

# Drug testing your patients for marijuana (THC)

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# Today's topic

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## Introduction

- Urine drug testing is a key diagnostic and therapeutic tool that is useful for monitoring of adherence to a controlled substance treatment regimen (eg, for chronic pain)
  - Also used to identify drug misuse or substance use disorder prior to starting or during treatment with controlled substances
- Drug testing is associated with many complexities including how, when, what to order, and how to interpret the results
- With more patients and consumers than ever showing an interest in marijuana-based products, understanding drug testing relating to marijuana is of clinical importance
- This podcast will review our current understanding of tetrahydrocannabinol (THC) and CBD and explain how you as a clinician can go about testing for these substances in your practice

# Marijuana

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- Marijuana is the most-often used illegal drug in the US (approximately 10%)<sup>1</sup>
  - delta-9-tetrahydrocannabinol (THC) is the primary psychoactive component
- Marijuana is illegal at the federal level
  - CSA1970 relegated all cannabis products to Schedule I classification reserved for compounds without any accepted medical use and a high potential for abuse. Most US-based researchers still cannot study the effects of cannabis products
- Cannabis potency has increased over time<sup>2</sup>
  - It is estimated that the average marijuana cigarette <1980s contained 1% to 3% THC; 6% to 20% in the 1990s; current strains have achieved 40% to 90% potency
- There is a worldwide push for medicinal and even recreational use, with growing evidence for its medicinal support

1. Prevalence of Marijuana Use Disorders in the United States Between 2001-2002 and 2012-2013. JAMA Psychiatry. 2015;72(12):1235-1242

2. ElSohly M, Mehmedic Z. Changes in Cannabis Potency over the Last Two Decades (1995-2014) - Analysis of Current Data in the United States. Biol Psychiatry. 2016 Apr 1; 79(7): 613-619.

# The effects of THC...

- The chemicals in marijuana are found in the leaves and flowers, of which THC is the most well-known
- Users can become dependent on or addicted to marijuana, just as someone can with alcohol and tobacco
  - A person has a marijuana use disorder when they use larger amounts over a longer period of time or their drug use interferes with many aspects of life [finances, school, work, social life...]¹
- Students who use marijuana may find it hard to study and learn because it affects one's ability to focus. THC affects timing, movement, and coordination in athletes
- Harmful effects have been recognized including decreased short-term memory² and ability to do difficult tasks, decreased reaction time (and hence motor vehicle accidents), as well as increased risky behavior
  - There is a strong link between drug use, unsafe sex, and the spread of sexually transmitted infections
- There are some man-made “synthetic” chemicals that act like THC: including spice and K2, which can have even more harmful effects
  - Hallucinations, kidney damage, seizures, and even death have been reported with these products

1. Prevalence of Marijuana Use Disorders in the United States Between 2001-2002 and 2012-2013. JAMA Psychiatry. 2015;72(12):1235-1242

2. Filbey, FM, et al., Long-term effects of marijuana use on the brain. (2014) Proc Natl Acad Sci USA. 111(47): p. 16913-8.

# The pharmacology of THC

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- One of the primary classes of compounds found in marijuana is called cannabinoids. There are up to 60 cannabinoids in marijuana (endo [CB1,2] and phyto-[CBD]) with delta-9-tetrahydrocannabinol (THC) being the primary psychoactive component
  - Humans have a robust cannabinoid system; CB<sub>1</sub> receptors are located mostly in the brain and CB<sub>2</sub> receptors are located mostly throughout the immune system
- When marijuana is smoked, THC is rapidly absorbed through the lungs and enters the bloodstream in minutes, whereas it takes a few hours to reach the circulation following oral ingestion
  - THC has a clearance half-life of less than 30 minutes, so most tests performed hours or days later will not detect THC itself
    - For this reason, most drug tests measure its metabolites once excreted into the urine
- THC is either absorbed into body tissues (organs and fat) or transformed by the liver into metabolites, mostly carboxy-THC
  - THC metabolites are stored in body fat and are released from these sites slowly over time
  - Urine may contain carboxy THC for a week or 10 days after light or moderate use and as long as 4 to 6 weeks after heavy use
- Drug tests cannot show the exact day or hour that marijuana was last used, or estimate how much was used and by what route (smoking, vaping, ingesting, topical...)

# Drug testing for THC and its metabolites

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- Urine drug testing is an accurate and reliable way to detect marijuana use
  - Blood (and saliva) tests are a better indicator of recent use, since they measure the presence of active THC in the system
- As you recall, there are 2 main types of drug testing: screening and confirmatory tests
  - Initial or screening tests are typically performed utilizing immunoassay technology and are conducted either at “point-of-care” or in a laboratory setting. The screening test results are considered presumptive, and clinicians use the patient’s history and clinical judgement to decide if further detailed testing is necessary. These tests are usually qualitative, ie “positive” or “negative”
  - False-positive THC results occur rarely with immunoassay testing when patients are taking certain Rx including NSAIDs and Efavirenz
  - The more confirmative and recommended method, known as: definitive testing, is typically laboratory based using high-level chromatography and mass spectrometry technology. Definitive urine drug test (UDT) usually reports the results of drugs present quantitatively, ie in concentrations of ng/mL

# THC testing

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- The length of time cannabinoids may be detected in the human body depends upon many factors including the sensitivity and specificity of the assay, and individual variables such as the frequency, dose, last time of use, genetic composition, and the function of the metabolic, digestive, and excretory systems
- While immunoassay cross-reactivity to non-cannabinoid compounds is rare, it is recommended that positive presumptive results are confirmed by mass spectrometry-based analytical methods such as GC-MS and LC/MS/MS which provide definitive test results
- Testing positive due to “passive inhalation” from others smoking around you is highly unlikely. Lab screening thresholds have been set at such levels so as not to detect minute quantities in the system
  - (Quest Diagnostics 50 ng/ml cutoff)
- In summary, with legalization of marijuana for medical and recreational use and increasing potency of THC levels in marijuana products, more attention needs to be focused on marijuana usage and testing

# CBD

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- Cannabidiol, or CBD, is another cannabinoid derived from the cannabis plant. The growing popularity of CBD products is leading to more positive tests for THC, the psychoactive component in marijuana
- CBD is being touted as an analgesic, anti-inflammatory, hypnotic, muscle relaxant, antiemetic, anti-anxiety/depressant, anticonvulsant, and has anecdotally ascribed antioxidant, neuroprotectant and anti-tumor effects
  - The four main formulations are sublingual tinctures/sprays, topical lotions/balms, oral edibles/capsules, and inhalation by vaporization or smoking
- Currently, the legal status of CBD is not clear
  - CBD and cannabis laws vary from state to state and it is up to you to know the exact laws for where you live. It is legal to use in states which allow medical and recreational cannabis use and in states which allow for the use of hemp products
  - CBD is metabolized through the hepatic P450 enzyme system and can therefore interact with warfarin and increase the risk of bleeding complications. Both share the same isoforms in their metabolism (CBD acts on CYP1A1, CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP3A4, and CYP3A5 and warfarin acts on five of them). CBD can competitively compete with the metabolism of warfarin by occupying the same isoforms, thereby decreasing the degradation of warfarin. Patients on warfarin who will be using cannabis should have their international normalized ratio monitored to detect any interaction between both drugs



## CBD (continued)

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- CBD is a non-psychoactive compound; under federal law products must have less than 0.3 percent THC to be legal
  - Regulation of these products is often suboptimal, and some unrefined products do contain higher amounts of THC (>40% products tested)
  - A clinician might not be able to tell whether a positive test for THC was caused by use of CBD rather than marijuana
- If someone tests positive for THC, a clinician should have a conversation with the person to see if he or she can explain the test result, which may be related to unregulated CBD products

# Summary

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- With a growing interest in marijuana-based products, understanding drug testing relating to marijuana is of clinical importance, especially when prescribing concomitant pain or ADHD controlled medications.
- An example of a clinical recommendation for therapeutic drug monitoring for marijuana in chronic pain patients on controlled substances management would include:
  - Baseline THC/carboxy-THC testing prior to initiation of opioid therapy
  - Compliance monitoring within 1 to 3 months after baseline monitoring
  - Random monitoring over the next 12 months with provision for more frequent monitoring if unexpected results, complaints, or behavior patterns are documented

# Quest Diagnostics

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- The abuse and misuse of prescription drugs remains epidemic in the US
- Quest serves 1 in 3 adult Americans and half the physicians and hospitals in the United States
  - Quest Diagnostics has the world's largest database of clinical lab results; our diagnostic insights help improve healthcare management
- A properly implemented drug testing program is an important step in tackling drug misuse and abuse
- By performing more than 10 million drug tests annually, Quest Diagnostics has the experience to help you implement a successful PDM program—one that helps protect your practice, safeguards your patients, and keeps your community safe
  - Rx Tox Line available to help clinicians with test ordering or result interpretation
    - 1.877.40.RXTOX (1.877.407.9869)