LETTER TO THE EDITOR

Nontobacco sources of cotinine in the urine of nonsmokers

To the Editor:

The report by Apseloff et al.[1] and your editorial[2] are both timely and provocative. These articles propose that positive urinary cotinine levels indicate some tobacco smokers lie that they are nonsmokers. There is no doubt that tobacco smoking is the major contributing factor to urinary cotinine levels. A still-unexplored issue that necessitates further research is what are other sources of nicotine and cotinine in humans. Apseloff et al. appropriately referenced Idle's article[3] in which the latter, in referring to cotinine, uses the phrase, "a minefield of misunderstandings." Urinary cotinine levels resulting from consumption of nicotine in tomatoes, potatoes, eggplant, green peppers, green tea, and some brands of instant tea are said not to exceed 50 ng/ml unless large quantities are consumed. What are large quantities of these substances?

Our own research experience is qualitatively similar to that of Apseloff et al.[1]: that some nonsmokers have measurable cotinine levels in their body fluids and yet vigorously deny exposure to tobacco products. As a result, we decided to confirm the presence of nicotine in certain vegetables using gas chromatography–mass spectrometry techniques.[3,4] After this research was published, I received a large number of telephone calls, letters, threats, and criticism of our findings and their "out of context" interpretation.[6] In our very limited study of vegetables, the greatest content of nicotine was 7.1 ng/gm of fresh potato pulp. A review of the literature indicates the greatest content of nicotine is 100 ng/gm of eggplant.[7] If we assume that a urinary cotinine level of 50 ng/ml is a reasonable cutoff and that 1000 ml of urine is produced in 24 hours, then 50 μg total of cotinine must be excreted in 24 hours. If we assume that the conversion of nicotine to cotinine and cotinine to 3′-transhydroxycotinine results in only 50% of the nicotine appearing in the urine as cotinine, then $50 \times 2 = 100$ μg nicotine must be ingested in 24 hours for a detectable cutoff of 50 ng/ml urinary cotinine. This is only one-tenth of the nicotine absorbed after smoking one average cigarette. Yet, 50 ng/ml of urinary cotinine in a nonsmoker would require the ingestion of 1 kg of eggplant or, in our study, about 14 kg of potatoes. Based on the report of Davis et al.,[9] one would need to eat about 6.5 kg of potatoes. Both of these latter quantities are impossible to eat in 1 day. It is also unlikely that 1 kg of eggplant is a reasonable portion to eat in 1 day. However, not all dietary or other nontobacco sources of cotinine have been studied, and most humans eat a varied diet. Perhaps the above calculations, based on ingestion of one vegetable, are erroneous.

It does seem that the contribution of nicotine to urinary cotinine levels from foods is negligible. I would agree with Apseloff et al.[1] and our Editor[2] that urinary assays of cotinine have a place in clinical pharmacologic research. Some tobacco smokers surely do lie about their smoking behavior. However, I would like to encourage more research on the sources of cotinine found in body fluids of nonsmokers who insist they are not active or even passive tobacco smokers. In my own research, I have had volunteers insist that they are nonsmokers who actively[7] avoid smoking areas, and yet they have detectable cotinine levels in their body fluids. Why?

I find it hard to believe that 25% of people who volunteer for clinical trials who claim to be nonsmokers of tobacco are really smokers. Maybe I am naive, but let us do a lot more research on nontobacco sources of nicotine and cotinine before we call one of four nonsmoking volunteers liars.

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References

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