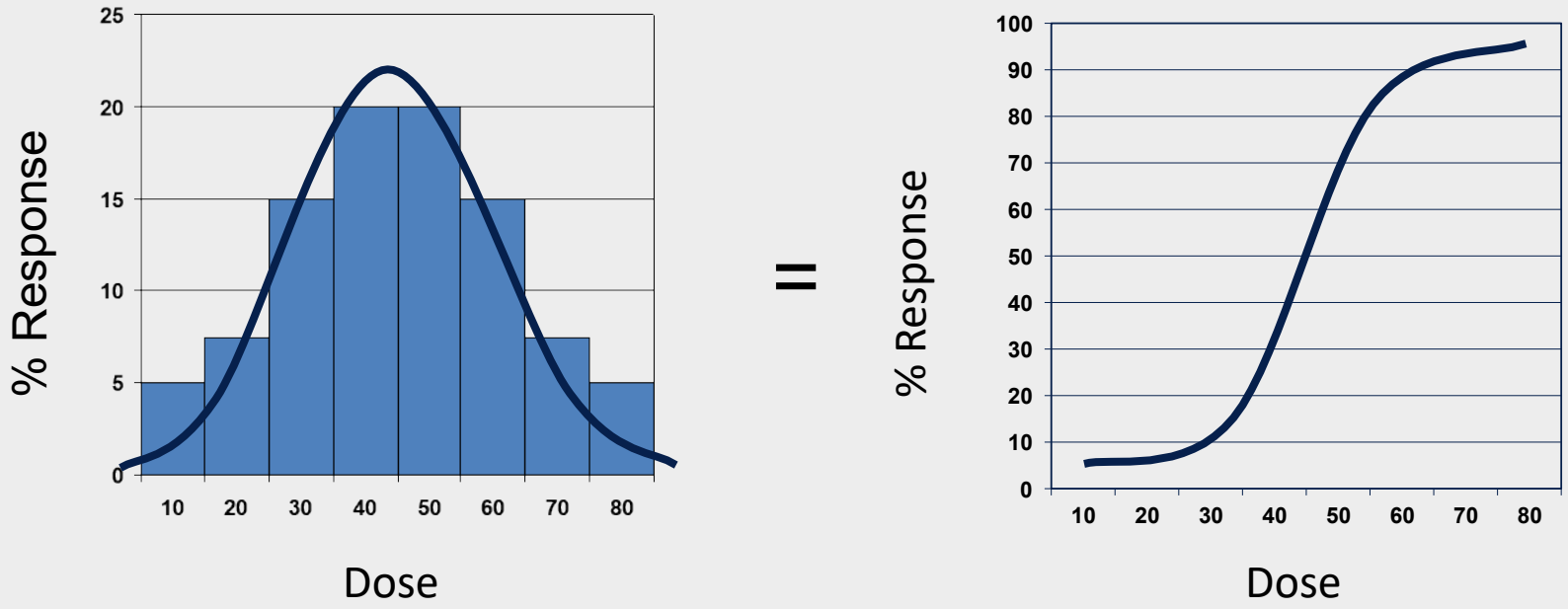
Addiction Medicine IS Pharmacology

- Drugs have to get to the brain to elicit a response.
  - Blood brain barrier is an effective barrier
- Euphoria – rate of rise
- Dependence – duration of exposure

Pharmacokinetics and Pharmacodynamics

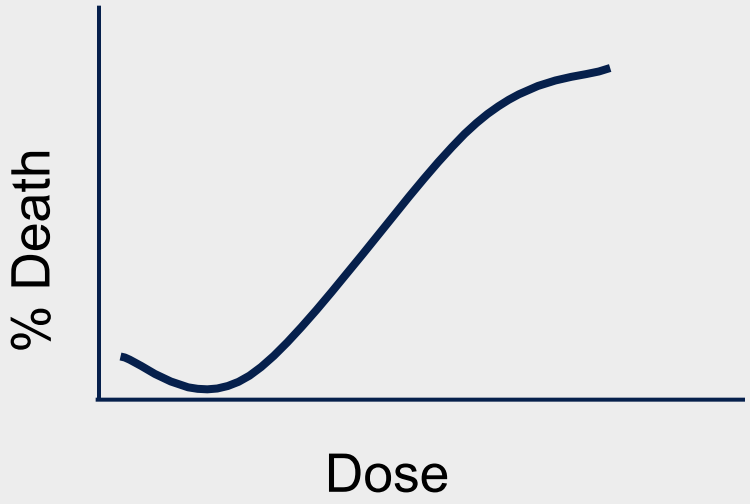
Absorption (Bioavailability)	Distribution	Elimination
Biotransformation	Dose Response (Clinical Effect)	Potency
Drug interaction	Tolerance	Dependence

Dose-Response

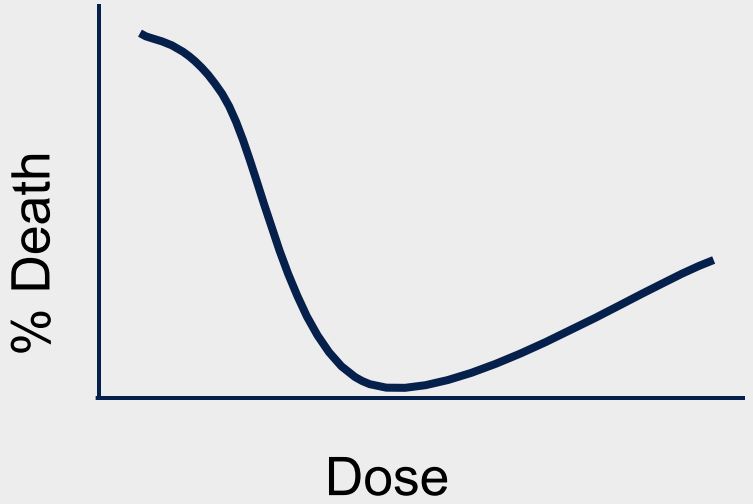


Response = Anything (Blood pressure, Euphoria, Death)

Dose-Response



Ethanol
Vitamins



Oxygen
Water

Response = Death

Potency

Rank order the potency at causing death:

Agent	LD50 (approx.)
Ethanol	5,000 (mg/kg)
Nicotine	2 (mg/kg)
Morphine	1 (mg/kg)
Fentanyl	0.01 (10 µg/kg)
Botulinum	0.000001 (2 ng/kg)

Don’t confuse potency with clinical effect

Which has more potent THC?

1980’s weed

Trick question:

The THC is the same potency

The higher concentration weed is more “potent”

Don’t confuse potency of a drug with its concentration

2020 weed

Potency doesn't really matter

Agent	Potency (vs morphine)
Tramadol	0.2
Morphine	1
Oxycodone	1.3
Methadone	4
Heroin	4
Buprenorphine	30
Fentanyl	100
Carfentanil	10,000

Any of these drugs will kill you if you take enough

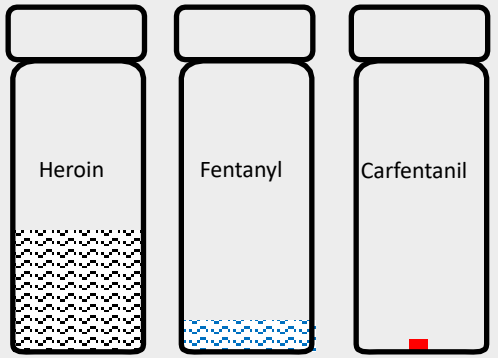
Dose Makes The Poison

"What is there that is not poison? All things are poison and nothing [is] without poison. Solely the dose determines that a thing is not a poison"

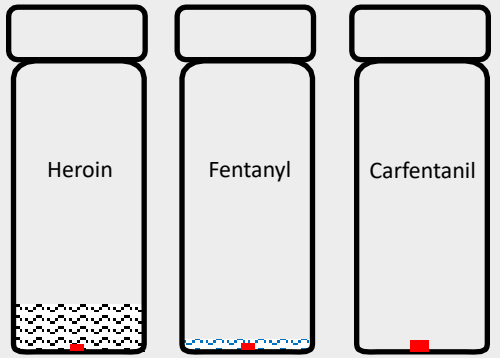
Paracelsus (1493-1541)
in *Third Defense*

Philip Theophrastus Bombast von Hohenheim
aka PARACELSUS (1493-1541)

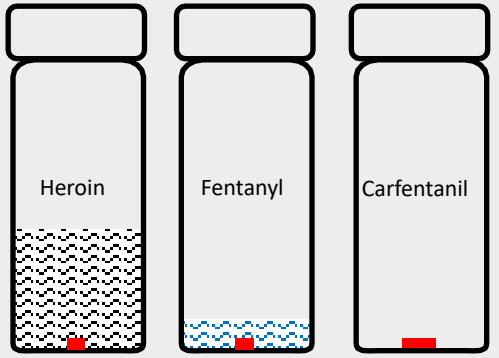
Potency doesn’t really matter



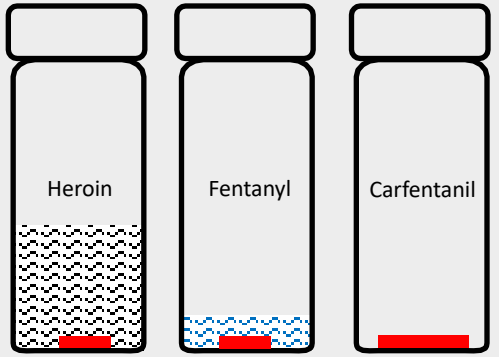
Equi-effective “safe” doses



Equi-effective “safe” doses



Dangerous doses



Deadly doses

Absorption

Routes of Administration

- Oral
  - Potentially extensive first-pass
- IV, IN, IM, SC, SL, buccal, inhalational, rectal
  - Bypass hepatic first-pass
- Intrathecal
  - Unique –bypass Blood Brain Barrier
- Transdermal
  - Bypass hepatic first-pass
  - Depot in skin/body fat can influence absorption
- Intranasal
  - May directly access CNS (nose-to-brain)

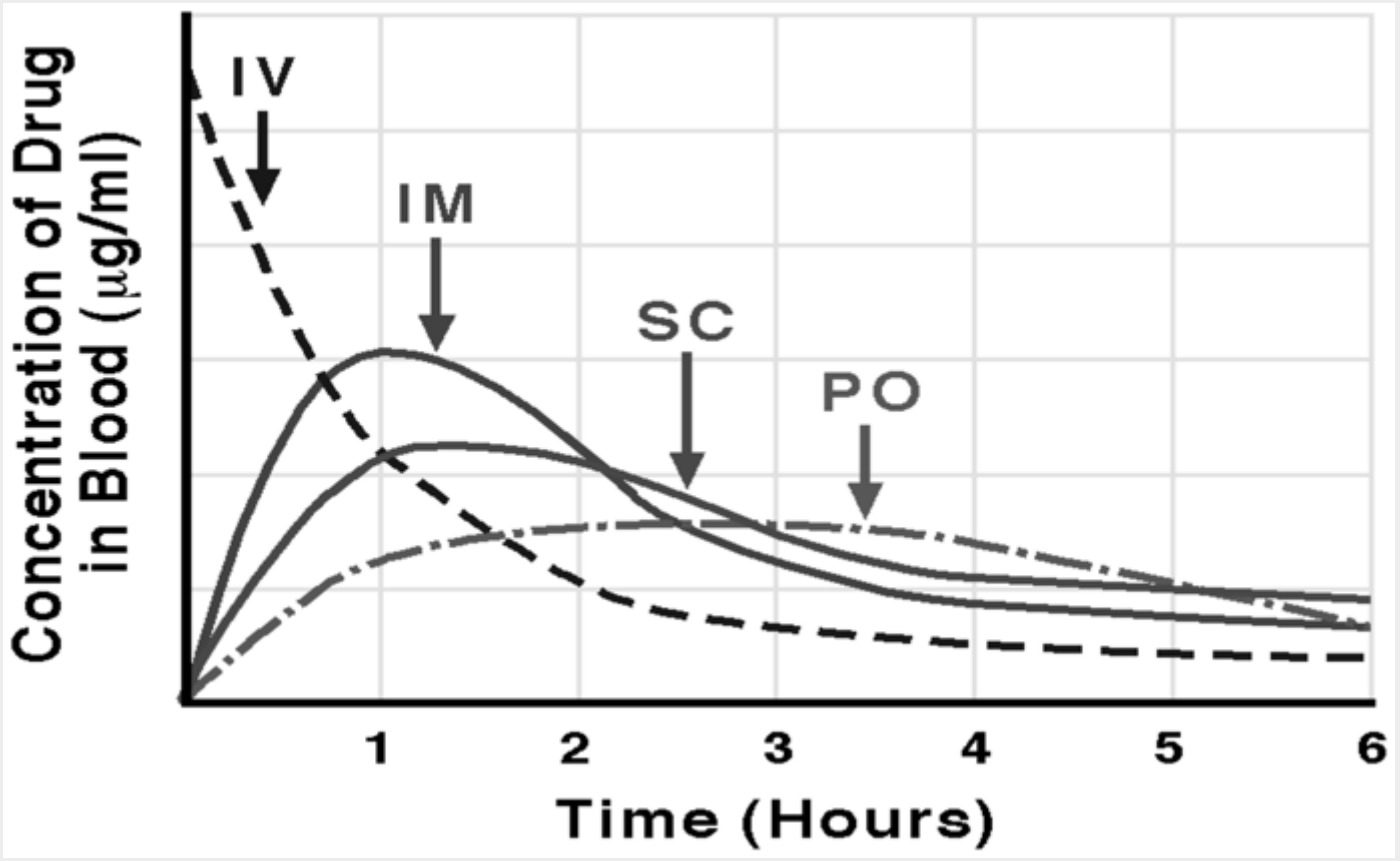
Bioavailability

- The amount of unchanged drug reaching systemic circulation after administration is the bioavailability (F).
- F depends upon:
  - Route (IV is 100%)
  - Site specific membrane permeability
  - Drug transporter activity (p-glycoprotein)
  - First-pass metabolism (hepatic)

	Route		
	Oral	**Sublingual**	**Buccal**
Buprenorphine	10%	50%	30%
	Oral	**Sublingual**	**Intranasal**
Naloxone	1%	20%	50%
	Oral		
Morphine	33%		
Oxycodone	75%		

Kuhlman JJ, et al. J Anal Toxicol 1996;20(6):369–78.

Area Under the Curve (AUC)



Wolff K, et al. The SAGE Handbook of Drug & Alcohol Studies

Q12h

OxyContin® CII

(OXYCODONE HCl CONTROLLED-RELEASE) TABLETS

10mg 20mg 40mg 80mg 160mg

Small, color-coded tablets (actual size)

OxyContin 80 and 160 mg Tablets for use
tolerant patients requiring daily oxycodone
dosages of 160 mg and 320 mg respective

OxyContin® Tablets are to be
are not to be broken, chewed or
broken, chewed or crushed OxyCont
lead to the rapid release and absorption
toxic dose of oxycodone.

One OxyContin 160 mg Tablet is comparable
two 80 mg tablets when taken on an empty stomach.
With a high fat meal, however, there is a 25% greater
peak plasma concentration following one 160 mg
tablet. Dietary caution should be taken when patients
are initially titrated to 160 mg tablets.

OxyContin® Tablets are to be swallowed whole, and are not to be broken, chewed or crushed. Taking broken, chewed or crushed OxyContin Tablets could lead to the rapid release and absorption of a potentially toxic dose of oxycodone.

section in package insert.)

For more information about pain management and prevention, visit our Web site: www.partnersagainstpain.com

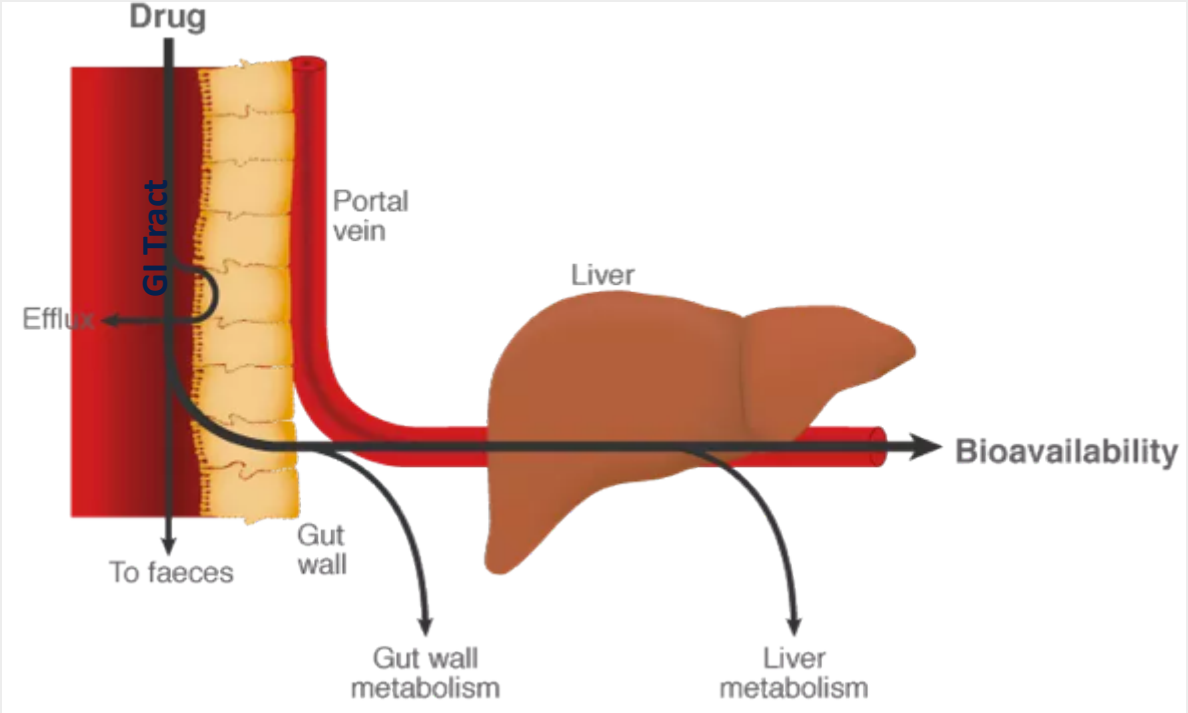
Please read attached professional prescribing information.

B6571

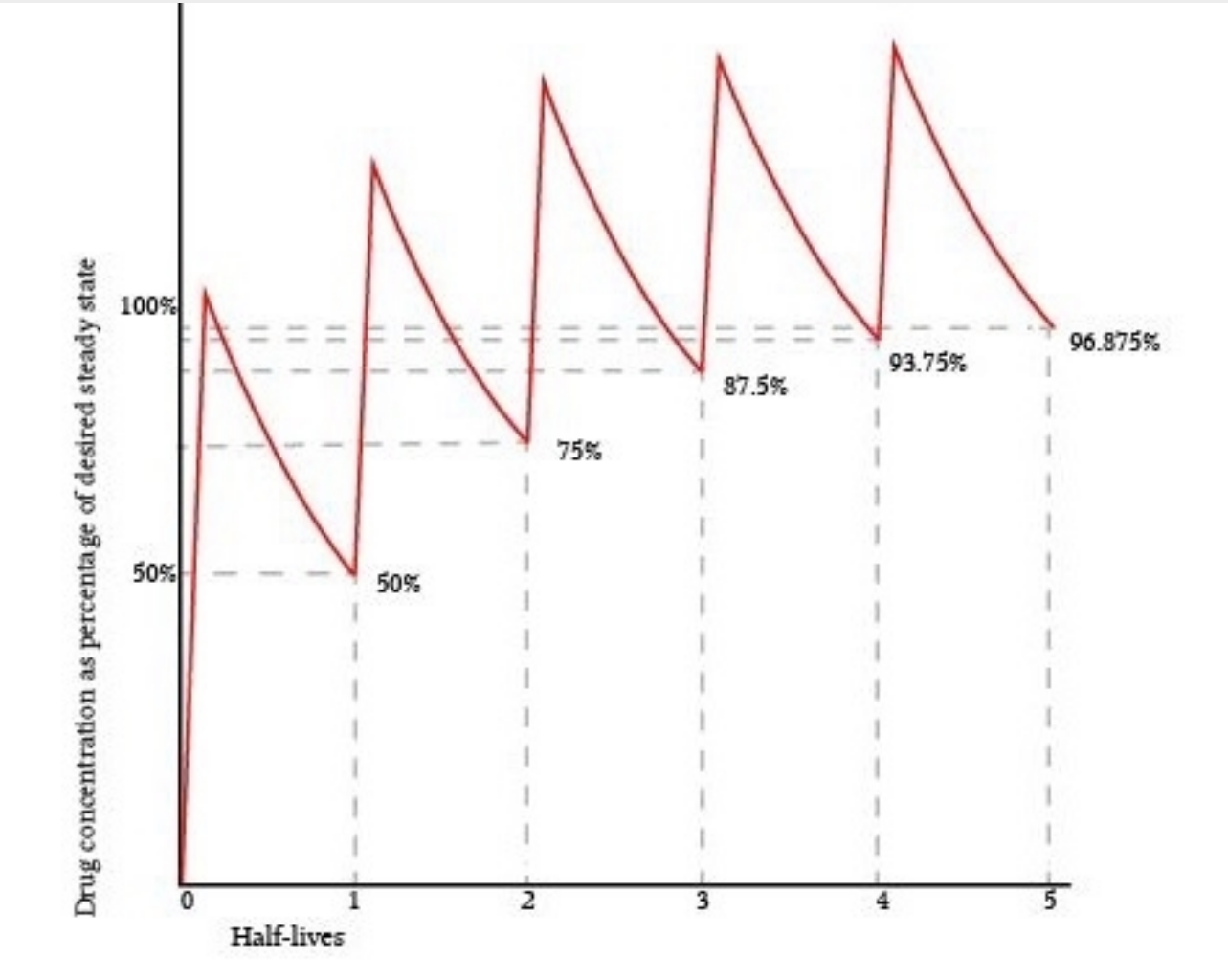
Distribution

First Pass Hepatic Metabolism

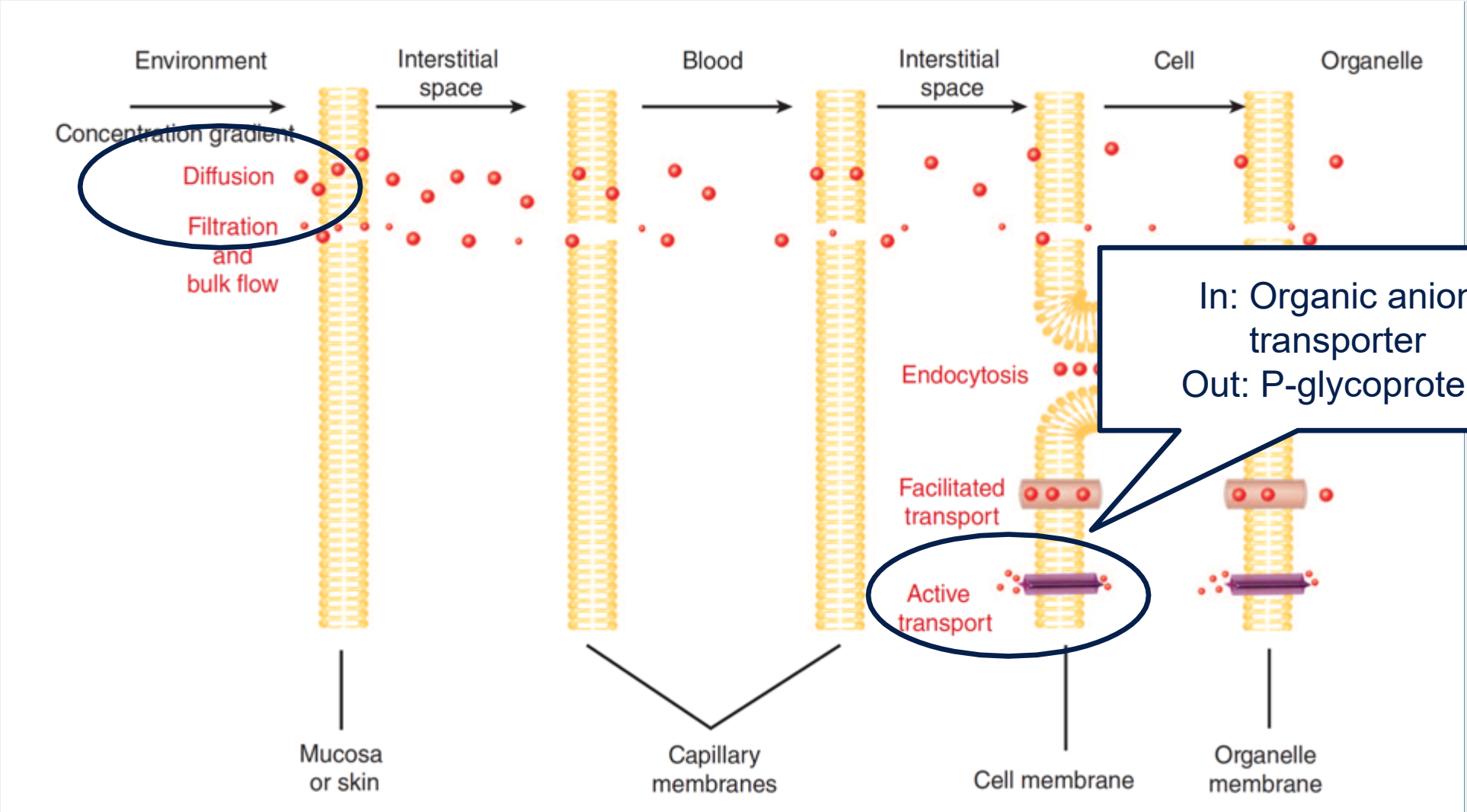
Bypass first pass



Steady State



- Requires approximately 5 half-lives
  - Regardless of the compound's half-life
- Explains (in part) the risk and difficulty of methadone induction
  - T½ ~24 hr (12-36 hr)



Goldfrank's Toxicologic Emergencies, 11th

P-Glycoprotein

Loperamide the OTC fentanyl (reason for no CNS activity) [A...
www.bluelight.org/vb/archive/index.php/t-217933.html
Aug 21, 2005 - 50 posts - 30 authors
I have found many commonly available items (herbal extracts, supplements or food items) which are **p-glycoprotein inhibitors**, but inhibition at ...

Immodium, BBB, and PGp inhibition [Archive]	8 posts	Jan 12, 2013
(**Loperamide**/cimetidine/quinine) Veteran. Wasn't a ...	13 posts	Oct 2, 2012
Forcing **Loperamide** through the BBB [Archive] - Page 2	30 posts	Jun 21, 2011
Forcing **Loperamide** through the BBB [Archive]	50 posts	May 23, 2006

More results from www.bluelight.org

Loperamide and P-glycoprotein inhibition: assessment of ...
www.ncbi.nlm.nih.gov/... National Center for Biotechnology Information
by J Vandenbossche - 2010 - Cited by 12 - Related articles
Loperamide and P-glycoprotein inhibition: assessment of the clinical relevance. ... coadministration of **loperamide** with a **P-glycoprotein inhibitor** or substrate.

Combinations - **Loperamide** Potentiation + **p-glycoprotein** in...
www.drugs-forum.com › ... › DRUG-FORUMS › Opiates & Opioids
Mar 2, 2012 - 3 posts - 2 authors
SWIM is going to be performing an experiement with **Loperamide**, he is ... SWIM is aware of the dangerous of **inhibiting p-glycoprotein** but is not ...

Addiction - metabolite of **loperamide** is possible PGP ...	4 posts	Feb 28, 2013
Combinations - Cheap Opiate High-potential ...	22 posts	Dec 27, 2012
Experiences - **Loperamide** Report	22 posts	Jan 16, 2012
Blood brain barrier permeation	17 posts	Dec 4, 2010

More results from www.drugs-forum.com

Pepper **Inhibits P-Glycoprotein** (just add **loperamide**??) [Ar...

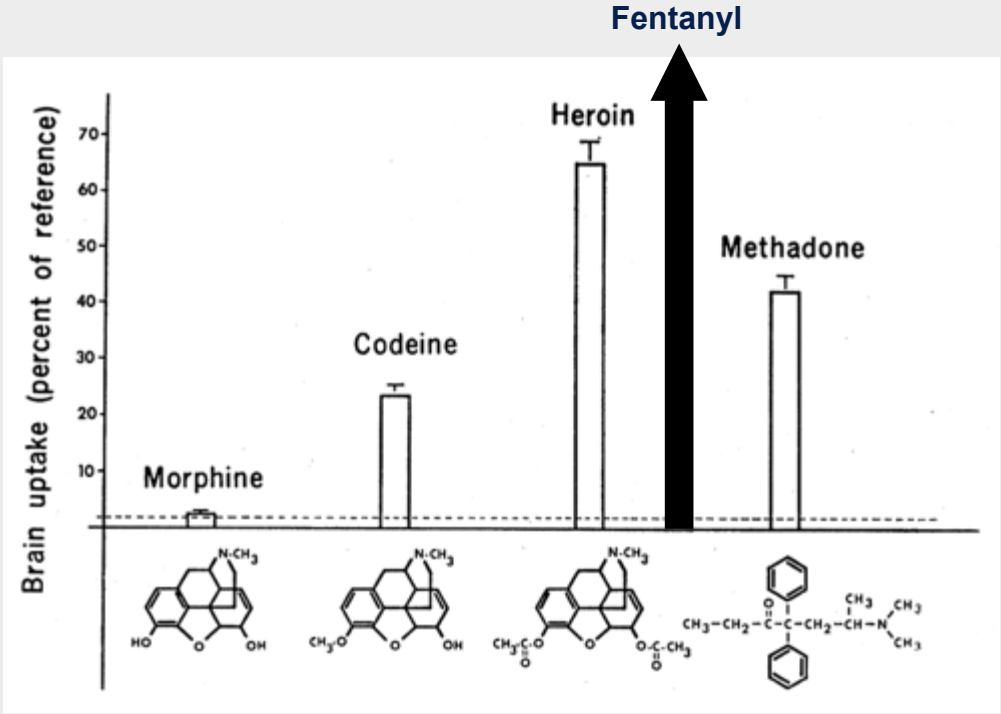
"Street pharmacologists" understand these principles

Loperamide and p-glycoprotein inhibitors

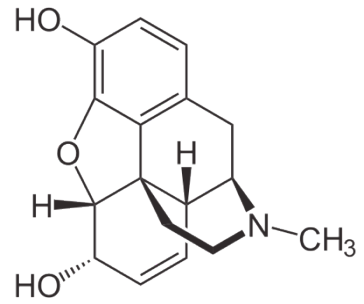
Lipophilicity

Lipophilicity = Reward = Abuse liability

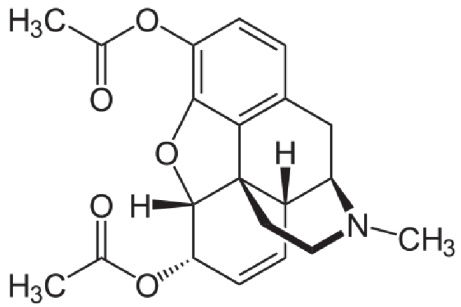
Drug	LogP
Buprenorphine	4.98
Fentanyl	4.05
Methadone	3.93
Naloxone	2.09
Hydromorphone	1.6
Heroin	1.58
Morphine	0.89



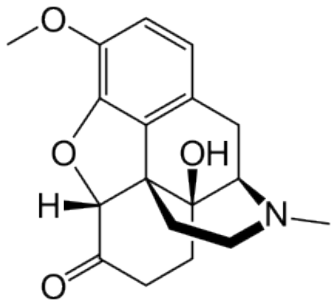
Oldendorf WH. Science. 1972



Morphine

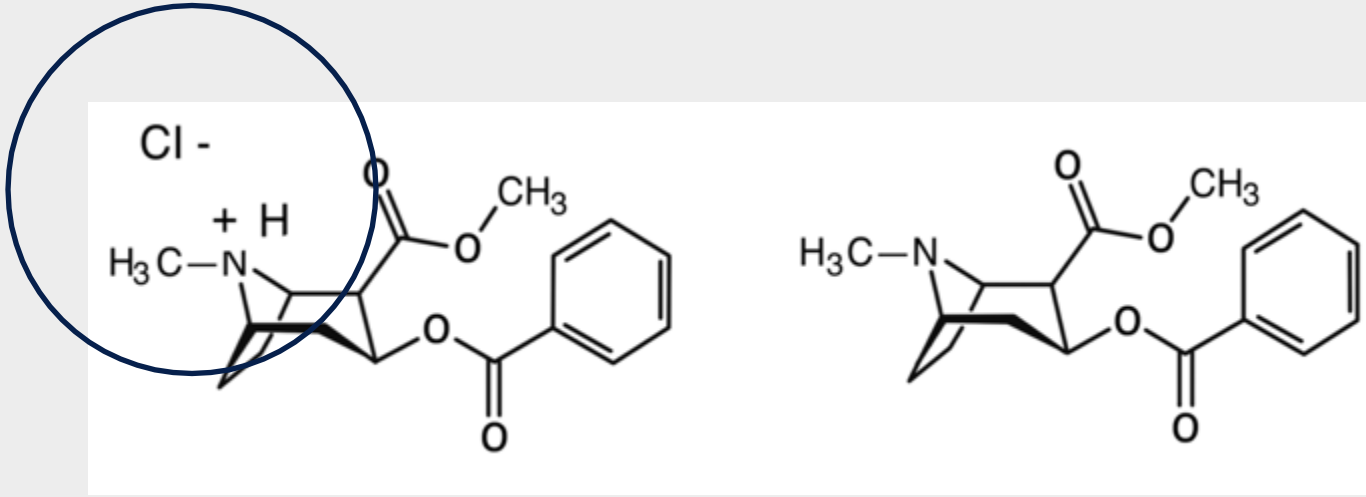


Heroin (diacetyl morphine)



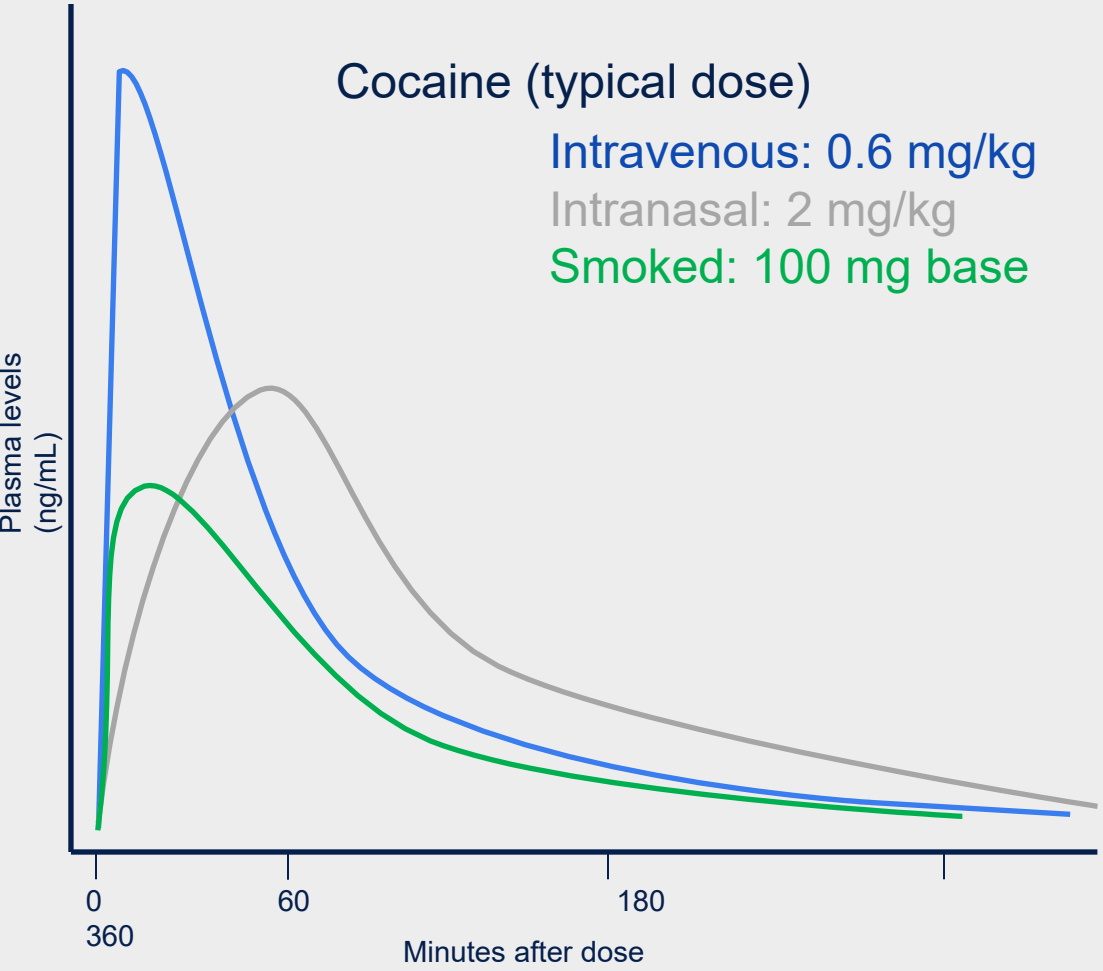
Oxycodone

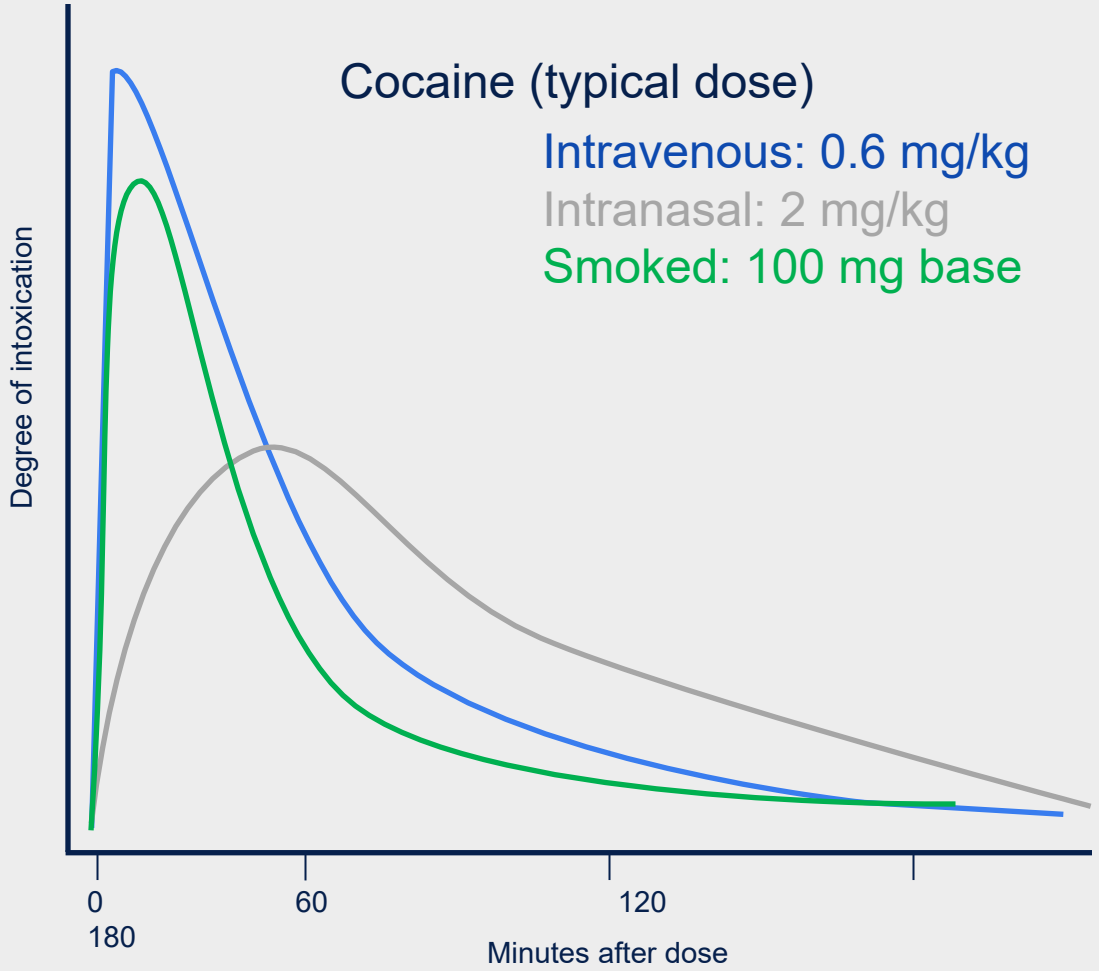
Addiction Medicine IS Pharmacology



Cocaine hydrochloride
(salt)

Cocaine base
(alkaloidal)





C_{max} and T_{max} depend on route of administration and dose

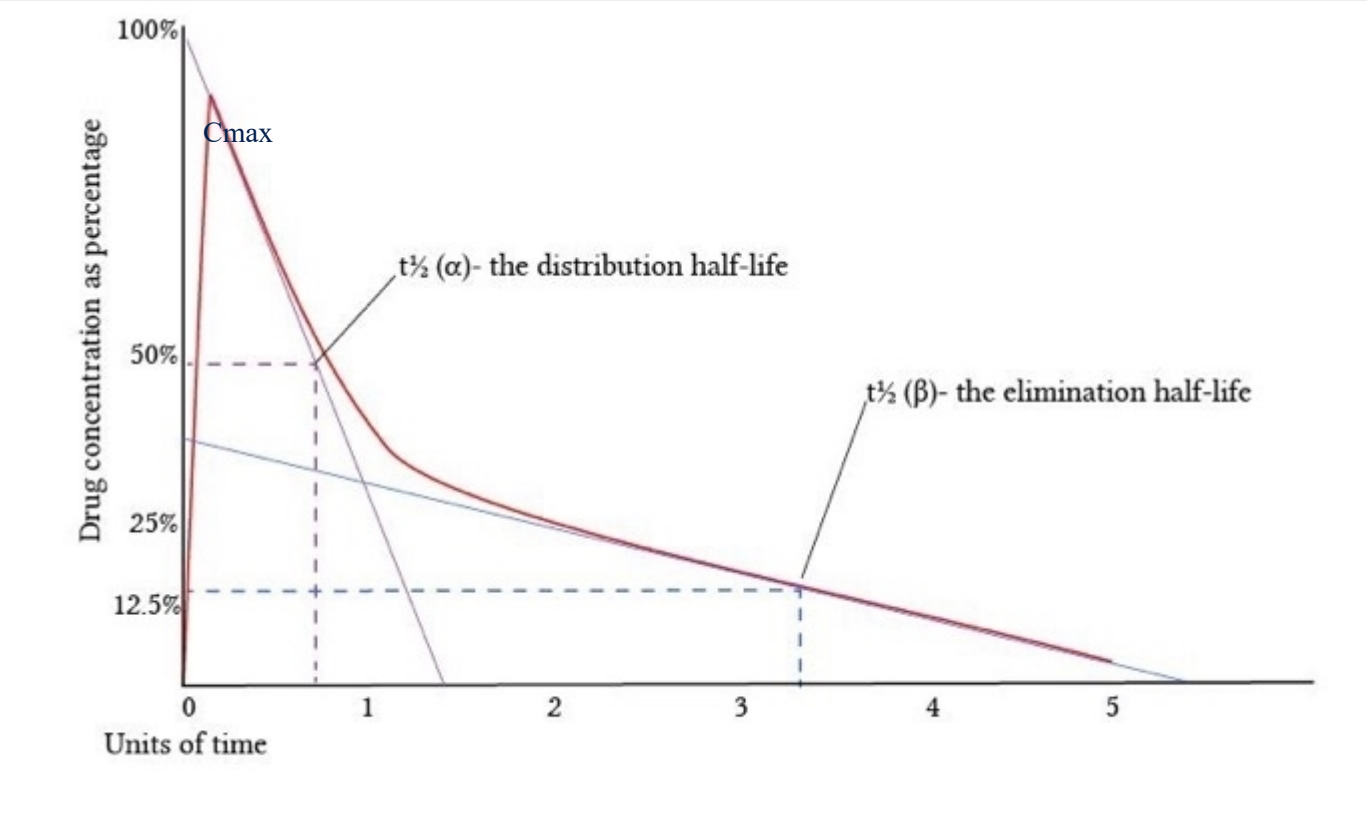
(C_{max} : IV → *Nasal* → *Smoked*)
(T_{max} : IV = *Smoked* → *Nasal*)

Subjective 'high' (0-100) by route
(*IV* → *Smoked* → *Nasal*)

NIDA Research Monograph 1992, 120

Elimination

T1/2 (Half-life) is The Time For Cmax to Fall by Half

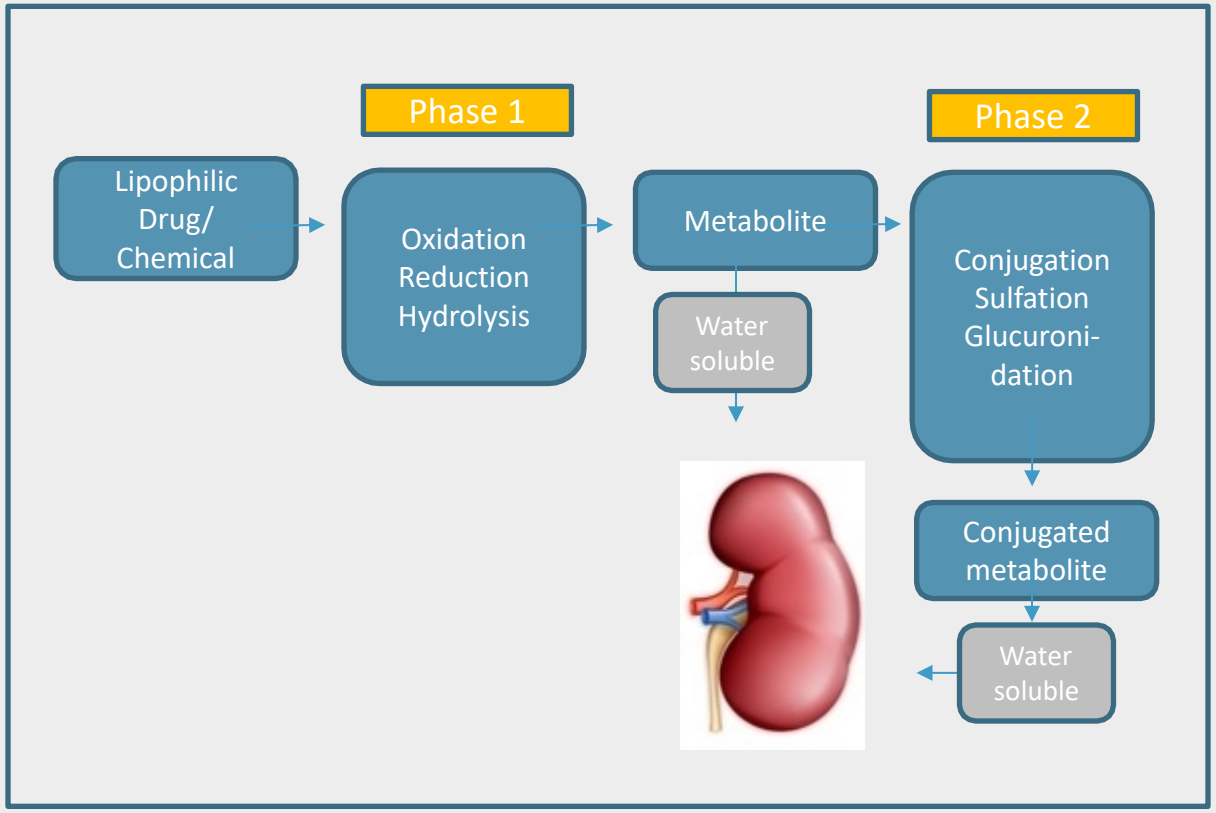


- Distribution t½
  - Redistribution t½
- Terminal elimination t½
  - Context sensitive t½
  - Apparent t½

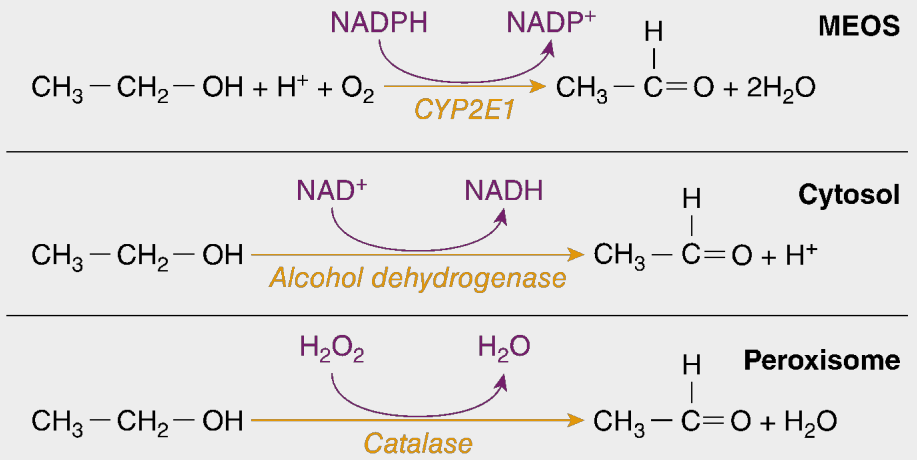
Drug	Half life (distrib)	Half life (redistrib)	Half life (term)	LogP
Fentanyl	2 min	12 min	480 min	4.05
Methadone	120 min	---	1440 min	3.93

Note: all half-lives have ranges, not shown

Biotransformation



Ethanol Metabolism

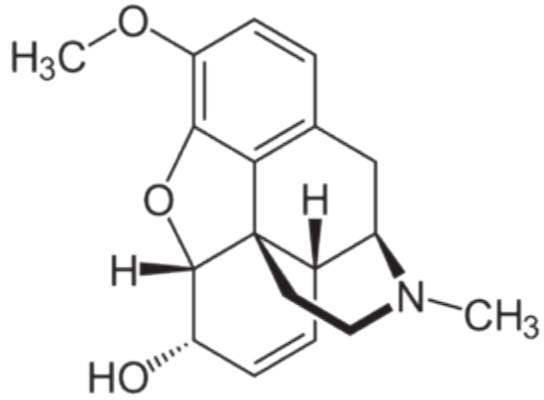


Goldfrank's Toxicologic Emergencies, 11th

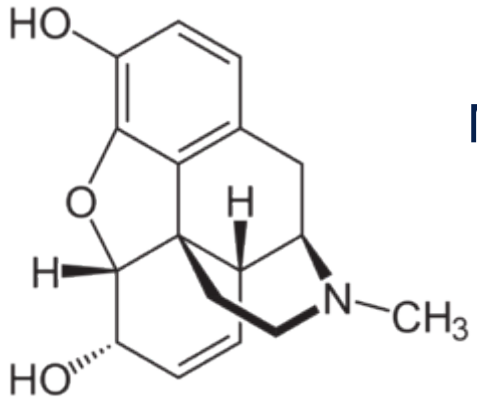
Activation through Biotransformation

- Codeine is demethylated in the liver to morphine
  - Occurs via CYP2D6
  - Codeine is a “pro-drug” (drug undergoes hepatic biotransformation or ‘metabolism’ to its active component
  - Lisdexamfetamine (Vyvanse™) is another example of a pro-drug

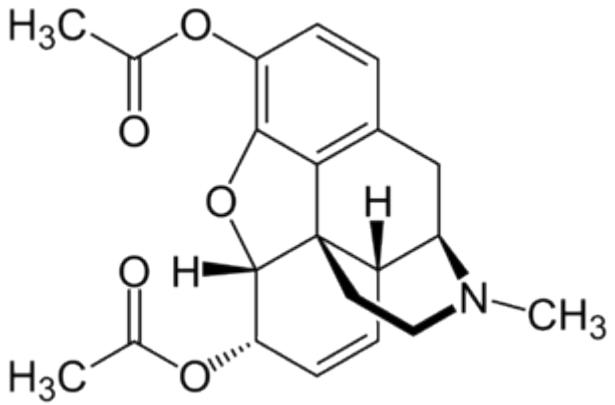
Fun pharm fact: *heroin does not bind to the mu receptor. Metabolism occurs in the CSF. Heroin is a pro-drug for morphine.*



Codeine



Morphine



Heroin

Biotransformation

TABLE 11–1 Characteristics of Different Cytochrome P450 Enzymes[26,33,123]

CYP Enzyme	*1A2*	*2B6*	*2C9*	*2C19*	*2D6*	*2E1*	*3A4*
Percent of liver CYPs	4%–16%	2%–5%	5%–29%	1%–4%	1%–4%	6%–17%	15%–37%
Contribution to enterocyte CYPs	None	None	Minor	Minor	Minor	Minor	70%
Organs other than liver with enzyme	Lung	Kidney	Small intestine, nasal mucosa, heart	Small intestine, nasal mucosa, heart	Small intestine, kidney, lung, heart	Lung, small intestine, kidney	Much in small intestine; some in kidney, nasal mucosa, lung, stomach
Percent of metabolism of typically used pharmaceuticals	9%	7%	13%	7%	20%	3%	30 %
Polymorphisms[a]	No	Yes	Yes	Yes	Yes	No	No
Allelic Frequency							
Decreased Activity							
African American		38%–62%	0%–3%	10%–17%	14%–30%		
Asian	—	14%–25%	2%–8%	25%–39%	47%–94%	—	—
Caucasian		23%–39%	16%–23%	6%–16%	31%–45%		
Increased Activity							
African American		0%–25%		15%–27%			
Asian	—	5%–15%	—	0%–2%	1%	—	—
Caucasian		6%		21%–25%	1%–9%		
Ethiopian					30%		

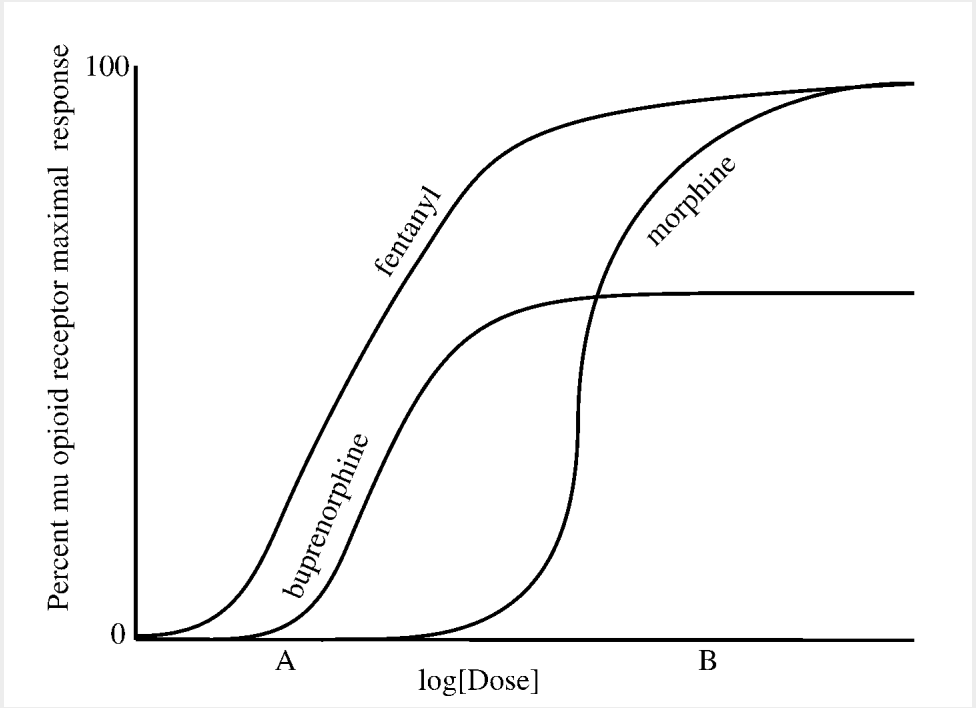
[a] Polymorphism is a genetic change that exists in at least 1% of the human population. Interpersonal allelic variations exist even in those listed as "No" for polymorphism.

Goldfrank's Toxicologic Emergencies, 11th

Receptor Pharmacology

Efficacy

Ligand	% Efficacy
Full agonist	E = 100
Partial agonist	0 < E < 100
Antagonist	E = 0
Inverse agonist	E < 0

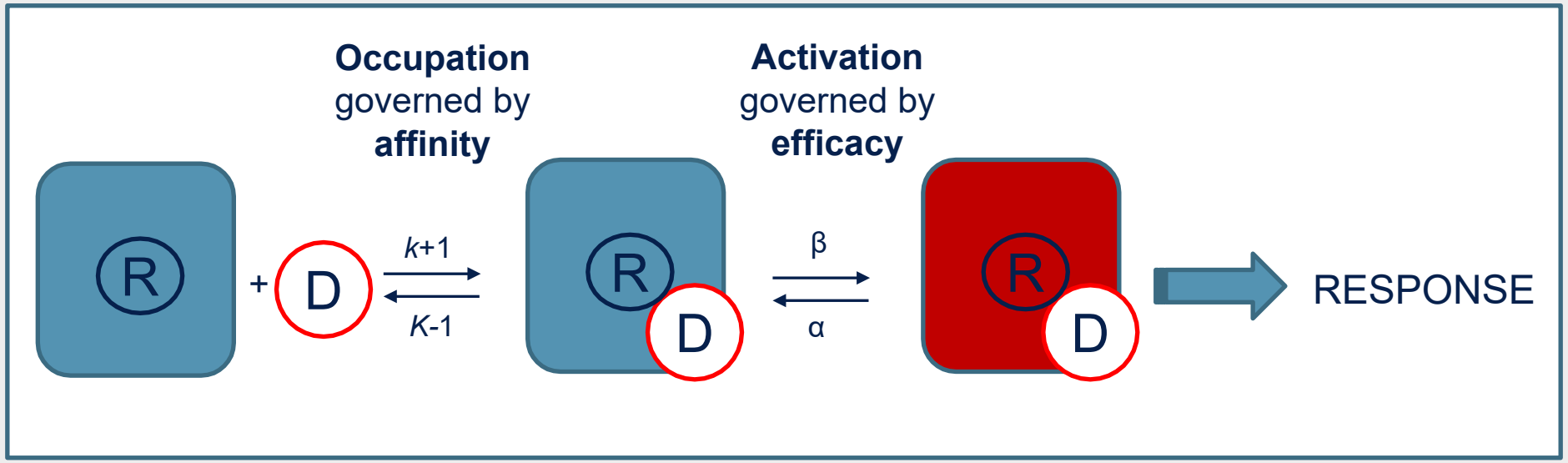


Affinity

Ligand	Ki (Affinity) (nmol)
Hydrocodone	41.58
Oxycodone	25.87
Heroin	9.6
Methadone	3.38
Fentanyl	1.35
Morphine	1.14
Naloxone	1.1
Hydromorphone	0.6
Buprenorphine	0.21

Volpe DA. Uniform assessment and ranking of opioid Mu receptor binding constants for selected opioid drugs. Reg Toxicol Pharmacol 2011

Receptor kinetics
On-off

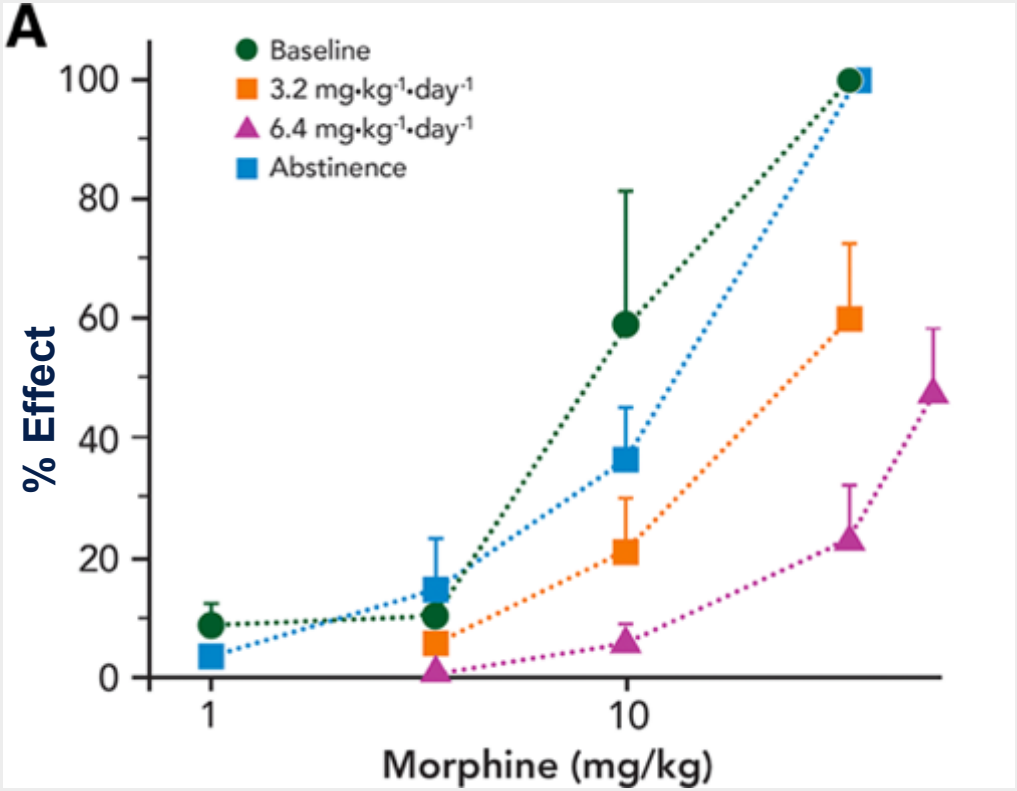


Pharmacodynamics

Tolerance

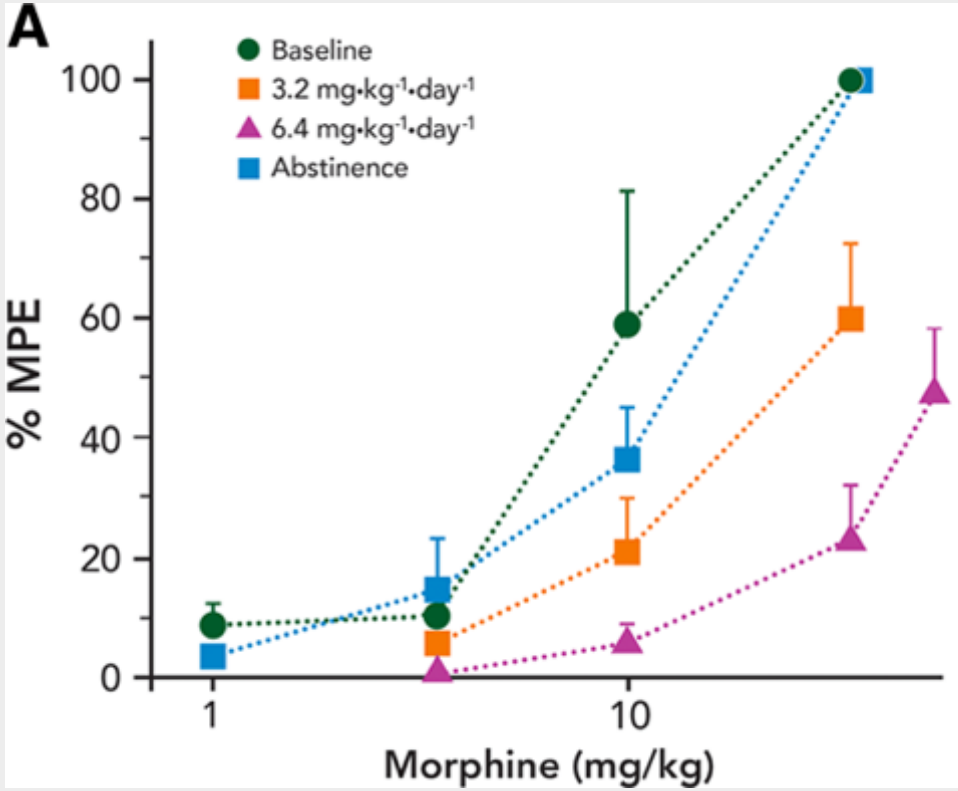
- Tolerance is the reduction in response to a drug after its repeated administration
- Tolerance shifts the dose-response curve to the right
  - Higher doses than initial doses to achieve the same effect

Analgesia

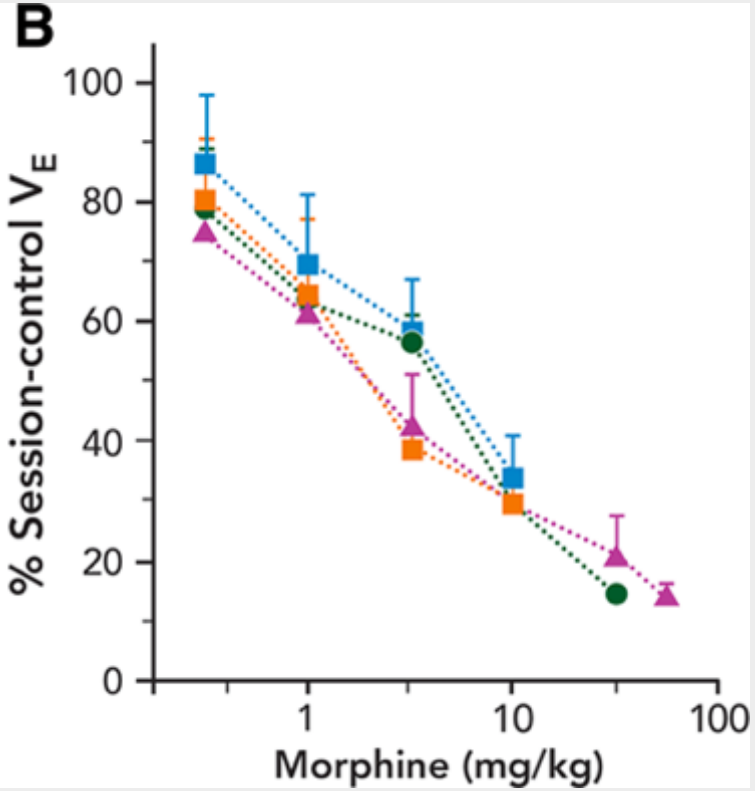


Differential Tolerance

Analgesia



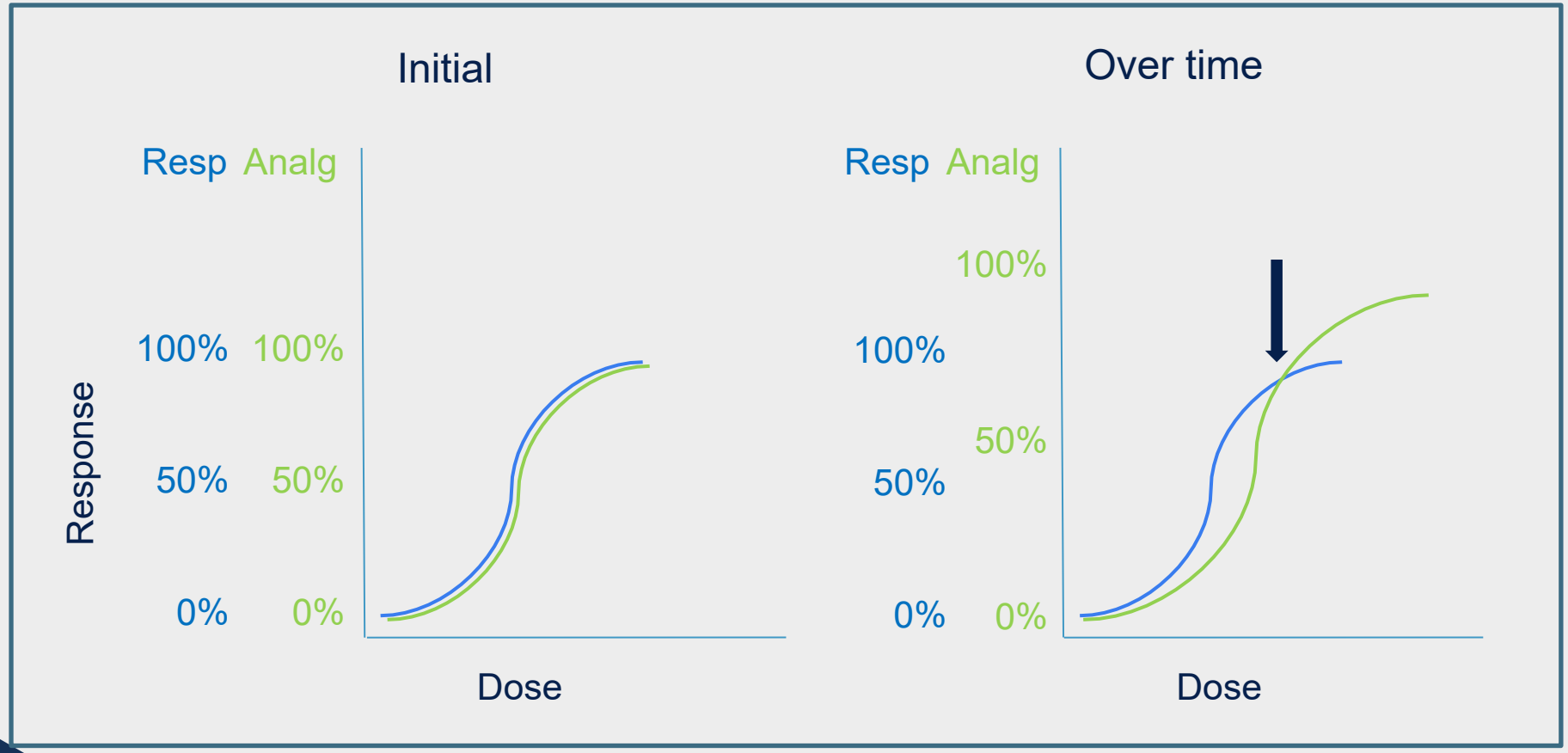
Respiratory depression*



*limited development of tolerance

Hayhurst. Anesthesiology 2016;124:483-8

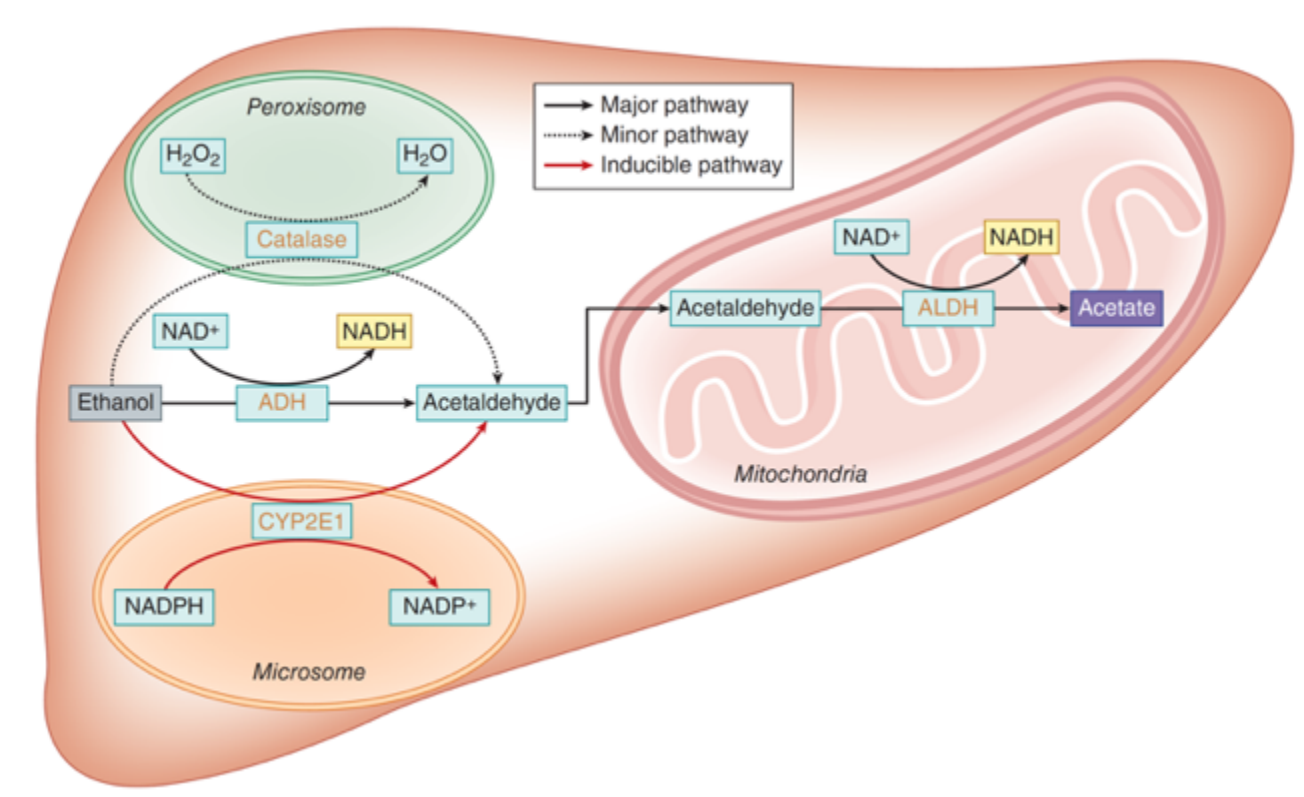
The Paradox of Differential Tolerance



Tolerance to analgesia is rapid
Tolerance to respiratory depression is slow

Pharmacokinetic Tolerance

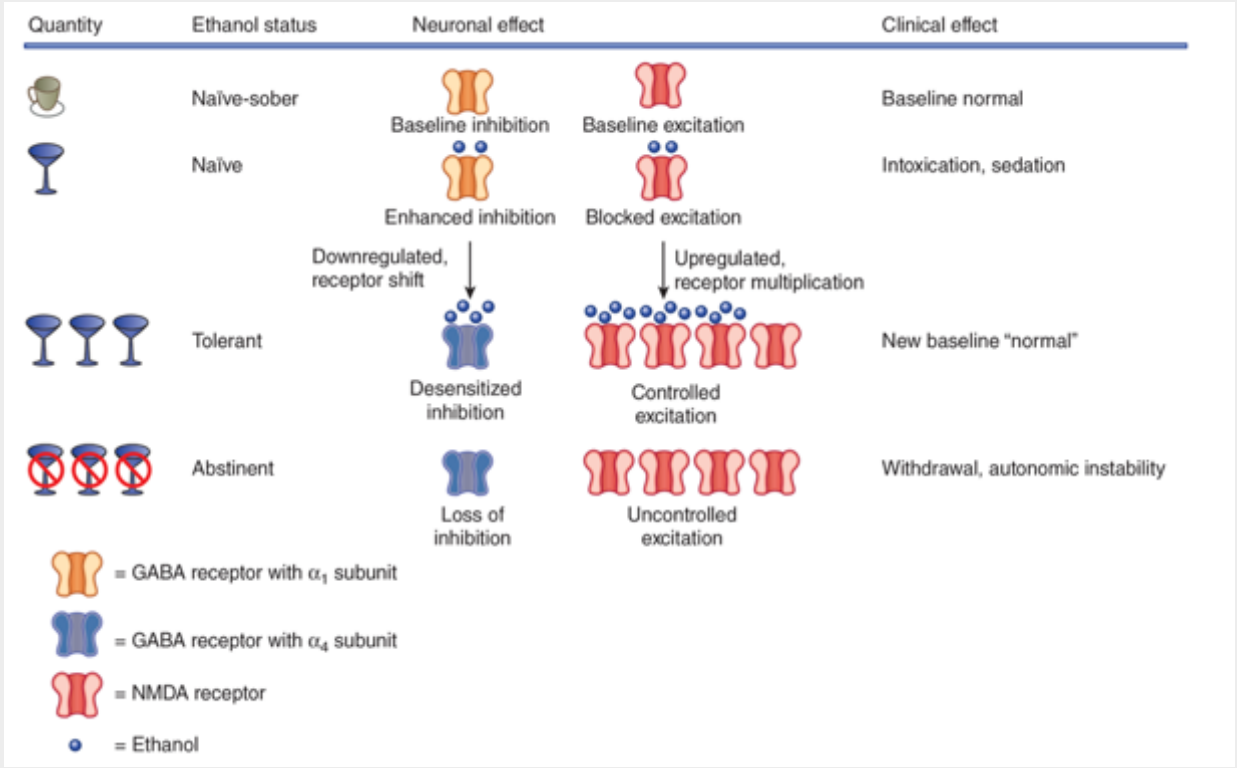
- A consequence of increased metabolism after a drug is repeatedly administered
- Results in less drug being available at the receptor for drug activity.
- Ethanol
  - Although ADH is not inducible, CYP2E1 is
  - Accounts for more rapid elimination of alcohol in heavy, chronic users



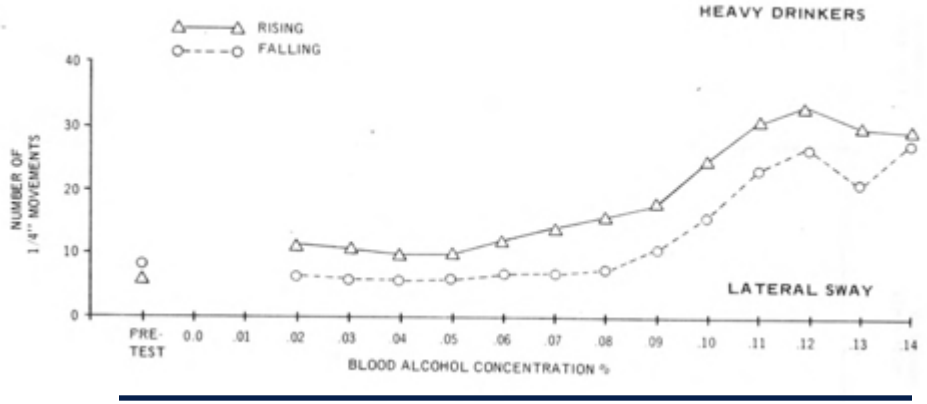
Goldfrank's Toxicologic Emergencies, 11th

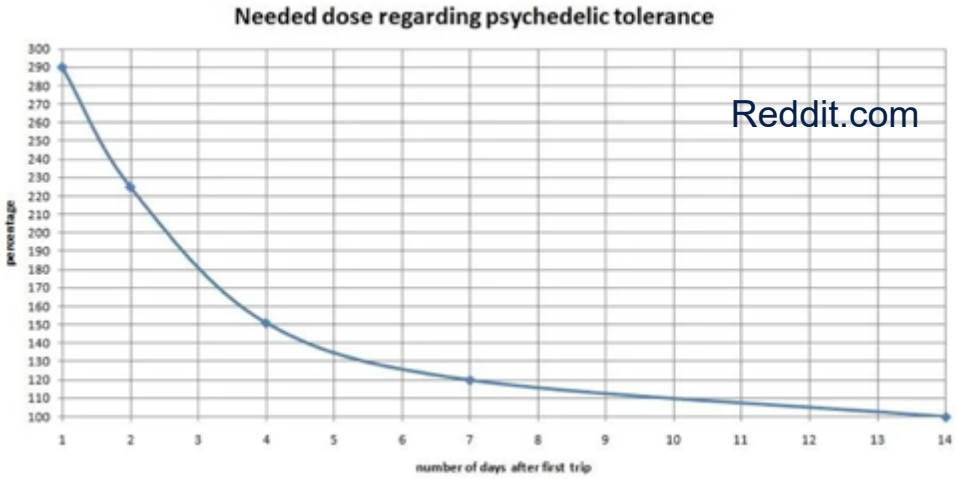
Pharmacodynamic Tolerance

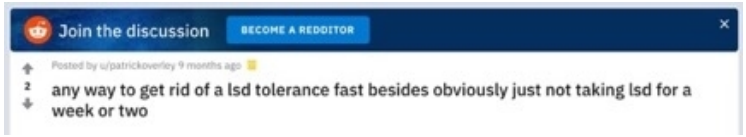
- Down-regulation of receptors (higher drug concentration needed)
  - Desensitization of GABA (ethanol)
    - Receptor conformation
  - Desensitization of MOR (opioid)
    - Signal transduction
    - Decreased density (internalization)
- Up-regulation of receptors
  - Increased number of NMDA



Goldfrank's Toxicologic Emergencies, 11th







Other Clinical Examples of Tolerance

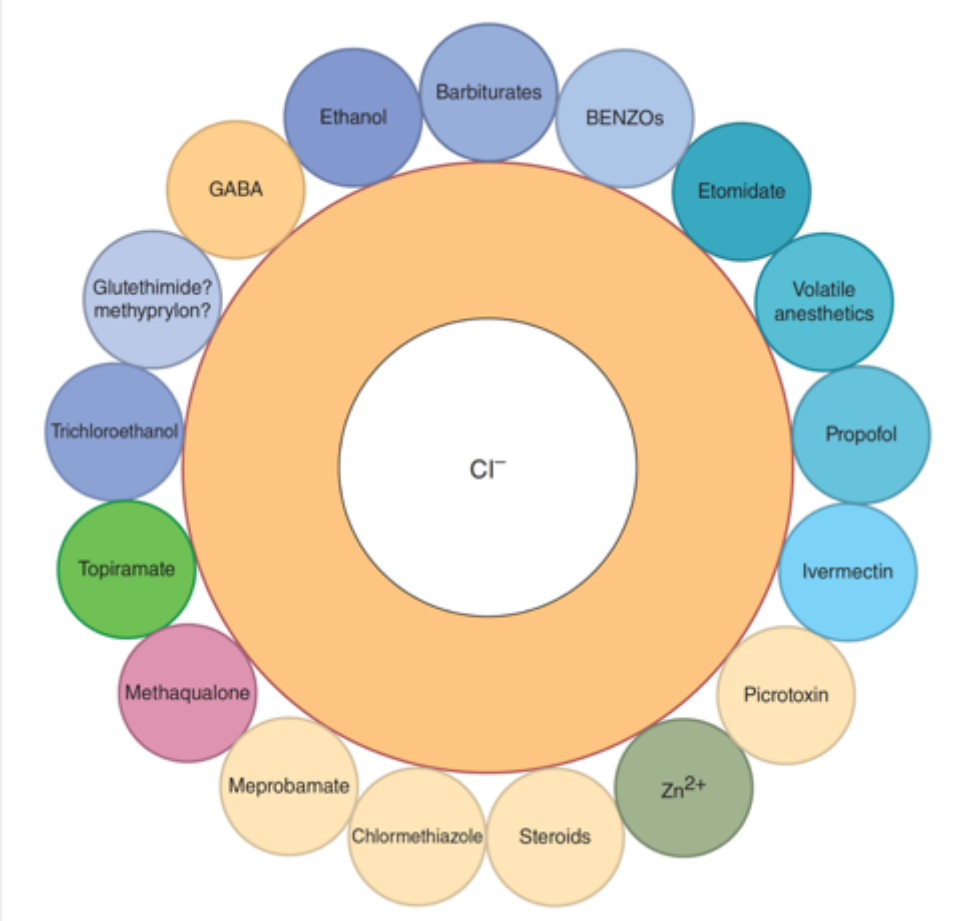
- Mellanby effect
  - Less “intoxicated” on descending limb of BAC curve
- MDMA, psilocybin, and LSD
  - Serotonin receptor
- BZD resistant alcohol withdrawal from IV (less with PO) diazepam
  - Tachyphylaxis

Mellanby E. Medical Research Committee. Special Report Series No 31, 1919.

Conditioned Tolerance

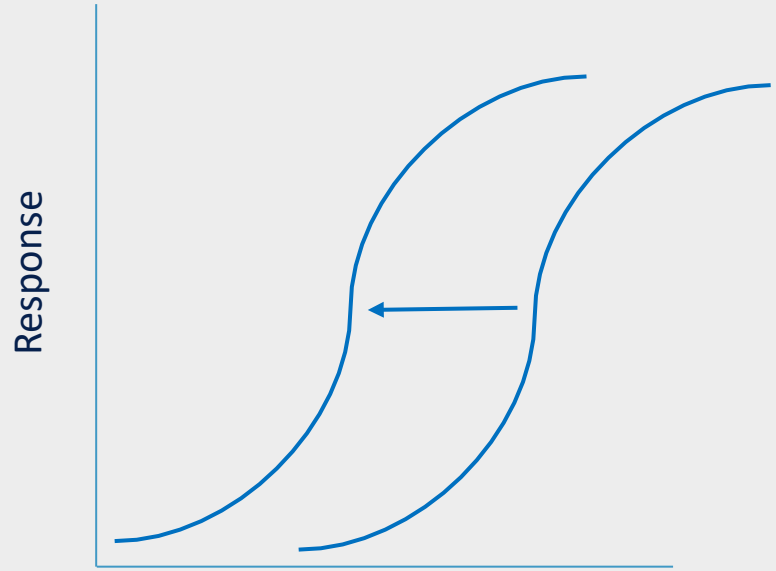
Cross-Tolerance

- Tolerance to the repeated use of a specific drug in a given category is generalized to other drugs with the same structural or mechanistic category.



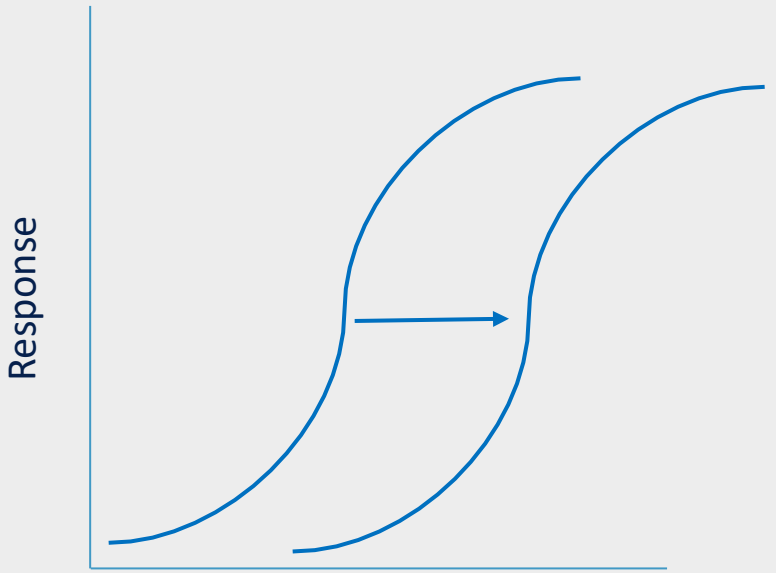
Goldfrank's Toxicologic Emergencies, 11th

Opioid-induced Hyperalgesia



Lowering of the pain threshold

Opioid Tolerance



Decreased efficacy of the opioid

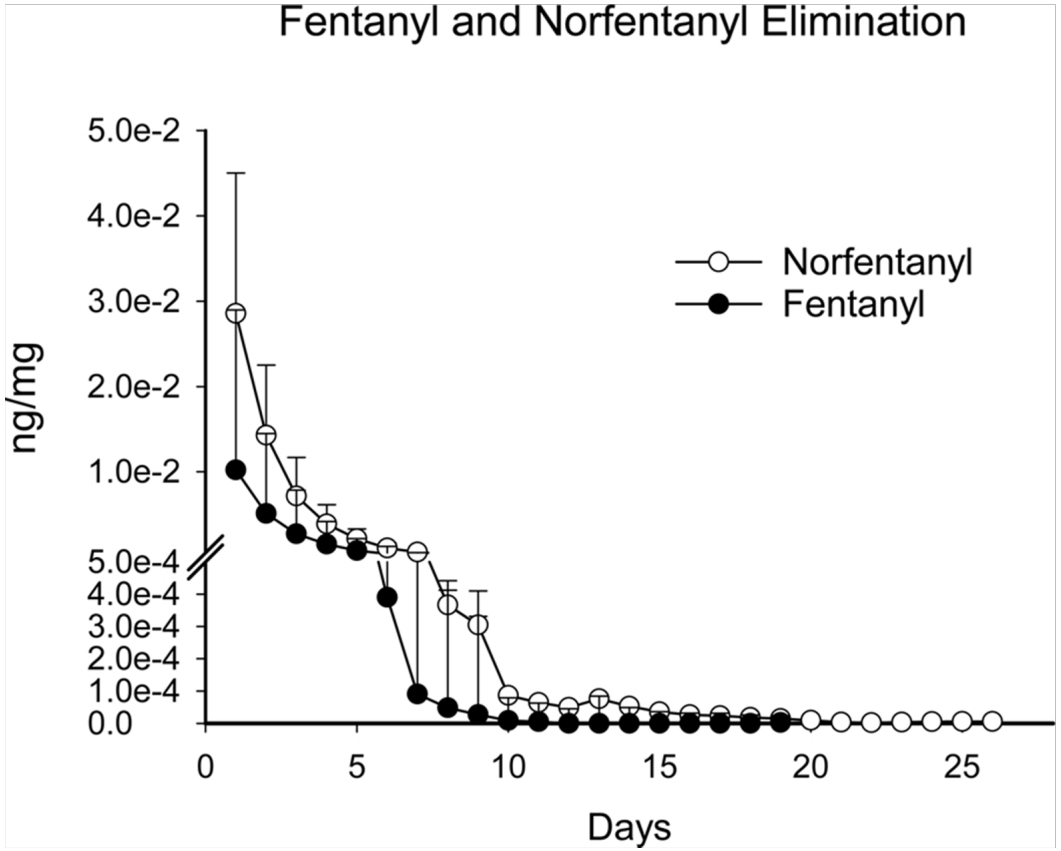
Superficially clinically indistinguishable

Physical Dependence

- A state that develops as a result of adaptation and the resetting of homeostatic mechanisms
- Withdrawal syndrome can occur in physically dependent person when the drug is abruptly stopped or dose reduced
  - Typically improves on restarting the drug
  - There can be a “point of no-return”
- Can occur with both addictive and non-addictive use of drugs
  - Caffeine, nicotine
- And with therapeutic use
  - Clonidine

Physical Dependence
Withdrawal Severity

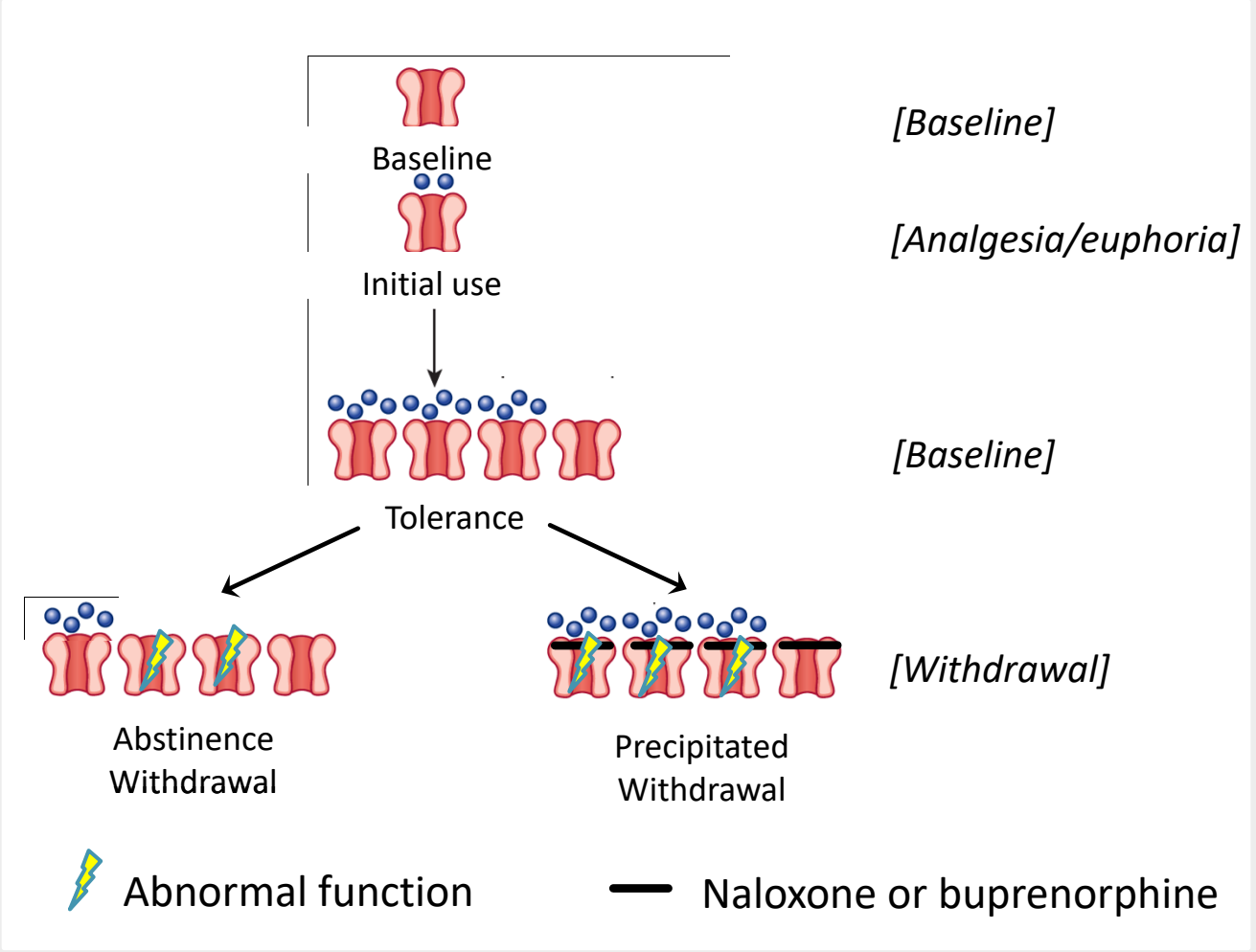
- Depth of dependence is related to extent and duration of exposure
  - Receptor adaptation



Huhn AS, et al. Drug Alcohol Depend 2020;108:147

Physical Dependence
Withdrawal Severity

- Related to rapidity of development of withdrawal



Drug Interactions

Physiological Drug Interactions (Pharmacodynamic)

Heroin and cocaine

Alcohol and benzodiazepines

Physiological Drug Interactions (Pharmacodynamic)

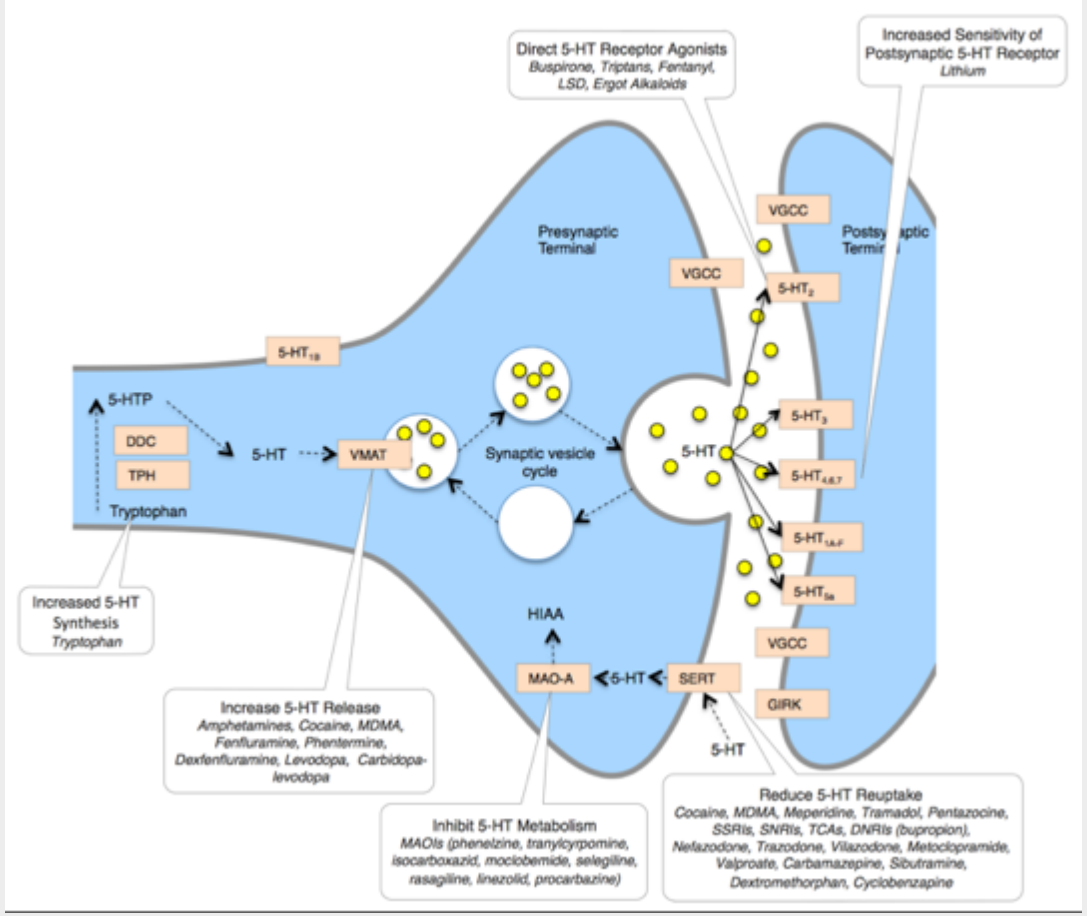
The New York Times

Tranq Dope: Animal Sedative Mixed With Fentanyl Brings Fresh Horror to U.S. Drug Zones

A veterinary tranquilizer called xylazine is infiltrating street drugs, deepening addiction, baffling law enforcement and causing wounds so severe that some result in amputation.

Jan. 7, 2023

PK/PD Drug Interactions



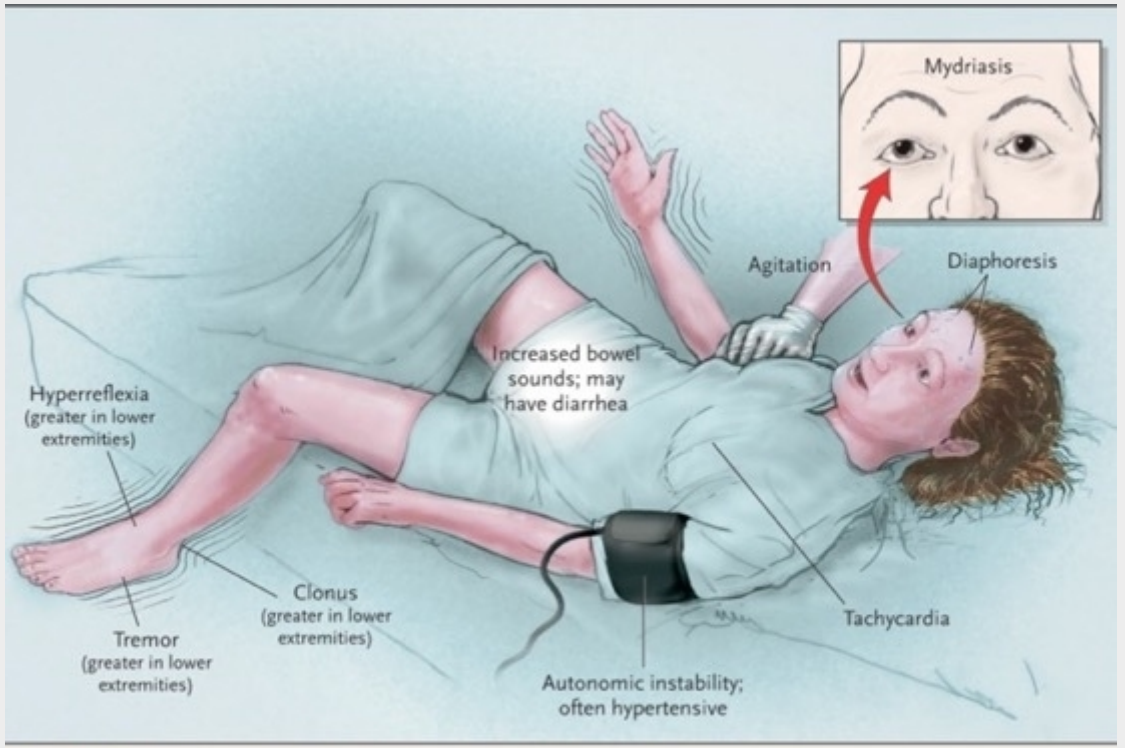


Figure 2. Findings in a Patient with Moderately Severe Serotonin Syndrome.
Hyperkinetic neuromuscular findings of tremor or clonus and hyperreflexia should lead the clinician to consider the diagnosis of the serotonin syndrome.

www.real-psychiatry.blogspot.com

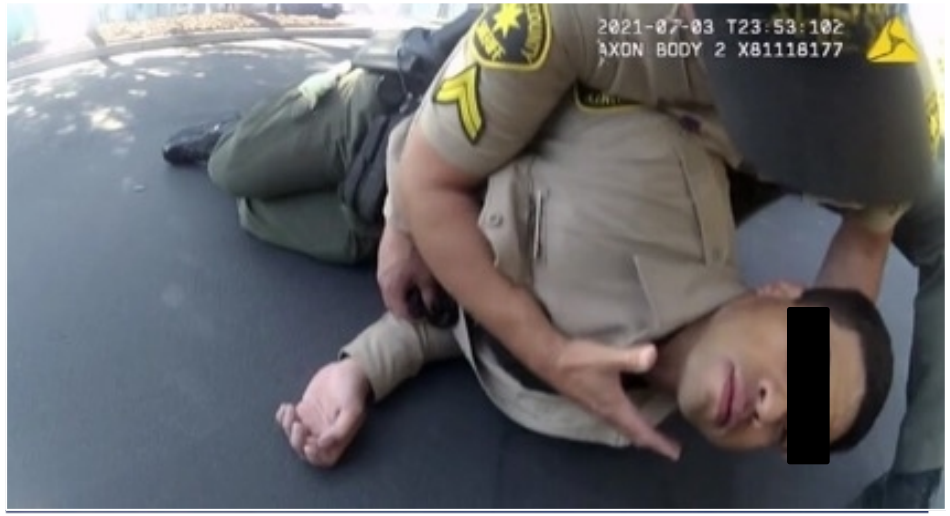
Boyer E. NEJM 2005

Exposure Pathway

Sheriff's deputy overdoses after exposure to fentanyl during arrest

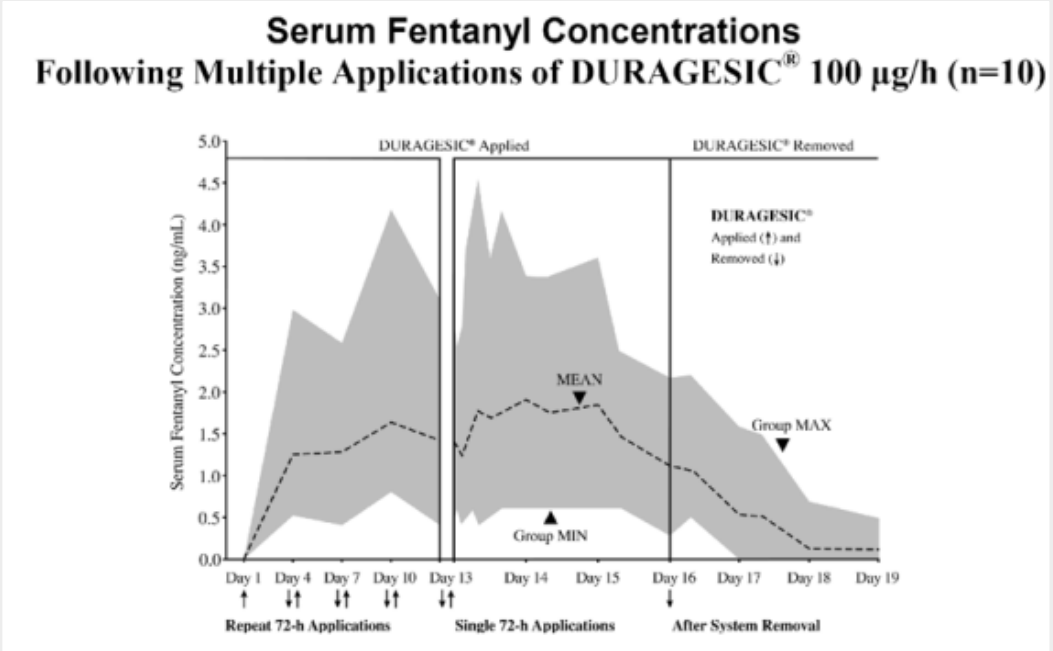
The video was released to promote public safety.

By ABC NEWS
August 6, 2021, 4:51 PM



What to know about the deadly drug fentanyl
Fentanyl was first developed in 1959 and introduced in the 1960s as an intravenous anesthetic.

The San Diego County Sheriff's Department released body camera footage of the crucial moments in which a deputy saved another's life after he was overdosed from fentanyl exposure during an arrest last month.



Duragesic prescribing information

CONSENSUS STATEMENT

Appropriate Use of Drug Testing in Clinical Addiction Medicine

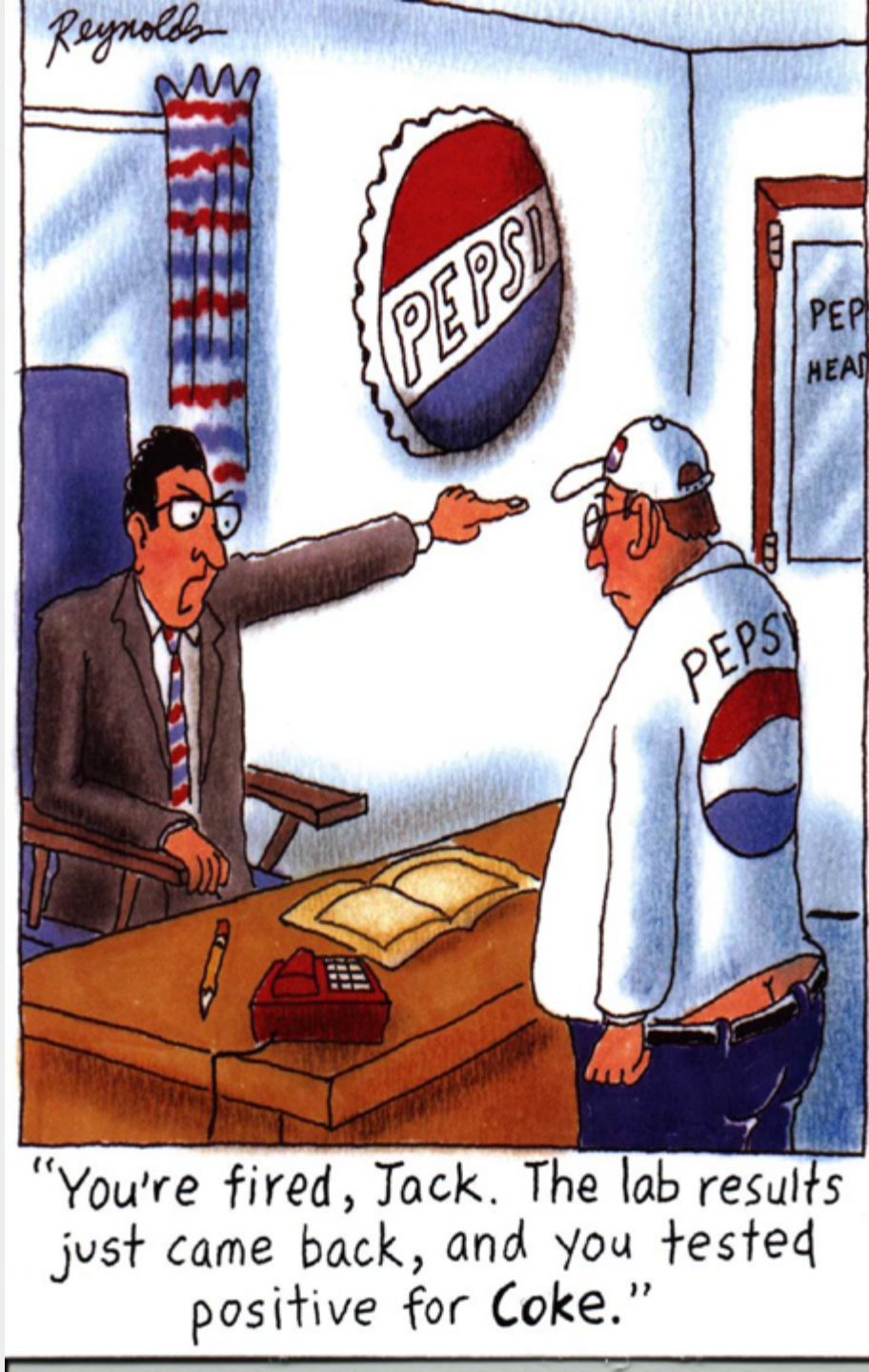
Effective Date: January 1, 2020
Rev. 0722

Medical Review Officer Guidance Manual for Federal Workplace Drug Testing Programs

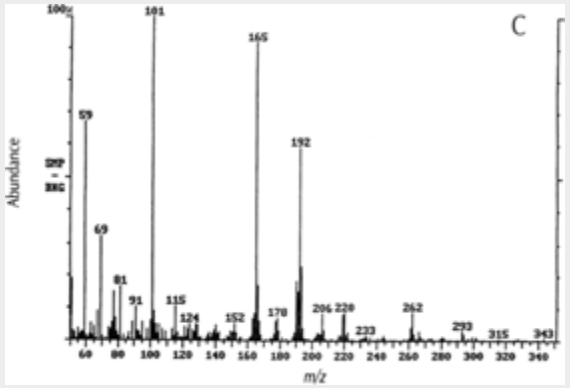
Department of Health and Human Services
Substance Abuse and Mental Health Services Administration
Center for Substance Abuse Prevention
Division of Workplace Programs

Philosophical Considerations (for substance use)

- Testing is not meant to "catch" the patient
  - Testing identifies recent use it does NOT identify addiction or impairment
  - A positive finding suggests need to review treatment plan
    - Not to prevent, limit, or punitively change treatment
- Tests must be interpreted in the context of patient self-report and other information from observed behaviors or reliable sources
- Language is important
  - e.g., clean vs dirty, pass/fail



Screening and Confirmatory Tests



Screening (Presumptive) Assays – indicate the presumptive presence of drugs

Highly sensitive

Rapid, inexpensive

Cutoff - Yes/No

Confirmatory (Definitive) Assays – specifically identify the drug detected in the screening assay

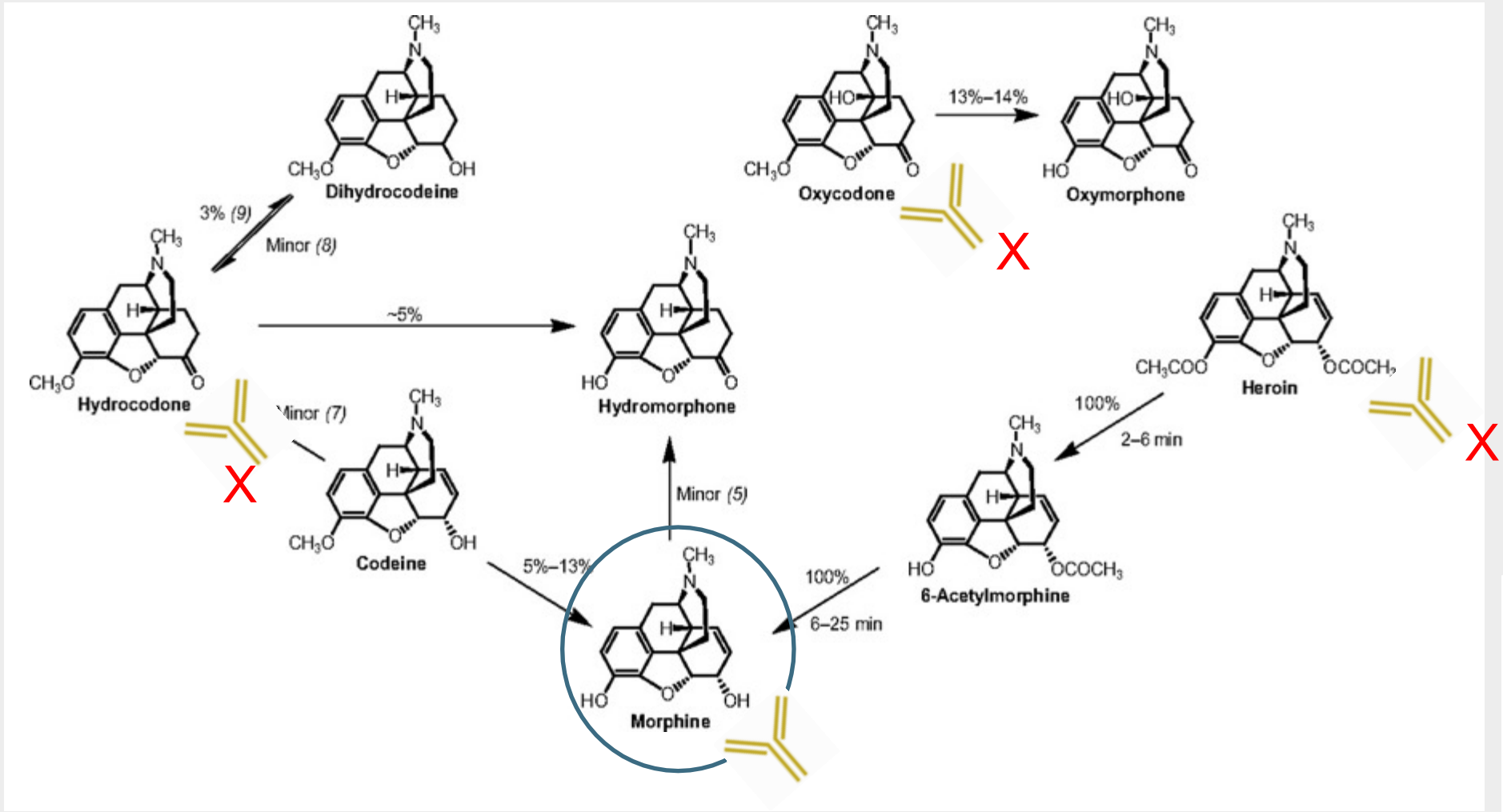
Highly specific

Quantitative

Complicated, expensive

Screening Tests for “Drugs of Abuse”

- Enzyme immunoassay
  - Based on a substance’s structure.
  - Relatively inexpensive, easily automated
- Analytical false positives are possible (e.g., amphetamine assay identifies pseudoephedrine)
  - Confirm “unconfirmed” positive screens in some clinical situations
- Analytical false negatives are uncommon (i.e., assay completely misses an expected analyte)
  - Clinical false negatives occur (e.g., opiate assay doesn’t detect a non-morphinan opioid)


Dihydrocodeine
3% (9)
Minor (8)
Hydrocodone
~5%
Hydromorphone
Oxycodone
13%–14%
Oxymorphone
Heroin
100%
2–6 min
6-Acetylmorphine
Minor (7)
Codeine
5%–13%
Minor (5)
Morphine
100%
6–25 min
X
X
X

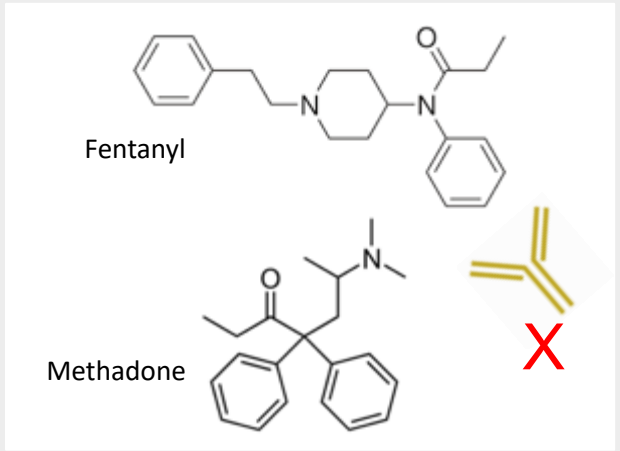

Fentanyl
Methadone
X

TABLE 7–4 Performance Characteristics of Common Urine Drug Screening Immunoassays[a]

Drug/Class	*Detection Limits (ng/mL)[b]*	*Confirmation Limits (ng/mL)[b]*	*Detection Interval[c]*	*Comments*
Amphetamine/ methamphetamine	500	500	1–2 days (2–4 days)	Decongestants, ephedrine, L-methamphetamine, selegiline, and bupropion metabolites are reported to give false-positive test results with some assays; MDA, MDEA, and MDMA are variably detected.
Barbiturates	200		2–4 days	Phenobarbital detection interval is up to 4 weeks.
Benzodiazepines	100–300		1–30 days	Benzodiazepines vary in reactivity and potency. Hydrolysis of glucuronides increases sensitivity. False-positive test results are reported with oxaprozin.
Cannabinoids	50	15	1–3 days (1 month)	Screening assays detect inactive and active cannabinoids; confirmatory assay detects inactive metabolite THCA. Duration of positivity is highly dependent on screening assay detection limits.
Cocaine	150	100	2 days (1 wk)	Screening and confirmatory assays detect inactive metabolite BE. False-positive test results caused by cross-reactive compounds are unlikely.
Opiates			1–2 days (1 week)	Semisynthetic opioids derived from morphine show variable cross-reactivity. Fully synthetic opioids (eg, fentanyl, meperidine, methadone, tramadol) have minimal cross-reactivity. Quinolones are known to cross-react with some assays.
Codeine/morphine	2,000	2,000		
Hydrocodone/hydromorphone	300	100		
Oxycodone/oxymorphone	100	50		
6-Acetylmorphine	10	10		
Methadone	300		1–4 days	Doxylamine is reported to cross-react with some assays.
Phencyclidine	25	25	4–7 days (1 month)	Dextromethorphan, diphenhydramine, ketamine, and venlafaxine is reported to cross-react with some assays.

[a]Performance characteristics vary with manufacturer and may change over time. For the most accurate information, consult the package insert of the current lot or contact the manufacturer. [b]Substance Abuse and Mental Health Services Administration recommendations[10] are shown for amphetamines/methamphetamines, cannabinoids, cocaine, opiates, and phencyclidine immunoassays. Other commercial immunoassay cutoffs are also listed. Other cutoffs may be set by individual laboratories. [c]Values are after typical use; values in parentheses are after heavy or prolonged use.

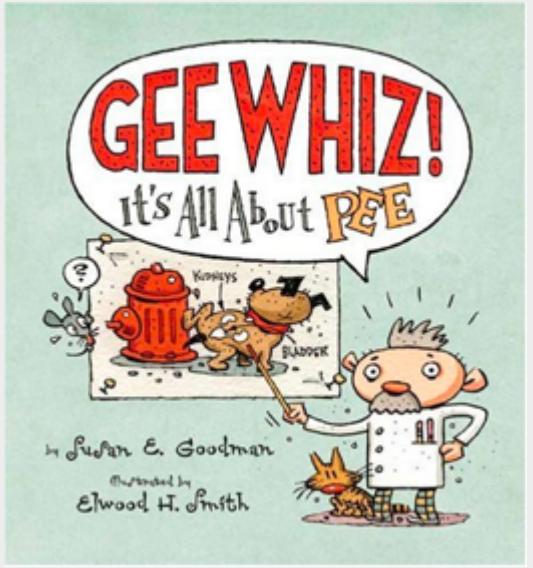
BE = benzoylecgonine; MDA = methylenedioxyamphetamine; MDEA = methylenedioxyethylamphetamine; MDMA = methylenedioxymethamphetamine; THCA = tetrahydrocannabinolic acid.

Complicated situation

- You are evaluating your long-standing patient who tests positive for “opiates” on routine testing. The patient assures you they have not used any drugs.
- Analytical true positive
  - Clinical false positive (need 6-MAM)
- Note for all screens
  - Unclear which substance (e.g., which opioid)
  - Does not correlate with impairment
  - Cannot tell route, time of use, or amount used

Interpretation of a Negative Opioid Screen

- Patient is not using (e.g., diversion)
- Clinical false negative
  - Collection/Lab error
  - Wrong assay used
    - e.g.: “Opiate” assay for oxycodone
  - Cutoffs are often used
  - Detection periods are short
  - Adulteration



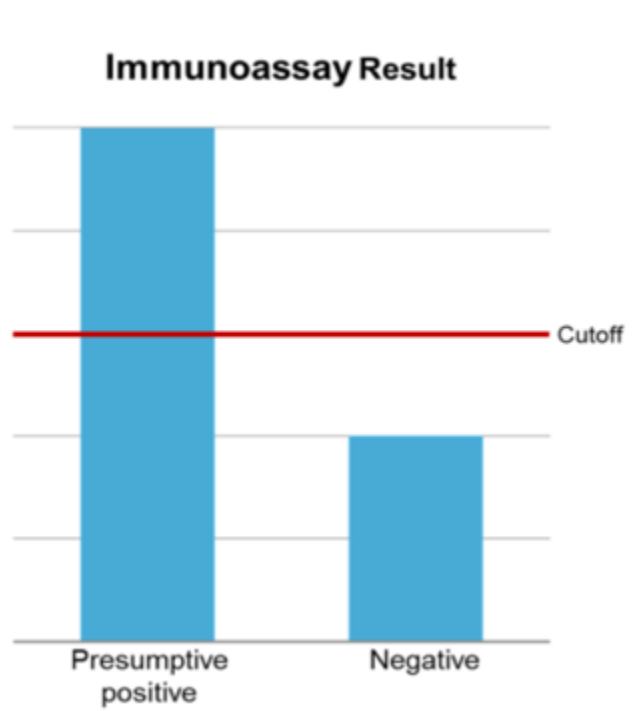
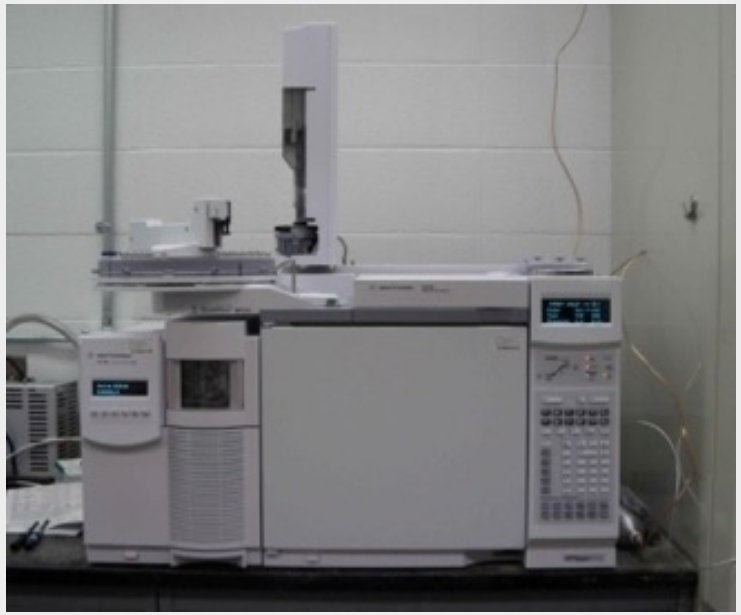


TABLE 2. **Length of Time Drugs of Abuse Can Be Detected in Urine**

Drug	Time
Alcohol	7-12 h
Amphetamine	48 h
Methamphetamine	48 h
Barbiturate	
Short-acting (eg, pentobarbital)	24 h
Long-acting (eg, phenobarbital)	3 wk
Benzodiazepine	
Short-acting (eg, lorazepam)	3 d
Long-acting (eg, diazepam)	30 d
Cocaine metabolites	2-4 d
Marijuana	
Single use	3 d
Moderate use (4 times/wk)	5-7 d
Daily use	10-15 d
Long-term heavy smoker	>30 d
Opioids	
Codeine	48 h
Heroin (morphine)	48 h
Hydromorphone	2-4 d
Methadone	3 d
Morphine	48-72 h
Oxycodone	2-4 d
Propoxyphene	6-48 h
Phencyclidine	8 d

Data from references 7 through 12.



The Gold Standards for Confirmation

- Gas Chromatography/Mass Spectrometry
  - Gold standard for confirmation
  - Chemical “fingerprint” of drugs
  - Sensitive and specific
  - Legally defensible

- Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS)
  - Emerging Standard for Confirmation
  - Less sample preparation

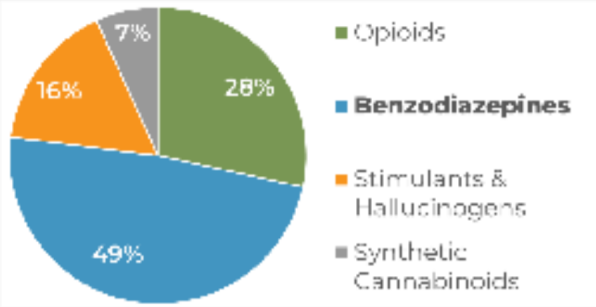
NPS Benzodiazepines in the United States

TREND REPORT | Q1 2024

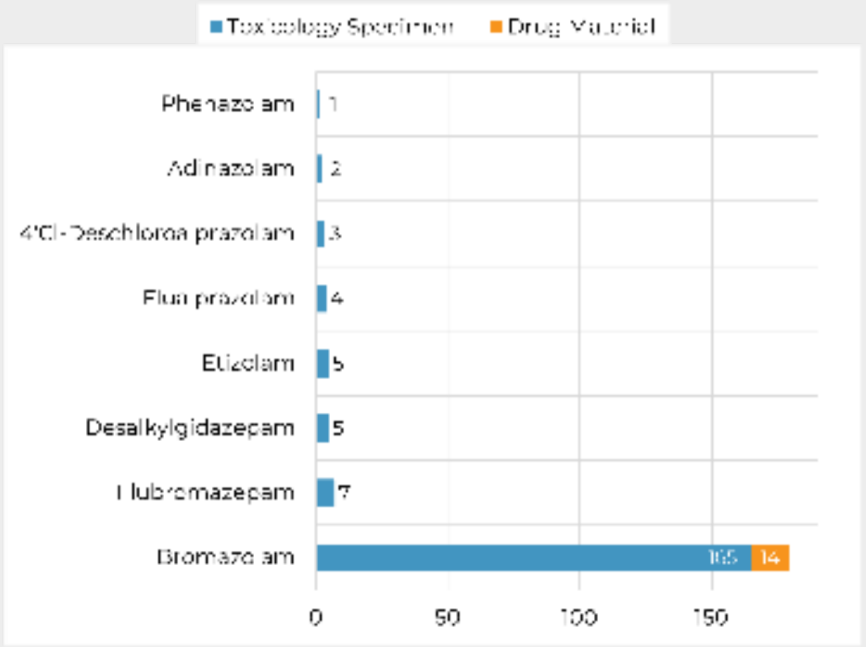
PURPOSE: This report provides up-to-date information regarding the status of NPS benzodiazepine prevalence and positivity in the United States.

OVERVIEW: Novel psychoactive substances (NPS), including NPS benzodiazepines, continue to pose great challenges for forensic scientists, clinicians, and public health and safety personnel. NPS benzodiazepines have been implicated in an increasing number of adverse health events, marked by emergency room admissions and death investigations, especially when ingested in combination with opioids. Maintaining a current scope of analysis can be challenging, requiring comprehensive analytical methodologies and reference materials for identification(s).

OBJECTIVE: Our laboratory utilizes novel approaches for the analysis of drugs in toxicology specimens and drug materials using comprehensive non-targeted data acquisition by gas chromatography mass spectrometry (GC-MS) and liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QTOF-MS). The scope of analysis contains more than 1,200 drugs, including a vast majority of NPS and their metabolites. This approach allows for real-time identification of new benzodiazepines and further data analysis of important trends. Cases and sample types linked to these results originate from recreational drug use, medicolegal death investigations, clinical intoxications, and/or driving under the influence of drugs investigations, among other circumstances. The results in this report represent the total number of NPS identifications at the CFSRE during this quarter, including those from sample-mining, data-mining, routine testing, and esoteric testing.

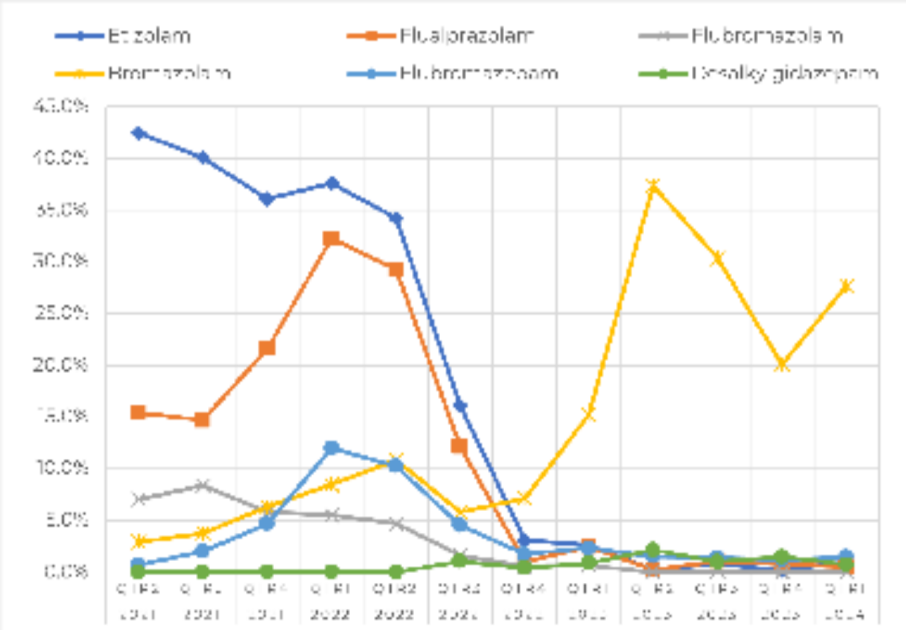


NPS BENZODIAZEPINES IDENTIFIED



SELECT POSITIVITY: Q2 2021 TO Q1 2024

Positivity plots are derived from a select toxicology data source that has been consistently monitored since 2018.



ACKNOWLEDGEMENTS: This report was prepared by Alex J. Krotulski, PhD; Sara E. Walton, MS; Joshua S. DeBord, PhD; Amanda LA. Mohr, MSFS, D-ABFT-FT; and Barry K. Logan, PhD, F-ABFT at the Center for Forensic Science Research and Education (CFSRE) at the Fredric Rieders Family Foundation. CFSRE's NPS Discovery program acknowledges scientists at the CFSRE and NMS Labs for their involvements and contributions. For more information about our programs and reports, please contact NPS Discovery at npsdiscovery@cfsre.org or visit our website at www.npsdiscovery.org.

FUNDING: CFSRE's NPS Discovery is supported by the National Institute of Justice, Office of Justice Programs, U.S. Department of Justice (Award Number 15PNIJ-22-GG-04434-MUMU, "Implementation of NPS Discovery – An Early Warning System for Novel Drug Intelligence, Surveillance, Monitoring, Response, and Forecasting using Drug Materials and Toxicology Populations in the US"). The opinions, findings, conclusions and/or recommendations expressed in this publication are those of the author(s) and do not necessarily represent the official position or policies of the U.S. Department of Justice.

Buprenorphine analysis

- Can only generalize about expected levels
  - No credible way to say “X” dose should give “Y” level
  - Patients tend to stay within a certain range over time unless dose change
    - Trending helpful and can detect aberrancy
- Adulterated specimen
  - Bup without metabolite (always)
  - Bup >1000 ng/mL, even with metabolite (suggestive)
- Higher Bup levels than Norbup levels due to:
  - Dosing shortly before urine test
  - CYP 3A4 inhibitor or substrate which slows conversion to metabolite

Matrix Considerations

- Window of detection
- Time to obtain results (availability of POCT)
- Ease of collection (need for trained personnel, collection facilities)
- Invasiveness/unpleasantness of collection
- Availability of the sample (e.g., renal health, shy bladder, baldness, dry mouth)
- Susceptibility of the sample to tampering

Where Can I Get Help with Interpretation?

- Medical or forensic toxicologist
- Staff at the testing laboratory
- A physician with MRO certification

What property of fentanyl accounts for its enhanced psychoactive effects compared to morphine?

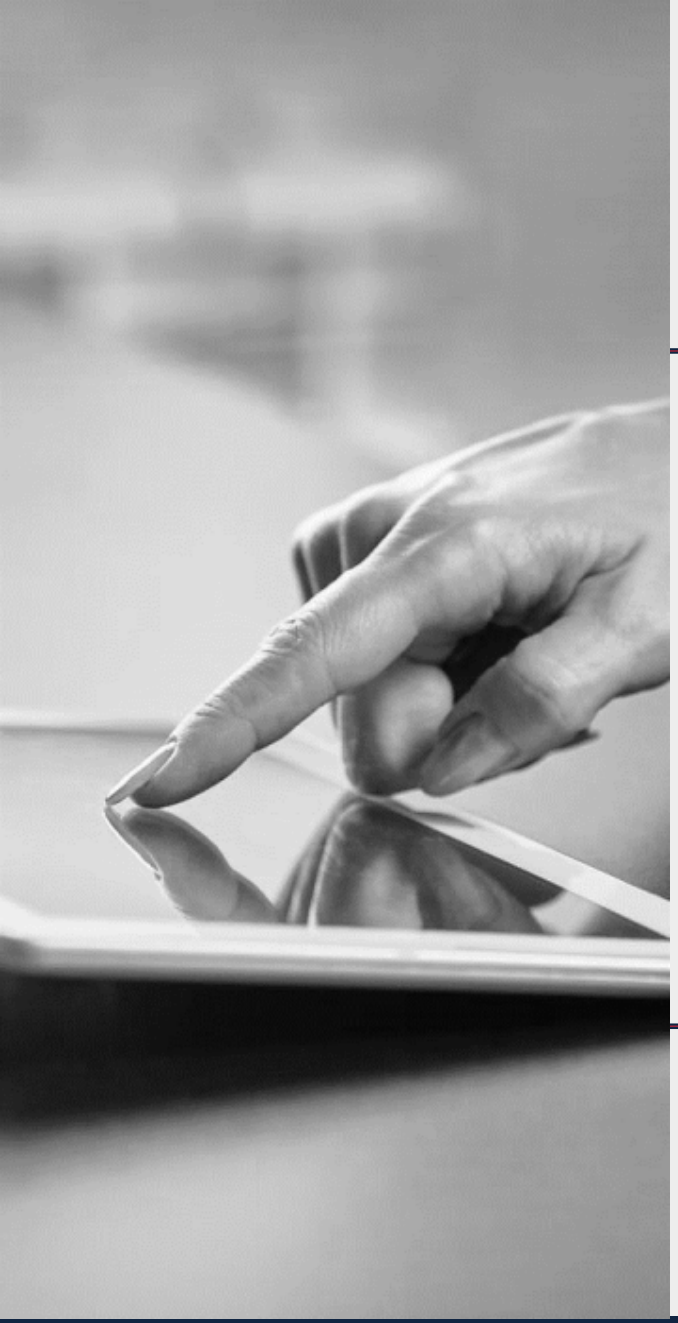
A. Charge
B. Lipophilicity
C. Molecular weight
D. Potency

A patient started on opioids requires increasing doses of medication to get adequate pain relief. At the same time, painful stimuli elicit more pain that they previously did. What does this represent?

A. Hyperalgesia
B. Pharmacodynamic tolerance
C. Pharmacokinetic tolerance
D. Withdrawal

Which of the following drug screening tests is associated with the lowest rate of false positive results?

A. Amphetamine
B. Cocaine
C. Opioids
D. Phencyclidine



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