Laboratory Testing for Substance Use

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(Slide 1)

I. Introduction **(Slide 2)**

A. Background on substance use in the U.S.

1. Prevalence from 2018 national survey for age 12+ [1]

a. 140 million (>50% of U.S.) used alcohol past month

b. 53 million used an illicit substance past year

c. 20 million had repeated substance problems past year

2. But detection and diagnosis of substance problems problematic

a. Dx criteria are imperfect

b. Screening for dx and relapse is challenging

1'. Some patients hide their use

2'. Relatives/friends often don't know of use

B. Drug testing might occur in: **(Slide 3)**

1. Legal/criminal situations where law is broken

2. Preemployment or random testing at work

3. Athletics to ID performance-enhancing substances

4. Medical settings where staff need to know recent use

C. Physicians need to know: **(Slide 4)**

1. Reasons to test for drugs

a. Help direct clinical care [2]

1'. Identify substances in medical emergencies

2'. Support initial diagnosis of a Substance Use Disorder (SUD as defined below)

3'. Monitor abstinence in individuals with a SUD

4'. Monitor adherence in individuals rx'ed controlled meds

b. Not used for universal screening or punitively

2. Methods of drug testing

a. Urine & blood toxicology: most common in clinical settings

b. Less common tests: sweat, saliva, hair & nails

3. Interpretation of urine drug screen (most commonly used)

a. Physicians have poor knowledge re: interpretation [3, 4]

b. Standard urine drug screens identify a limited # of drugs

c. May need further analysis to identify drugs not on standard screens

d. False-positives and false-negatives are common

D. Therefore this lecture covers: **(Slide 5)**

1. Important definitions

2. Role of laboratory testing in substance use

3. Drug-specific considerations with urine testing

4. Limitations of drug testing

II. Important Definitions

A. Using Diagnostic and Statistical Manual Amer Psychiatric Assn (DSM-5) [5]

B. Substance Use Dx (SUD): 2+ in same 12 months: **(Slide 6)**

1. Tolerance

a. ↑ Drug needed for effects OR

b. ↓ Effect with same amt drug

2. Withdrawal (defined below: symptoms begin when stop or cut down)

3. Use longer/more than intended

4. Desire but unable to ↓ or stop use

5. Much time spent obtaining, using, or recovering from effects

6. ↓ Activities in order to use

7. Use despite medical or psychological problems (liver failure, depression)

8. Craving or strong urge/desire to use

9. Failing roles from use (parenting/home, work, school)

10. Hazardous use (i.e., while driving)

11. Social/interpersonal problems from substances (divorce, loss of friends)

B. Substance intoxication [5] (note: use alone ≠ SUD) **(Slide 7)**

1. Recent ingestion of substance

2. Causes problematic physiologic, behavioral and/or psychological Δs

3. Δs are effect of drug on brain

C. Substance withdrawal **(Slide 8)**

1. Symptoms are opposite of acute effect of that drug

2. Cessation (or ↓) of substance after heavy use

3. Using alcohol as i.e., must have 2+ days of the following

a. ↑ Blood pressure, +/or pulse, +/or sweating

b. Hand tremor

c. Insomnia

d. Nausea +/or vomiting

e. Anxiety

D. Technical definitions used in lecture **(Slide 9)**

1.Metabolite = breakdown product of drug metabolism

2. Pharmacokinetics = what body does to the drug, including the 4 steps of:

a. Absorption – how and how much drug enters the body

b. Distribution – where drug goes in body (blood, fat, urine, hair, etc.)

c. Metabolism – how body alters drug in the process of breaking it down

d. Elimination – how drug/metabolite is eliminated

3. Half-life = time taken for [drug] in body to decrease by ½

III. Characteristics of laboratory testing in substance use **(Slide 10)**

A. Test clinical suspicion of drug use based on: **(Slide 11)**

1. History suggesting substance use [6, 7]

a. Past history of substance misuse

b. Family or romantic partner with history of SUD

c. Ongoing issues suggesting SUD:

1'. Sleep disturbances

2'. Failure to fulfill responsibilities

3’. Disrupted familial and social relationships

4’. Engagement in high risk sexual behavior

2. Physical exam findings suggesting substance use [8]

a. Poor grooming/hygiene (i.e. unkempt, body odor)

b. Signs of injection drug use (i.e. scars at injection sites)

c. Significant weight ↑ or ↓

d. Evidence of acute intoxication:

1’. Slurred speech

2’. Unsteady gait

3’. Dilated or constricted pupils

4’. Bizarre or atypical behavior (i.e. aggressive behavior or laughing inappropriately)

5’. Abnormal vital signs (i.e., rapid pulse or high blood pressure)

6’. Skin flushing or sweating

B. Lab testing for substance use affected by: **(Slide 12)**

1. Pharmacokinetics

a. Fast metabolism can → ↓ drug in blood/tissues

b. Drug use missed if concentration too low

c. Affected by time remains in tissue

1’. Diazepam (Valium) sometimes positive up to 30 days

2’. Cocaine may be positive for only 2 days

d. Absorption: not detected if tested too early after use & drug not in tissues

2. Strategies for detection

a. Direct = detect drug or metabolite (breakdown product)

b. Indirect = detect secondary effects (alteration of body tissue/structure)

C. Types of testing

1. Urine testing [9] **(Slide 13)**

a. First drug screen usually antibody (Ab)-based immunoassay

1’. Antibody binds to molecules → rxn = drug present

2’. Advantages [10]

a’. Urine collection is non-invasive

b’. Results quickly available

c’. Low cost

3’. Disadvantages

a’ Cross-reactivity w/ similar molecules→ false-positive (i.e, poppy seed vs opioid)

b’. Doesn’t identify all drugs/metabolites→ false-negatives

c’. Cheating can occur (i.e. using a friend’s urine)

d’. Detection rates vary b/t different manufacturers [11]

e’. Package info from manufacturers not always reliable [12]

b. Confirmatory urine testing usually gas chromatography-mass spectroscopy

1’. Need order to confirm first test or for additional info

2’. Quantify & identify specific drugs/metabolites

3’. Requires an expert to do

4’. More expensive, time-consuming & cost →less available

2. Blood testing **(Slide 14)**

a. Direct biomarkers

1’. Advantages

a’. Can quantify amount substance consumed

b’. Can monitor concentration Δs over time

c’. Results quickly available

2’. Disadvantages

a’. Detects recent ingestion only

b’. Will be negative after short period of abstinence

3’. Example – blood alcohol concentration (BAC) [13] **(Slide 15)**

a’. Determine amount of EtOH used

b’. Monitor Δs in BAC over time

c’. Can predict impairment with BAC, i.e.:

1’’. 0.05g/100 ml blood (50 mg/100 ml) → ↓coordination

2’’. 0.08% = legal limit, above which considered unsafe to drive

3’’. 0.40% (400 mg/100 ml) = coma or death may occur

b. Indirect biomarkers [14, 15] **(Slide 16)**

1’. Advantages

a’. Will detect heavy, chronic use of substance

b’. Slower return to normal levels after abstinence (i.e., 2+ weeks for some)

2’. Disadvantages

a’. Can be falsely ↑ from meds, health, etc.

b’. Some take up to 5 days for results

3’. Serum aminotransferases (i.e. liver functions tests or LFTs) **(Slide 17)**

a’. LFTs incl. aspartate aminotransferase (AST) & alanine aminotransferase (ALT)

b’. AST and ALT part of complete metabolic profile (CMP)

c’. AST/ALT ratio of > 2:1 may indicate liver damage due to EtOH

4’. Mean corpuscular volume (MCV)

a'. Measure of red blood cell size

b'. MCV ↑ w/ chronic, heavy EtOH use

c'. Timing: abstinence → ↓ MCV in 3 months

3. Sweat testing [16] **(Slide 18)**

a. Swab collection

1'. Used to verify intoxication

2'. Detects recent use only (<24 hours)

b. Patch collection

1'. Collect drug over longer periods of time (~1 week)

2'. Possible to provide cumulative measure

3'. Drugs may be reabsorbed

c. Advantages

1'. Non-invasive

2'. Difficult to cheat on test

3'. Can electronically monitor – data collected remotely

4'. Many substances can be detected

d. Disadvantages

1'. Limited quantification (results = "largely present" or "absent")

2’. Unclear effects of exercise (= ↑ sweat production)

4. Hair testing [17] **(Slide 19)**

a. Drug deposited in follicles → presence in hair

b. Hairs cut and sent for testing

c. Advantages

1’. Difficult to cheat

2’. Detects patterns of long-term use

3’. Non-invasive

d. Disadvantages

1’. Limited substances can be detected

2’. Significant time lag until results

3’. Positive test → expensive replication

4’. Cosmetic hair treatments (bleaching/perming) → false-negatives [18]

5. Saliva testing [19, 20] **(Slide 20)**

a. Drug travels to blood or ingested via mouth → drug in saliva

b. Saliva absorbed into pad for testing

c. Advantages

1’. Can use to detect acute intoxication

2’. Non-invasive

3’. Difficult to cheat

d. Disadvantages

1’. Short window of detection (< 24 hours)

2’. Positive test → expensive replication

6. Nail testing [21, 22] **(Slide 21)**

a. Drugs via blood supply to nail bed → creates layers of history as nails grow

b. Detects chronic substance use

c. Advantages

1’. Highly stable and easy to ship/store

2’. Drugs detected 3-6 months after use

3’. Can use to detect prenatal drug exposure

d. Disadvantages

1’. Environmental exposure to drug → false-positive

2’. Does not detect single time drug use

IV. Drug-specific concerns w/ urine testing (most common test in practice) **(Slide 22)**

A. Important general considerations **(Slide 23)**

1. Diff. manufacturers have urine tests w/ varying detection of drugs

2. Therefore, best practice → call the lab you are using for info about urine test

3. Ask for assistance to interpret results when unsure

B. Cannabis screen **(Slide 24)**

1. 1° psychoactive component is tetrahydrocannabinol (THC)

2. Detects inactive metabolite of THC

3. Dronabinol, efavirenz, pantoprazole → false-positive

4. THC = stored in fat tissues → slowly released back into blood

5. Detected 3-5 days (for rare use); 10-30 days (for chronic use)

6. Positive test identifies past use ≠ level of impairment/acute intoxication

B. Opioids [10] **(Slide 25)**

1. Opiates = naturally occurring opioids; "opioids" includes synthetic

a. Opiate screen

1'. Reliably detects morphine & codeine (in Tylenol #3)

2'. Other opioids may be +/- on screens

a'. Hydrocodone (in Norco)

a'. Hydromorphone (Dilaudid)

a'. Oxycodone (OxyContin)

b. Detected for 1-2 days

c. Positive result w/ heroin b/c breaks down → 6-monoacetylmorphone → morphine

d. To differentiate heroin & morphine test for 6-monoacetylmorphone

2. False-positives may occur w/: **(Slide 26)**

a. Dextromethorphan (Robitussin)

b. Diphenhydramine (Benadryl)

c. Poppy seeds

d. Verapamil (Isoptin: blood pressure med)

e. Rifampin (Rifadin: antibiotic)

3. Semisynthetic & synthetic opioids [10] **(Slide 27)**

a. I.e., oxycodone, hydromorphone, oxymorphone, buprenorphine, fentanyl, methadone

b. Metabolites don't include morphine or codeine → false-negative on screens

c. Urine test for specific opioid of concern needs to be ordered

d. Detection times vary (i.e. methadone up to 11 days; buprenorphine up to 4 days)

C. Benzodiazepine screen **(Slide 28)**

1. Each manufacturer's test is unique → difficult to interpret

2. Typically detects oxazepam (1° metabolite of some benzos i.e. diazepam)

a. Not all benzos metabolize to oxazepam → false-negatives may occur w/:

1'. Alprazolam (Xanax)

2’. Clonazepam (Klonopin)

3’. Lorazepam (Ativan)

b. Benzo-like hypnotics (sleeping agents) are not detected in benzo screen

1’. Eszopiclone (Lunesta)

2’. Zaleplon (Sonata)

3’. Zolpidem (Ambien)

3. Drugs w/o oxazepam as a metabolite need special order to detect

4. Benzos w/ long half-lives (i.e. diazepam) → detected up to 30 days **(Slide 29)**

5. Benzos w/ short half-lives (i.e. lorazepam) → detected up to 3 days

6. Few false-positives except for:

a. Sertraline (antidepressant)

b. Oxaprozin (anti-inflammatory)

c. Efavirenz (antiretroviral)

D. Amphetamine screen [23] **(Slide 30)**

1. “Amphetamines” = amphetamine and methamphetamine

2. Amphetamine screen → detects amphetamine (metabolite of methamphetamine)

3. Mass spectrometry confirmation needed to identify methamphetamine

4. Testing isomer distribution determines source of methamphetamine [24]

a. ↑ D-methamphetamine in rx medication or illicit source

b. ↑ L-methamphetamine in OTC vasoconstrictors

c. >20% D-methamphetamine in sample = rx med or illicit source

5. Detected 1 day (rare use); 2-4 days (chronic use)

6. Cross-reactivity w/ other agents → many false-positives, i.e.: **(Slide 31)**

a. Attention-deficit/hyperactivity disorder (ADHD) meds

1'. Amphetamine (Adderall) & lisdexamfetamine (Vyvanse)

2'. Methylphenidate (Ritalin and Concerta) usually ≠ positive

b. Pseudoephedrine & l-methamphetamine (in OTC decongestants)

c. Propranolol & atenolol (blood pressure meds)

d. Bupropion, trazodone, selegiline, chlorpromazine & thioridazine (psych meds)

e. Ranitidine (anti-histamine; for heartburn)

E. Cocaine screen **(Slide 32)**

1. Detects benzoylecgonine (1° metabolite of cocaine)

2. No cross-reactivity w/ other substances

3. Coca tea → false-positive b/c contains cocaine [25]

4. Detected 2-4 days

F. Phencyclidine (PCP) screen **(Slide 33)**

1. False-positives may occur w/

   a. Detromethorphan (Robitussin)

   b. Ibuprofen (Advil)

   c. Tramadol (Ultram)

   d. Venlafaxine (Effexor) and o-desvenlafaxine (Pristiq)

2. Detected up to 8 days (rare use) or 21 days (chronic use)

V. Limitations **(Slide 34)**

A. Some drugs not easily detected - require additional analysis: **(Slide 35)**

1. Synthetic marijuana [26]

   a. ≠ THC metabolites

   b. Chemistry Δing as new compounds produced

   c. Additional testing for cannabinoids in synthetic marijuana (i.e. JWH-018 or JWH-073)

2. Club drugs like 3,4-methylenedioxymethamphetamine (MDMA) a.k.a. ecstasy

   a. Not usually positive under amphetamines screen [27]

   b. Detected 1-2 days [28]

B. Common clinician errors **(Slide 36)**

1. Using standard urine screen only to r/o drug use

   a. Many substances not tested in standard urine screen

b. Not knowing drugs included in hospital's standard urine screen

2. No knowledge of causes of false-positives and false-negatives

a. False-positives: cross reactivity, contamination of sample

b. False-negatives: Low [drug] does not meet threshold for detection

C. There can be tampering with urine samples [29] **(Slide 37)**

1. Adulterants

a. Substances added to urine sample (i.e., OTC eye drops, ammonia)

b. Suspect w/ abnormal urine chemistry (↓/↑ acidity, ↑ [nitrate])

2. Dilution

a. Intentional fluid over-ingestion ↓[urine drug]

b. Suspect w/ dilute urine (↓ [creatinine], ↓specific gravity)

3. Substitution **(Slide 38)**

a. Use of another person's, old, or synthetic urine

b. Suspect w/ abnormal urine properties (i.e., temperature, chemistry)

4. False attribution – claimed use of one chemical to hide another [28]

a. Amphetamines – phenylephrine (OTC decongestant)

b. Opioids – poppy seeds, quinolones (antibiotic)

c. Benzodiazepines – sertraline (anti-depressant)

d. PCP – dextromethorphan (cough suppressant)

e. Cannabinoids – proton pump inhibitors (OTC heartburn Rx)

D. Lab errors can occur – i.e. samples can get mixed or contaminated

VII. Conclusions/Take Home messages **(Slide 39)**

A. Various methods of lab testing are clinically useful in addiction medicine

B. Direct and indirect biomarkers provide different types of data in blood testing of alcohol

C. Physicians need to understand limitations of urine drug screen to correctly interpret

D. Understanding limitations of testing can guide further assessment

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