

Letter to the Editor

Reducing False-Negative Tests in Urinary Drugs-of-Abuse Screening

To the Editor:

The urine samples analyzed for the presence of drugs of abuse are more subject to adulterations than other biological matrixes (hair, blood, saliva) (1).

The addition of different substances to urinary samples (sodium chloride or bleach [2–3]) or the ingestion of common drugs (e.g., aspirin [4–5]) may cause a reduction of the immunoassay signal, potentially yielding falsely negative results.

The dilution of the urine sample, either by ingestion of considerable volume of liquids or by assumption of diuretic substances, is another common method of deception to push the analyte concentration below the adopted cutoff.

In this context, the urinary creatinine concentration can be used to verify the extent of the urine dilution.

An extended study on the importance of urinary creatinine measurement for detection of presumably false-negative samples tested for abused drugs was reported by Lafolie et al. (6).

In that paper, the authors suggest that a creatinine value < 4.0 mmol/L can be used as a cutoff in discriminating between physiologically and nonphysiologically diluted samples. Moreover, they propose to simply concentrate the urine to test the authenticity of the sample.

Following this approach, 100 samples, all of which were negative for all the drugs by the initial immunoassay (Cloned Enzyme Donor Immuno Assay [CEDIA] Boehringer Mannheim, Tutzing, Germany) and all of which displayed a "suspect" urinary creatinine value (< 4 mmol/L), were concentrated at 37°C under a stream of nitrogen.

The samples were evaporated until the creatinine concentration approached a normal value (3- to 6-fold concentration).

Of these samples, 27 were positive when retested by the CEDIA immunoassay, and all the positive results were confirmed by gas chromatography–mass spectrometry (Table I).

We developed this procedure following a request of our Addiction Treatment Centers (Servizi Tossicodipendenze, SERT), which is equally interested in lowering the number of falsely positive and falsely negative results. As a matter of fact, both of these errors are detrimental to the recovery programs of drug addicts. At the moment, whereas samples positive after the immunoassay undergo confirmation by chromatographic techniques, the negative ones are not further investigated.

The procedure we described is very simple, rapid, and effective in any case of adulteration that is due to dilution and can reduce falsely negative results in urine testing for abused drugs.

Table I. Modification of Creatinine Content and Drug Positivity Following Urine Concentration (n = 100)

	Creatinine (mmol/L)		Morphine (>300 mg/L)	Cocaine (>300 mg/L)	Cannabinoids (>25 mg/L)	Amphetamines (>300 mg/L)	Benzodiazepines (>100 mg/L)
	mean	range*					
Before concentration	2.74	0.53 – 4.42	0	0	0	0	0
After concentration	9.91	7.52 – 11.50	14	1	5	2	5

*lowest and highest value

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References

1. R.H. Liu and B.A. Goldberger. *Handbook of Workplace Drug Testing*. AACC Press, Washington, DC, 1995.
2. A.H. Wu, E. Forte, G. Casella, K. Sun, G. Hemphill, R. Foery, and H. Schanzenbach. CEDIA for screening drugs of abuse in urine and the effect of adulterants. *J. Forensic Sci.* **40**: 614–18 (1995).
3. A. Warner. Interference of common household chemicals in immunoassay methods for drugs of abuse. *Clin. Chem.* **35(4)**: 648–51 (1989).
4. M.W. Linder and R. Valdes. Mechanism and elimination of aspirin-induced interference in Emit II d.a.u. assays. *Clin. Chem.* **40(8)**: 1512–16 (1994).
5. R.E. Wagener, M.W. Linder, and R. Valdes. Decreased signal in Emit assays of drugs of abuse in urine after ingestion of aspirin: Potential for false-negative results. *Clin. Chem.* **40(4)**: 608–12 (1994).
6. P. Lafolie, O. Beck, G. Blennow, L. Boréus, S. Borg, C.E. Elwin, L. Karlsson, G. Odelius, and P. Hjemdahl. Importance of creatinine analyses of urine when screening for abused drugs. *Clin. Chem.* **37(11)**: 1927–31 (1991).