

Dr Pierre M. Durand

COTININE AND CANNABIS TESTING

It wasn't long ago when I had to have a blood test for cotinine levels. As is typical when these tests are required, the request came from an insurer to pass on to the army of actuarialists to work out my health risk.

I was sitting in a restaurant at the time watching the smokers huddled in a glass room and wondered how vulnerable I may be to second hand smoke each time the door opened. Cotinine testing suddenly became very important, so I wanted to share the latest with you. And while we on that, let's talk about cannabis testing as well.

PART 1 Cotinine

Nicotine is found in the leaves of tobacco plants and after drying and fermenting, the leaves are consumed by smoking, chewing, and sniffing. It is also absorbed via the skin by those handling tobacco, or through second hand smoke. Nicotine salts can also be produced synthetically and used in replacement therapies or tobacco-free products like e-cigarettes. Some foods, such as cauliflower, eggplant, potatoes, tomatoes, and sweet peppers, also contain nicotine.

Nicotine is highly addictive, but it is the other tobacco-related compounds that are the main causative agents of disease. It is also true that while e-cigarettes may contain less tobacco products, they are still harmful due to other carcinogens in the e-liquid. Testing for nicotine is, therefore, used as a marker for all recreational uses of tobacco and e-cigarette products.

Cotinine is the nicotine metabolite tested for in urine, blood, saliva and hair because nicotine is short lived (a few hours) compared to cotinine, which lasts days. Blood and urine are the samples routinely used for testing.

False positives

The most frequently asked question when a positive result is recorded is: Is this a false positive? When the levels are very high this is extremely unlikely but what about cases where the level is, say, less than 75ng/mL.

This requires discretion because factors like passive exposure, dietary intake of nicotine-containing plants, or even some medical conditions (renal, hepatic, cardiac and medications) may cause elevated levels. Furthermore, age and rates of nicotine metabolism also play a role. It is also important, therefore, to consider sources of second and third hand exposure as well as diet. And, of course, always exclude that the person is using therapeutic nicotine (patches, lozenges, strips, gels, etc.)

Without going into the technical complexities of sensitivity, specificity, etc., as a general guideline these levels are used a rule-of-thumb:

Cotinine levels in a nonsmoker are generally less than 10 ng/mL. Cotinine levels in a light smoker or someone exposed to second-hand smoke are usually between 11 ng/mL and 30



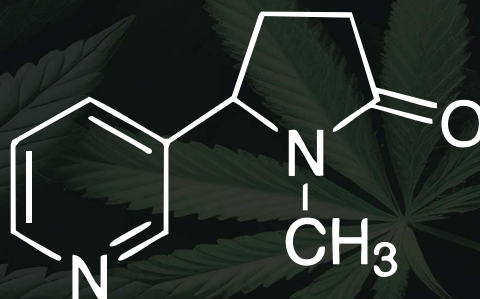
When is a Cotinine Level Positive?

The cut-off value for cotinine is actually a range and something that requires careful interpretation. In blood, levels as low as 3.0ng/mL (sensitivity approximately 75%) can be identified, but such a low level is seldom helpful.

Identifying whether someone has been exposed to tobacco third hand, e.g., through residue on surfaces is of no clinical relevance, yet the level in the individual's blood may cross this very low level. For medical purposes and assessing risk a higher level is warranted. A value of 15ng/mL in blood is a documented point at which tobacco users and nonusers are relatively well separated with a sensitivity of 89.5% and specificity of 98.5%.

Technically this is a helpful cut-off especially when clinical guidance is required, however, for medico-legal purposes one wishes to have a very high degree of certainty that an individual regularly consumes dangerous amounts of nicotine-related products. The cut-off for making such a call is therefore elevated to either 25ng/mL or 50ng/mL. In practice, the higher level of 50ng/mL is more common because it minimises false positives. Whether the cut-off is 25 or 50 doesn't make much difference.

Cut-off levels for urinary cotinine are usually much higher because the compound is concentrated in urine. Different urine dipstick tests have different cut-off levels beginning at around 35ng/mL but may go as high as 500ng/mL.





PART 2 Cannabis and its derivatives

The cannabis plant *Cannabis sativa*, including both marijuana and hemp cultivars, is typically the source of delta-9-THC (THC), which is the psychoactive compound that gives the high associated with marijuana. The hemp cultivar contains much less THC and is usually grown for its fibre, seeds, etc.

THC is one of dozens of cannabinoids that include cannabidiol (CBG) and flavonoids that don't have psychoactive properties and approved for a host of medical uses like some kinds of pain, anorexia, nausea associated with chemotherapy, spasticity and anxiolysis, etc. There are also other interesting compounds (for connoisseurs of cannabis, you may wish to know that it is the volatile terpenes that give the different aromas) which are beyond this discussion.

Cannibis testing

THC is usually the compound of interest in medical testing and is reportedly the most frequently consumed illicit substance (but surely that statistic depends on where you live). CBD products on the other hand are legal in many parts of the world. Legalising THC is a complicated affair because it may depend on the level of THC in the product or the amount of the product being stored by the user. For example, in Switzerland only flowers with less than 1% THC are legal. And in South Africa, the legal amount of cannabis being kept in the house is limited to 600g per person but makes no

1. Testing and Critical Cut-off Levels

There are many ways of testing for THC in blood, sweat, serum, saliva, hair and urine. Saliva, sweat, and hair are less common and for forensic purposes, testing is fraught with 'ifs' and 'buts', so let's stay with the routine testing you are likely to come across. Bear in mind though that more accurate testing with GC-MS exists. Our routine tests don't differentiate THC from THC-like cannabinoids, so there is some cross-reactivity with medicinal cannabis, which always contains small amounts of THC or THC-like compounds (CBD doesn't cross react with THC). The important difference, however, is that the level of THC in those using medicinal cannabis products is generally too low to conclude that the person is a 'user' of drugtype cannabis.

The blood level cut-off to assume frequent consumption (more than twice a week) of drug-type cannabis is a concentration of THC of >50 ng/mL and users of medicinal cannabis rarely cross this threshold. In urine samples, a higher cut-off level is recommended because of the concentration effect (for interest, in the urine test metabolite of THC rather than THC itself is measured). The cut-offs for blood and urine levels are worked out to indicate whether someone is either a frequent user or has recently used cannabis. They are therefore set at a relatively high value to increase specificity.

2. General guidelines, some 'ifs' and 'buts'

Cannabis compounds are lipid-soluble and stored in fat cells. They are released slowly into the circulation, which is why there is a period of prolonged detection. With this in mind, it is clear that more frequent users will have greater stores, which is why they test positive for longer periods. And people with more fat cells may also have a longer duration of a positive result.

Broadly, we use the rough guidelines for interpreting a positive THC result:

1. In someone who smokes cannabis for the first time, tests may remain positive for up to 5 days after the last intake.
2. In someone who smokes cannabis more than twice a week, the detection window is up to a week or even longer.
3. In someone who smokes cannabis almost every day (or more), tests are almost always positive for at least one month and sometimes much longer.

Occasionally, a false positive blood test, possibly due to second hand smoke or handling products, can be considered when the level is borderline and then a sample should be repeated after 2-3 days. False positive urine tests due to second-hand smoke are considered almost impossible because of the high cut-off level. Similarly, the consumption of hemp-containing foods is extremely unlikely to cause a positive result. Finally, on urine dipstix tests, it is important to remember that there are some drugs that cross-react with the antibodies that bind THC metabolites. In South Africa, the commonest ones are proton pump inhibitors and efavirenz (for HIV).

References

Kim S. Overview of Cotinine Cutoff Values for Smoking Status Classification. *Int J Environ Res Public Health*. 2016. 13:1236
Sharma P, et al. Chemistry, metabolism, and toxicology of cannabis: clinical implications. *Iran J Psychiatry*. 2012. 7:149-56.



clientservices@togonalab.co.za



011 663 6300



FOLLOW US

