The Cotinine Test for Tobacco Use

BY JARROD SHAPIRO, DPM

Here's an important test you probably didn't know about.

Practice Perfect is a continuing every-issue column in which Dr. Shapiro offers his unique personal perspective on the ins and outs of running a podiatric practice.

One of my favorite parts about being involved with a residency program is the opportunity to learn things that you didn't know before. Recently, during an academic session, a PGY-1 resident presented information about the Cotinine test to evaluate the tobacco smoking status in patients. She did a great job comparing this test with the carbon monoxide test, and we learned a lot about this test that we didn't know much about before. Let's pay it forward and discuss the Cotinine test for those who may not know much about it.

After nicotine enters the body it's metabolized in the liver.

What Is Cotinine?

- Cotinine is the primary metabolite of nicotine.
- After nicotine enters the body (via smoking, vaping, or nicotine replacement therapy), it's metabolized in the liver.
- Cotinine has a longer half-life (~ 16–20 hours) than nicotine (~ 2 hours), making it a stable marker for recent tobacco use.

Purpose of the Cotinine Test

- Detect recent tobacco use (typically within the last 1–3 days for blood, 3–7 days for urine, possibly up to 10 days for saliva in heavy users).
- Differentiate active smokers from passive/second-hand smoke exposure.
- Monitor smoking cessation programs.
- Occasionally used in research studies to quantify nicotine exposure.

Types of Samples

Cotinine can be measured in several biological specimens (see Table 1).

Testing Methods

Immunoassays (ELISA, rapid tests)

1) Quick, inexpensive
2) Can be qualitative (yes/no) or semi-quantitative
3) Common in clinical and workplace screening

Chromatography-based methods (GC-MS, LC-MS/MS)

1) More accurate and quantitative
2) Can distinguish nicotine from cotinine and other metabolites
3) Used in research or forensic settings

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Table 1

Sample Type	Detection Window	Notes
Blood/serum	1-3 days	Gold standard; quantitative levels possible
Urine	3-7 days	Common; inexpensive; can be qualitative or quantitative
Saliva	4 days	Non-invasive; good for outpatient settings
Hair	Weeks to months	Long-term exposure, not acute use

Tobacco Use (from page 29)

Interpretation of Results (see Table 2)

Cutoff values vary by lab and context. Typical thresholds for urine cotinine:

- > 500 ng/mL: Likely active smoker
- 50–500 ng/mL: Possible passive exposure or occasional smoking
- < 50 ng/mL: Non-smoker or minimal exposure

Serum cotinine thresholds:

- > 10 ng/mL: Active smoker
- 1–10 ng/mL: Passive exposure
- < 1 ng/mL: Non-smoker

Note: Thresholds differ slightly depending on the assay and population studied.

Advantages

- *Objective:* Not reliant on self-report.
- *Sensitive:* Detects even low-level exposure.
- *Quantifiable:* Can monitor changes over time.

Limitations

- *Cannot distinguish nicotine source:* Smoking, vaping, nicotine replacement therapy, or even smokeless tobacco.

Metabolism varies:

Genetic differences in nicotine metabolism (CYP2A6 enzyme) can influence cotinine levels.

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Table 2

Test Type	Sample	Detection Window	Typical Cutoff/Interpretation	Pros	Cons/Notes
Blood/Serum	Serum/Plasma	1-3 days	>10 ng/mL = active smoker 1-10 ng/mL = passive exposure <1 ng/mL = non-smoker	Gold standard, quantitative, accurate	Invasive, requires lab processing
Urine	Urine	3-7 days	>500 ng/mL = active smoker 50-500 ng/mL = possible passive/ occasional use <50 ng/mL = non-smoker	Non-invasive, inexpensive, widely available	Cutoff varies by lab; hydration affects concentration
Saliva	Saliva	~ 4 days	>10 ng/mL = active smoker	Non-invasive, easy outpatient collection	Can be affected by recent oral nicotine use (gum, lozenges)
Hair	Hair shaft	Weeks to months	Varies by lab; reflects cumulative exposure	Detects long-term exposure	Cannot detect recent use; expensive; not routine clinically

Tobacco Use *(from page 30)*

• *Metabolism varies:* Genetic differences in nicotine metabolism (CYP2A6 enzyme) can influence cotinine levels.

• *Detection window limited:* Usually reflects only the past few days.

• *False positives:* Very rare, mostly from nicotine-containing products.

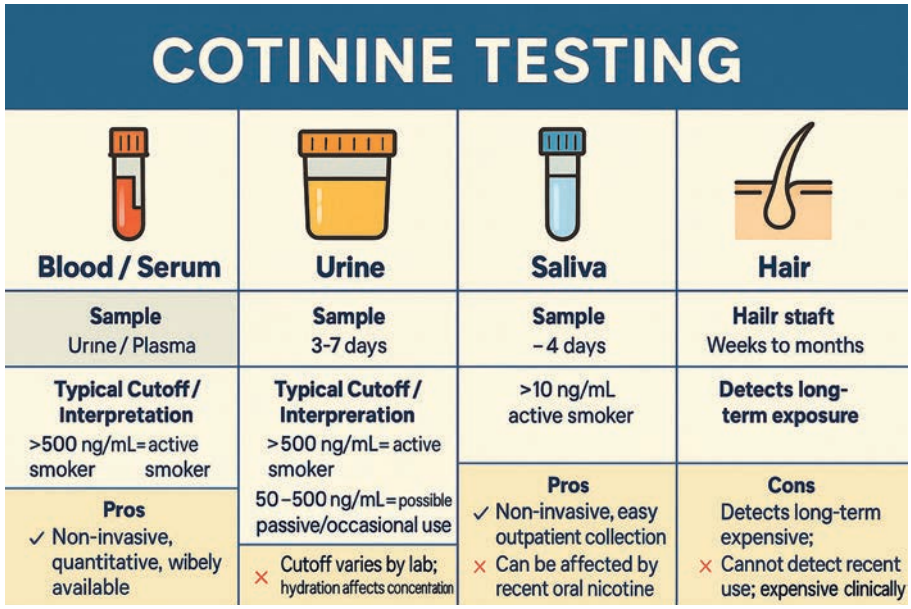

Figure 1

***Detection window limited:* Usually reflects only the past few days.**

For those reading who like infographics, see Figure 1, a nice AI-generated graphic to summarize the key points. **PM**

Dr. Shapiro is editor of PRESENT Practice Perfect. He joined the faculty of Western University of Health Sciences, College of Podiatric Medicine, Pomona, CA in 2010.