DRUG SCAN
AN ACM GLOBAL LABORATORY

ORAL FLUID TESTING

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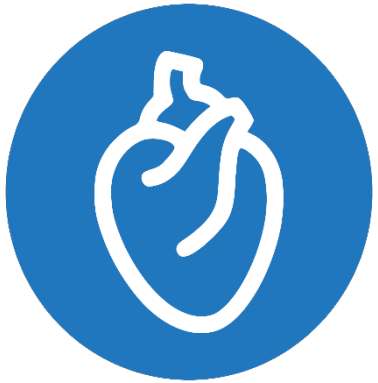
Objectives

1. Identify the role of drugs, drug testing using oral fluid as a matrix.
2. Discuss oral fluid collection using Quantisal™ Oral Fluid Collection Device.
3. Explain the unique features of identifying drugs and metabolites in oral fluid.

MATRICES FOR DRUG TESTING

Different Matrices

Hair

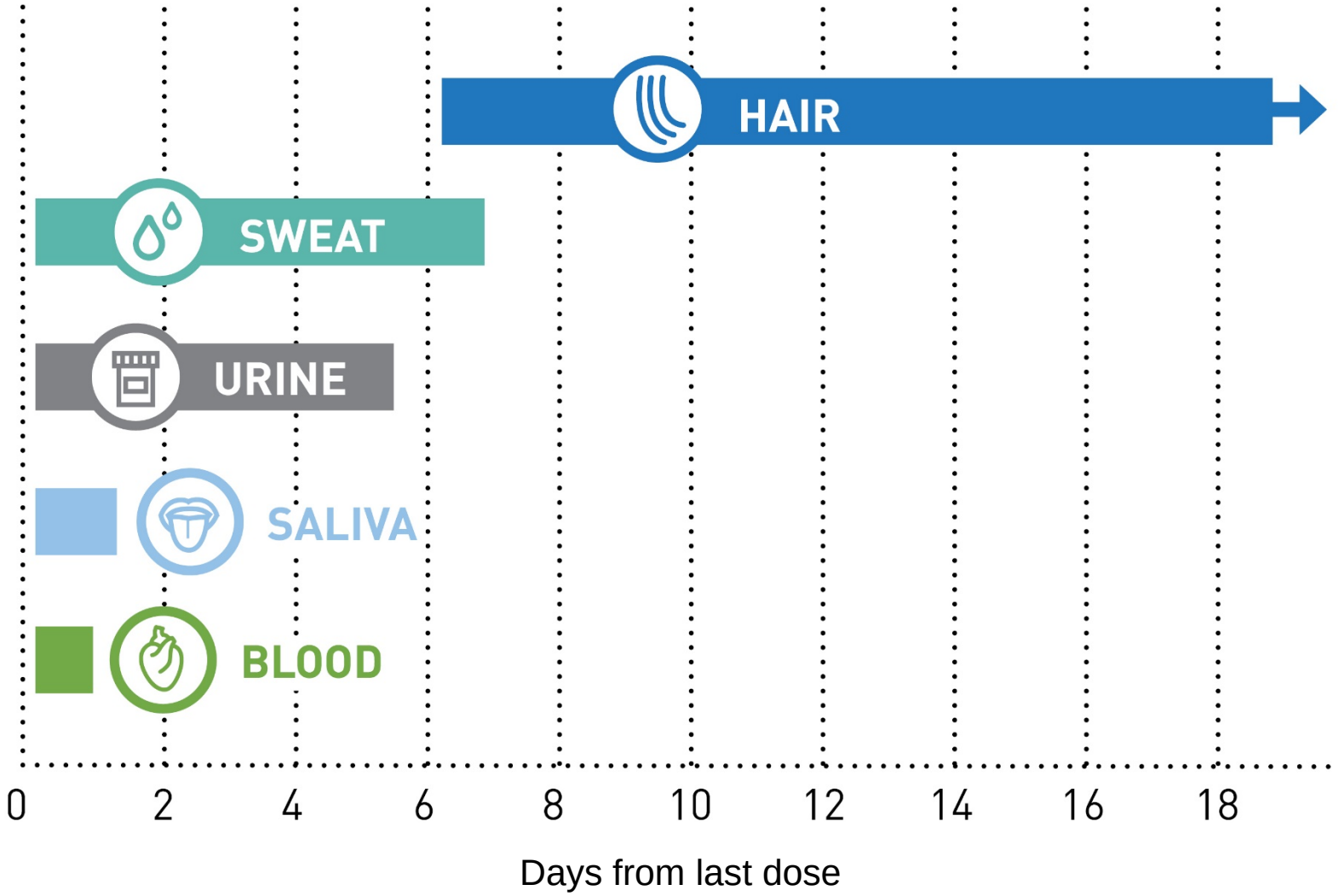


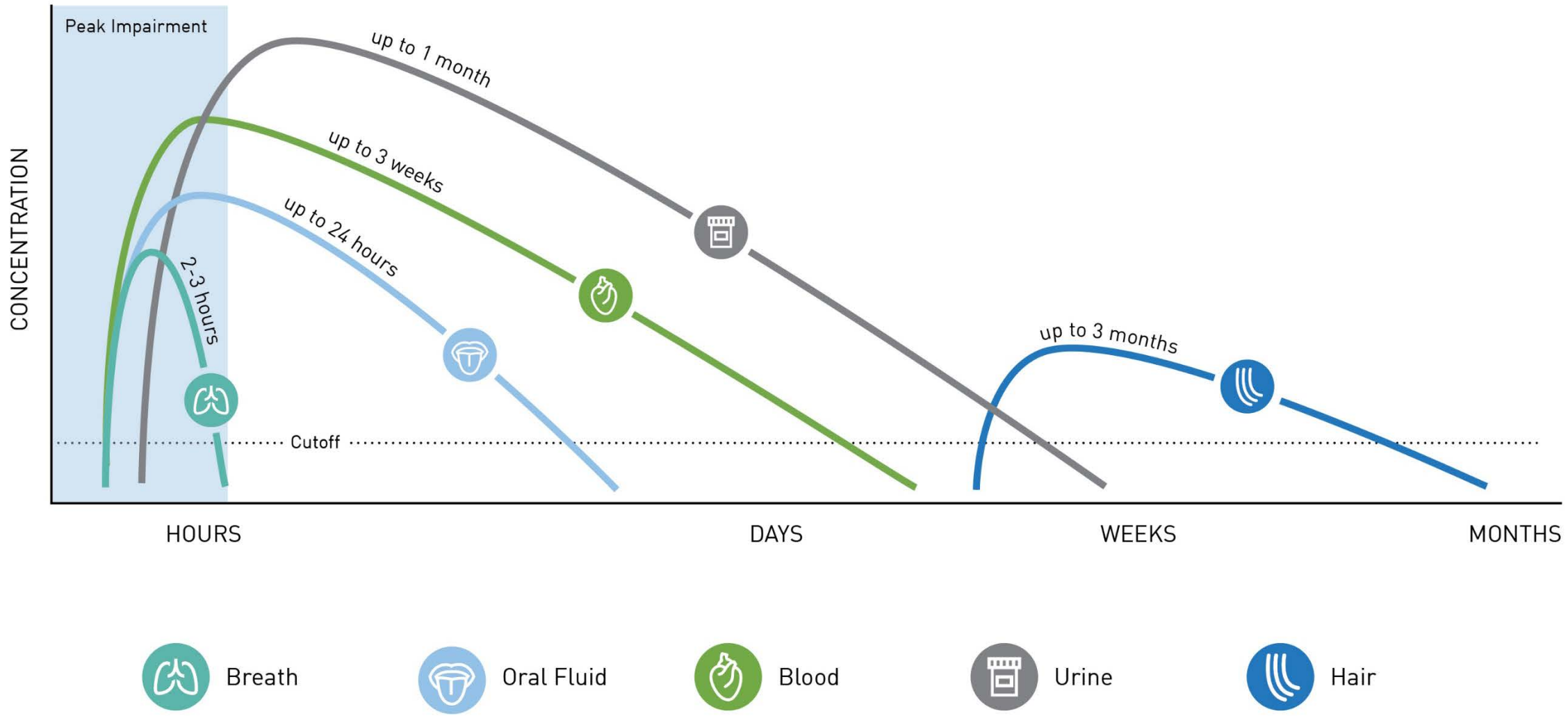
Blood

Urine

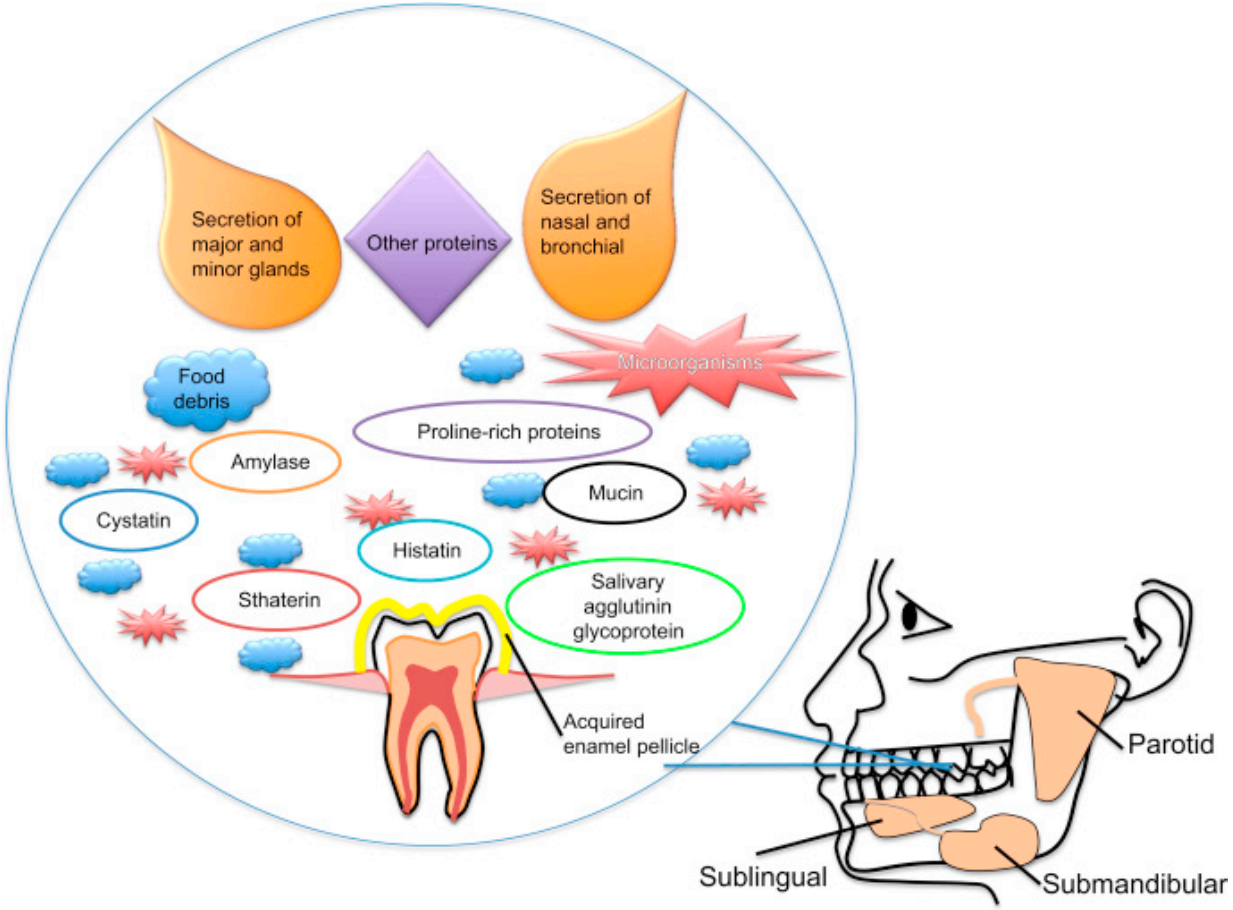
Oral Fluid

Drug Detection Times in Different Matrices





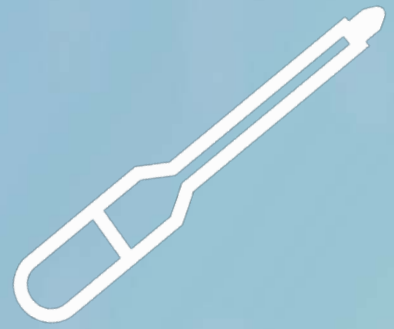
The components of whole saliva and the location of major salivary glands. Saliva is composed of secretions of major and minor salivary glands, a mixture of bronchial and nasal secretions, gingival crevicular fluid, as well as products from microorganisms, blood, cells, and food debris. The salivary proteins form the acquired enamel pellicle that is precursor of dental biofilm formation. [7]



Oral Fluid and Drug Deposition

- Highly perfused Salivary glands and oral cavity tissues allow rapid transfer of drugs from blood to saliva
- Transfer occurs primarily from passive diffusion and depends on numerous factors:
  - Chemical properties of the drug
  - Salivary pH
  - Lipid soluble parent drugs tend to diffuse across cell membranes into oral fluid more easily than metabolites
  - Concentration of un-ionized drug–ionized drug does not passively diffuse
  - Drug-protein binding–only free drug can diffuse

COLLECTION OF ORAL FLUID



Oral Fluid Collection Advantages

- Simple collection
- Non-invasive
- No need for special restroom facilities—can be collected in any location
- No need for same sex collectors
- Can be performed under direct observation or video monitored
- Reduced risk of adulteration and substitution
- Identification of recent drug use

Immunalysis Oral Fluid Collection Video

Oral Fluid Collection Disadvantages

- Some drugs may reduce salivation resulting in:
  - Reduced volume
  - Longer collection time
- Drug concentrations are frequently lower in Oral Fluid (OF) than in urine
- Not all drugs cross into the oral fluid
- Drugs that are smoked, inhaled or taken orally may
  - Contaminate the oral mucosa and OF
  - May lead to increased detection rates
  - Result in reduced correlation with blood concentrations

Oral Fluid and Drug Deposition

- Saliva is relatively acidic–meaning that basic drugs will often be found in higher concentrations than in plasma (blood)
  - Amphetamines and cocaine are examples of this

Oral Fluid Detection Times

- Most useful in detecting recent drug use
- Drugs and some metabolites can be detected for a period of several hours to a couple of days

Oral Fluid Drug Levels

- Drug levels are generally related to blood levels
- Drugs may be present as residual drug in the oral cavity
  - Drugs administered orally–sublingual Buprenorphine
  - Drugs smoked–marijuana

Average Oral Fluid to Blood Concentration Ratios for Selected Drugs

The average ratios are derived from pharmacokinetic studies and will change depending on a number of factors, including pH of oral fluid, protein binding and degree of contamination of the membranes in the oral cavity by recently consumed drug.[4]

Table 2. Average oral fluid to blood concentration ratios for selected drugs.

Drug (type)	Average oral fluid to blood concentration ratio
Alcohol (ethanol)	1.07
Barbiturates	0.3
Buprenorphine	1
Codeine (basic)	4
Methamphetamine (basic)	2
MDMA (basic)	7
Cocaine (basic)	3
Diazepam (acidic)	0.01-0.02
Methadone (basic)	1.6
Morphine (basic)	0.8
Δ9-Tetrahydrocannabinol (neutral)	1.2

IDENTIFYING DRUGS AND METABOLITES

Interpretation of Some Commonly Encountered Oral Fluid Drugs [1,2]

Amphetamine

- Appears rapidly in oral fluid
- Parallels plasma drug concentration
- Risk of a positive from passive exposure appears unlikely
- Possible sources–prescription ADHD medications such as Adderall® and Vyvanse®
- May be present as a metabolite of methamphetamine

Methamphetamine

- Appears rapidly in oral fluid
- Abused by numerous routes including smoking, snorting, injecting and oral administration
- Parallels plasma drug concentration
- Risk of a positive from passive exposure appears unlikely
- May be present along with amphetamine as its metabolite

Benzodiazepines

- Lipophilic drugs with high plasma protein binding (70-99%)
- Generally weakly acidic causing lower oral fluid detection[6]
- Blood and oral fluid levels peak in approximately 0.75 hour
- Does not correlate well with blood concentrations: 88-197% but can be used to confirm recent intake of benzodiazepines[3]

Cannabis

- Smoking is primary route of administration
- Ingestion of edibles is not uncommon
- THC Found in oral fluid following smoked and oral ingestion of cannabis

Marijuana Levels in Oral Fluid

- THC Identified in oral fluid following smoking and oral ingestion
- THCCOOH also found in very low concentrations
- Extremely high THC levels immediately after smoking and decline rapidly
- Recent study indicates passive inhalation did NOT produce false positive oral fluid tests[9]

Cocaine

- Short approximate 1 hour half life
- Rapidly hydrolyzed to benzoylecgonine (BZE)
- Cocaine and BZE show up rapidly in oral fluid following all routes of administration
- Oral fluid levels decline rapidly

Cocaine/BZE Levels in Oral Fluid

- Positive cocaine negative BZE use within approximately 8 hours
- Positive cocaine greater than BZE likely uses within 2-8 hours
- Positive cocaine less than BZE
  - Occasional users cocaine use likely within 12 hours
  - Cocaine use likely within 48 hours for daily users
- BZE levels positive NO Cocaine
  - Cocaine use likely within 48 hours for occasional users
  - Cocaine use likely within 48-96 hours for daily users

Opioids - Heroin

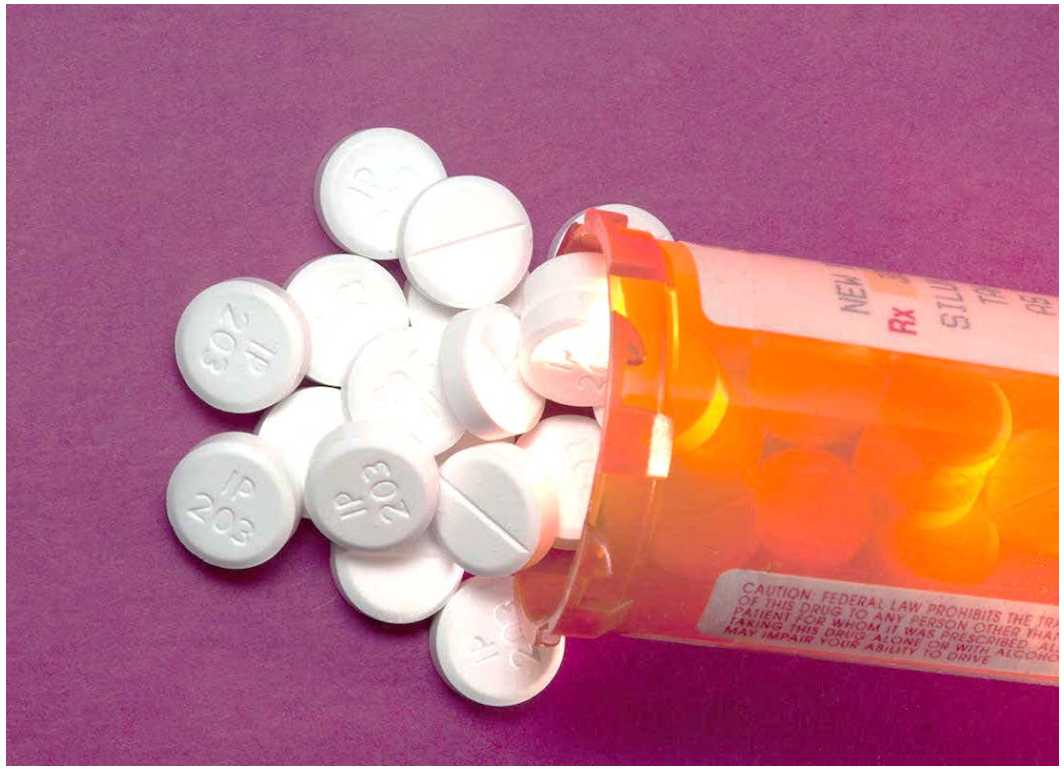
- Heroin - diacetylmorphine
  - Most commonly administered IV or smoked
  - Very short half life rapidly converted to 6-acetylmorphine (6-am)
- 6-am
  - Appears in oral fluid within 2 minutes following administration
  - Levels similar to blood when IV route used
  - Higher in oral fluid following smoking– probable oral fluid deposition of drug
  - 30-60 minutes after smoking heroin, oral fluid levels diminish and reflect blood

Opioids – Heroin Levels in Oral Fluid

- Positive for 6-am and morphine
  - Heroin use
- Positive morphine only
  - Heroin or morphine use; possible poppy seed ingestion within last hour
- Positive morphine and codeine
  - Codeine > morphine–codeine use
  - Morphine > codeine–possible heroin or morphine. Codeine may be impurity in heroin production generally very low codeine concentration
  - Possible recent poppy seed ingestion within the hour

Morphine

- Morphine appears rapidly in oral fluid
- High degree of glucuronidation but most likely found because high doses of morphine are more commonly prescribed or ingested
- Following parenteral administration, morphine appears rapidly in oral fluid
- Also a metabolite of heroin, codeine and a natural component of poppy seeds



Morphine Levels in Oral Fluid

- Positive morphine
  - Possible use of heroin, morphine or poppy seeds
    - Poppy seed ingestion may result in low concentration up to 1 hour after consumption
    - Codeine use has not been reported to produce detectable morphine levels
- Positive morphine and 6-am
  - Heroin use
- Positive morphine and codeine
  - Morphine > codeine
    - Heroin(codeine as an impurity) or combined morphine/codeine use

6-Acetylmorphine Levels in Oral Fluid

- Positive 6-am believed to be detectable in oral fluid and urine 8 hr and 34.5 hr after use respectively
- A study by Vindenes et al. showed that 6-am was detected in OF 4-8 days after use with undetectable UR and OF morphine levels which challenges the detection windows above[8]

Codeine

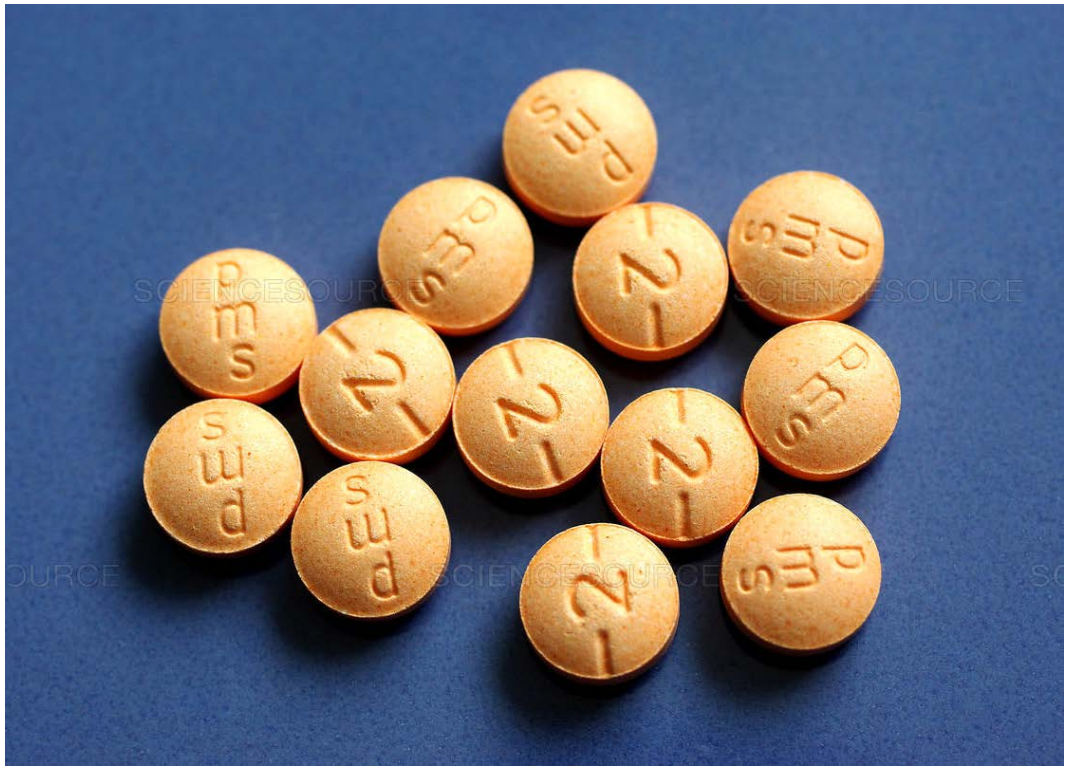
- Oral administration results in levels within an hour max 1.6-1.7 hrs
- Levels 3-4 times higher in oral fluid than plasma
- Metabolizes to morphine–detected in urine
- Detected in oral fluid following IV and smoked heroin administration and poppy seed ingestion by not following codeine administration

Codeine Levels in Oral Fluid

- Positive codeine
  - Codeine use
- Positive codeine and morphine
  - Morphine > codeine
    - Possible heroin
    - Secondary codeine use in combination with morphine
    - Possible poppy seed ingestion within an hour

Hydromorphone

- Oral administration plasma levels peak in approximately 1 hour
- Reported to appear in saliva rapidly following IV administration



Hydromorphone Levels in Oral Fluid

- Positive hydromorphone
  - Hydromorphone use
- Positive hydromorphone and morphine
  - Hydromorphone > morphine–hydromorphone and morphine use
  - Hydromorphone << morphine–possible hydromorphone use or showing up as a minor metabolite of morphine–rare

Hydrocodone

- Misuse primarily by the oral route
- May be abused intranasal, smoked or rectal administration
- Reaches maximal plasma concentration in 1 hour

Hydrocodone Levels in Oral Fluid

- Positive hydrocodone–no hydromorphone or codeine
  - Hydrocodone use
- Positive hydrocodone and hydromorphone
  - Hydrocodone > hydromorphone–Hydrocodone use
  - Hydrocodone < hydromorphone–likely combined use of hydrocodone and hydromorphone. Could occur at low concentrations toward the end of excretion following hydrocodone use
- Positive Hydrocodone and Codeine
  - Hydrocodone > or equal to codeine–combined hydrocodone and codeine
  - Hydrocodone << codeine–possible hydrocodone use but possibly hydrocodone as a minor metabolite of codeine

Oxycodone

- Oral fluid levels are more closely related to blood levels than urine
- In one study using 23 pairs of samples, the median concentration in oral fluid was 524 ug/L and blood was 53 ug/L. Projecting a oral fluid to plasma ratio of 12[5]
- Appears in oral fluid and blood within 15-30 minutes after oral administration

Oxycodone Levels in Oral Fluid

- Positive oxycodone–oxycodone use
- Positive oxycodone and oxymorphone
  - Oxycodone > oxymorphone
    - Oxycodone use–oxymorphone minor metabolite
  - Oxycodone < oxymorphone
    - Likely combined oxycodone and oxymorphone use but could occur at low concentrations toward end of excretion following oxycodone use

Oxymorphone

- Excreted in low levels in oral fluid

Oxymorphone Levels in Oral Fluid

- Positive oxymorphone
  - oxymorphone use
  - May be present in low concentration following oxycodone administration as a minor metabolite

Fentanyl

- Oral fluid levels are fairly well correlated with the respective plasma concentration. OF/plasma ratio of 3.0 has been reported[10]

Methadone

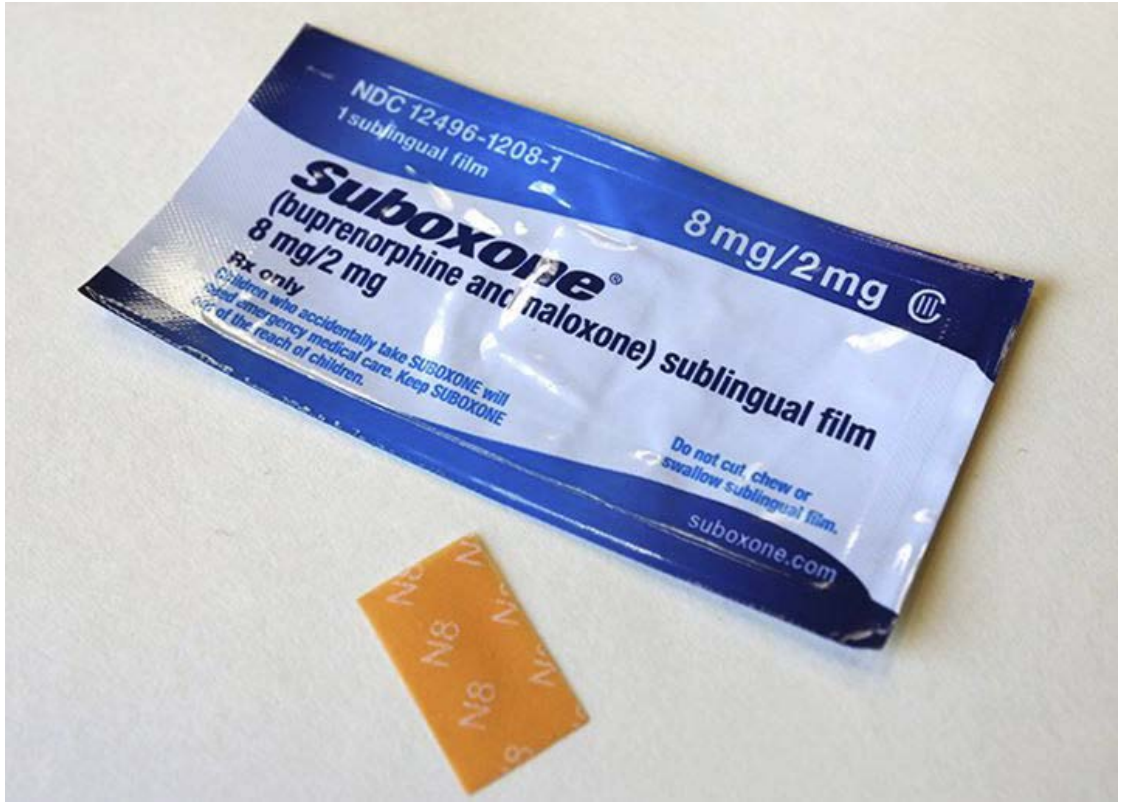
- Methadone and EDDP (metabolite) appear rapidly in oral fluid and correlate with plasma concentrations

Methadone and EDDP Levels in Oral Fluid

- Positive Methadone–No EDDP
  - Methadone use within 24-48 hours or possible methadone doping
- Positive Methadone and EDDP
  - Methadone use within 24-48 hours

Buprenorphine

- Following sublingual administration high levels may be due to an oral mucosal drug depot



Buprenorphine and Norbuprenorphine Levels in Oral Fluid

- Positive buprenorphine
  - Buprenorphine use
- Positive buprenorphine and norbuprenorphine
  - Buprenorphine >> norbuprenorphine–acute buprenorphine use
  - Buprenorphine < or equal to norbuprenorphine–chronic buprenorphine use

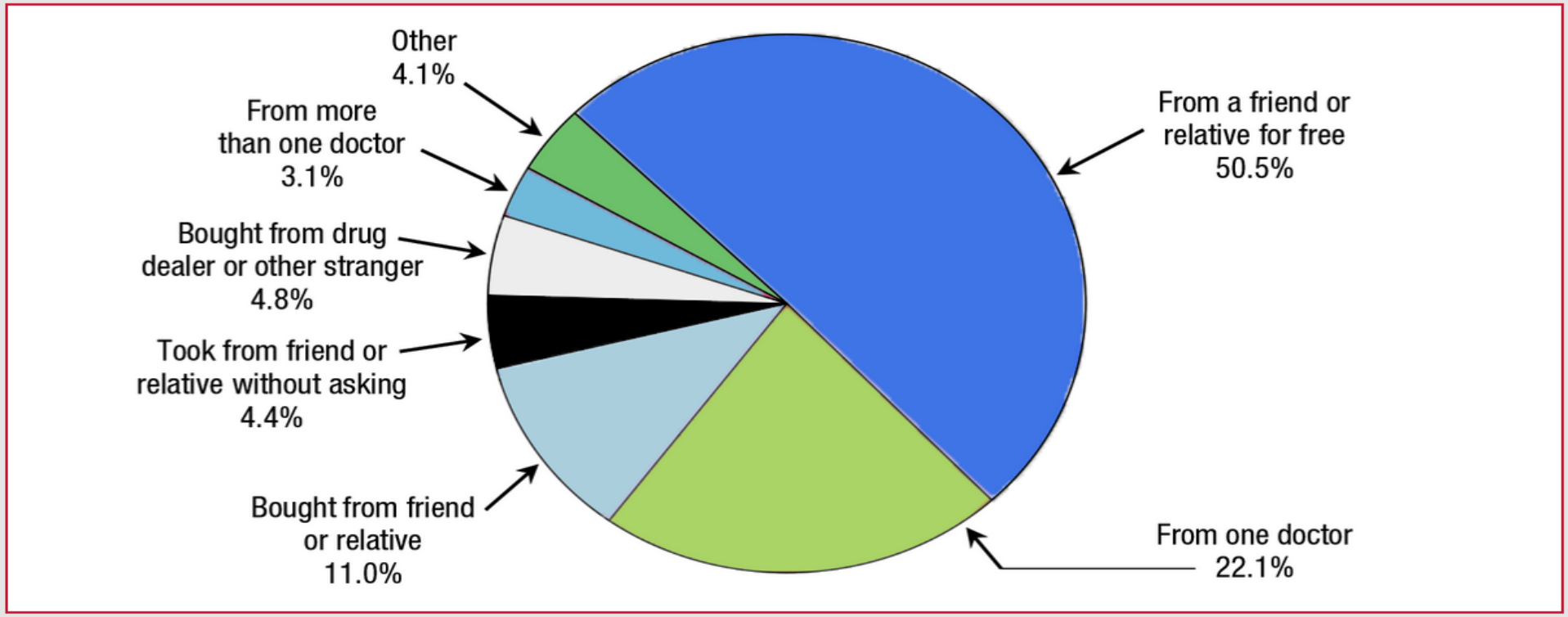
DRUGSCAN Oral Fluid Screen and Confirmation

SCREENING			CONFIRMATION			CONFIRMATION		
Drug	**ng/mL**	**Method**	**Drug**	**ng/mL**	**Method**	**Drug**	**ng/mL**	**Method**
Amphetamine	50	Elisa	**Amphetamines**			**Ethanol**		
Barbiturates	50	Elisa	Amphetamine	10	LCMSMS	Ethanol	20	HSGC
Benzodiazepines	20	Elisa	Methamphetamine	10	LCMSMS	**Methadone**		
Buprenorphine	5	Elisa	MDA	10	LCMSMS	EDDP	10	LCMSMS
Carisoprodol	50	Elisa	MDMA	10	LCMSMS	Methadone	10	LCMSMS
Cocaine Metabolites	20	Elisa	MDEA	10	LCMSMS	**Narcotics**		
Ethanol (Alcohol)	20	HSGC	**Benzodiazopines**			Buprenorphine	10	LCMSMS
Fentanyl	1	Elisa	Alprazolam	10	LCMSMS	Fentanyl	2	LCMSMS
Marijuana	4	Elisa	Bromazepam	10	LCMSMS	Meperidine	10	LCMSMS
Meperidine	50	Elisa	Clonazepam	10	LCMSMS	Norbuprenorphine	10	LCMSMS
Methadone	50	Elisa	Diazepam	10	LCMSMS	Norfentanyl	10	LCMSMS
Methamphetamine	50	Elisa	Estazolam	10	LCMSMS	Normeperidine	10	LCMSMS
Opiates	40	Elisa	Flunitrazepam	10	LCMSMS	Tramadol	10	LCMSMS
Oxycodone	40	Elisa	Lorazepam	10	LCMSMS	**Opiates**		
Phencyclidine	10	Elisa	Lormetazepam	10	LCMSMS	6-Acetylmorphine	2	LCMSMS
Tramadol	50	Elisa	Midazolam	10	LCMSMS	Codeine	10	LCMSMS
			Nitrazepam	10	LCMSMS	Dihydrocodeine	10	LCMSMS
			Nordiazepam	10	LCMSMS	Hydrocodone	10	LCMSMS
			Oxazepam	10	LCMSMS	Hydromorphone	10	LCMSMS
			Prazepam	10	LCMSMS	Morphine	10	LCMSMS
			Temazepam	10	LCMSMS	Oxycodone	10	LCMSMS
			Triazolam	10	LCMSMS	Oxymorphone	10	LCMSMS
			Barbiturates			**Soma**		
			Amobarbital	40	LCMSMS	Carisoprodol	20	LCMSMS
			Butalbital	40	LCMSMS	Meprobamate	40	LCMSMS
			Pentobarbital	40	LCMSMS	**Tapentadol**		
			Phenobarbital	40	LCMSMS	Tapentadol	2	LCMSMS
			Secobarbital	40	LCMSMS	**THC**		
			Cocaine			Carboxy THC	2	LCMSMS
			BE	2	LCMSMS	THC	2	LCMSMS
			Cocaine	2	LCMSMS	**PCP**		
						PCP	2	LCMSMS

Current COVID-19 & Substance Use Disorder

- Current situation highlights possible increased drug use
  - Less monitoring
  - More boredom
  - Higher risk of COVID-19 serious implications
  - Could hit individuals with SUD harder esp. tobacco, marijuana or vaping
  - Opiate use disorder (OUD) and methamphetamine use disorder may be more vulnerable since the virus attacks the lungs which are affected by OUD and Methamphetamine abuse
  - https://www.drugabuse.gov/about-nida/noras-blog/2020/04/covid-19-potential-implications-individuals-substance-use-disorders

Figure 1. Source of prescription pain relievers for the most recent nonmedical use among past year users aged 12 or older: annual averages, 2013 and 2014



Source: SAMHSA, Center for Behavioral Health Statistics and Quality, National Surveys on Drug Use and Health (NSDUHs), 2013 and 2014.

Source: https://www.samhsa.gov/data/sites/default/files/report_2686/ShortReport-2686.html
January 12 2017 SAMHSA Publication

American Society of Addiction Medicine Drug Testing Guidelines

- Drug testing should be used to explore denial, motivation and actual substance use behavior
- Test results that do not align with patient's self-report should generate therapeutic discussion with the patient
- In addition to measuring treatment efficacy, drug testing may also serve as a motivation and reinforcement for abstinence
- Providers should use negative test results as a source of encouragement
- Providers should persuade patients to the extent possible that drug testing is therapeutic and not punitive to avoid an "us versus them" mentality
- For testing that will inform an irreversible clinical decision, formal laboratory analysis – NOT POCT – remains the "gold standard" testing methodology

https://www.asam.org/docs/default-source/quality-science/appropriate_use_of_drug_testing_in_clinical-1-(7).pdf?sfvrsn=2

American Society of Addiction Medicine Drug Testing Guidelines

- The ability to consult with laboratory staff when needed is an important consideration in choosing a laboratory. The relationship between the testing laboratory and the addiction treatment center should be collaborative. Providers should be able to communicate with the testing laboratory about test panels, detecting sample tampering, test result interpretation, and regional drug use trends

https://www.asam.org/docs/default-source/quality-science/appropriate_use_of_drug_testing_in_clinical-1-(7).pdf?sfvrsn=2

ASRA American Society of Regional Anesthesia and Pain Medicine Recommendations

OPIOIDS

- Use telemedicine to evaluate and continue opioid Rx
- Ensure existing Rx to avoid withdrawal
- Provide naloxone education and Rx for high-risk patients
- DEA-registered practitioners can issue Rx for pts without in-person evaluation if
  1) legitimate medical purpose
  2) audio/ visual, real-time, two-way interactive communication system
  3) in accordance with applicable federal and state laws.

https://www.asra.com/page/2903/recommendations-on-chronic-pain-practice-during-the-covid-19-pandemic

DRUGSCAN Certifications

- SAMHSA
- CAP
- Numerous state certifications Including NYS

Questions

- Please use chat function

Video Oral Fluid Collection Monitoring

ORAL FLUID COLLECTION IN A VIRTUAL SPACE.
IT'S HERE. IT'S NOW.

At DRUGSCAN we recognize the importance of maintaining continuity of care for people throughout every community during COVID-19. As part of our commitment to this, we're bringing testing into a virtual space to deliver accurate and reliable results in a timely manner.

Virtual specimen collection is a key breakthrough in bringing essential patient medication monitoring and a smarter, efficient, more versatile collection solution to patients during the COVID-19 crisis, and in the future.

CONVENIENT
Sample collection from anywhere

SECURE
Online observed monitoring for sample verification

PATIENT-CENTERED
Keeps high-risk patients safe

References

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