Short communication

# Addressing discordant quantitative urine buprenorphine and norbuprenorphine levels: Case examples in opioid use disorder

Stephen R. Holt[a,*], Joseph H. Donroe[a], Dana A. Cavallo[b], Jeanette M. Tetrault[a]

[a] Department of Internal Medicine, Yale University School of Medicine, New Haven, CT, USA
[b] Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA

ABSTRACT

*Introduction:* Urine adulteration is a concern among patients treated for opioid use disorder. Quantitative urine testing for buprenorphine (B) and norbuprenorphine (NB), and the appropriate interpretation of B and NB levels, can facilitate constructive conversations with patients that may lead to modifications in the treatment plan, and strengthening of the patient-provider relationship.
*Case summary:* Three cases are presented in which discordant urine B and NB levels were recognized. Each patient was submerging buprenorphine/naloxone strips in their urine to mask ongoing illicit drug use. The authors used an approach to addressing intentional adulteration of urine samples that adheres to the principles of harm-reduction, the centrality of the patient-provider relationship, and the acknowledgment that ongoing illicit drug use and subsequent dishonesty about disclosure may be common among persons with substance use disorders. Each of the three patients ultimately endorsed diluting their urine, which allowed for strengthening of the patient-provider relationship and modifications to their treatment plans. Two of the three patients stabilized and achieved abstinence, while the third was eventually referred to a methadone treatment program.
*Conclusion:* Providers should routinely monitor B and NB levels, rather than qualitative screening alone, and discordant levels should elicit a timely conversation with the patient. The authors use of a nonjudgmental approach to address urine adulteration, including giving patients an opportunity to reflect on potential solutions, has been effective at helping patients and providers to reestablish a therapeutic alliance and maintain retention in treatment.

## 1. Introduction

Urine drug testing is a standard monitoring procedure for patients treated for opioid use disorder (OUD). Clinically, it offers information regarding use of illicit substances, relapse, and adherence to treatment medications such as buprenorphine/naloxone (SAMHSA, 2012; Kirsh et al., 2015). Quantitative urine testing strategies, such as liquid chromatography-tandem mass spectrometry (LC–MS/MS), are highly sensitive and specific for identifying concentrations of selected substances in the urine (ASAM, 2013). The interpretation of those levels can be clinically challenging, however, and should be done with an understanding of the limitations of the test and the metabolism of the drug of interest (SAMHSA, 2012; Sethi and Petrakis, 2014). For example, a low norbuprenorphine (NB) level may represent a normal finding, medication nonadherence, medication diversion, concomitant intake of a cytochrome P450 inhibitor, or intentional urine dilution (adulteration) to mask identification of other substances. While urine testing can provide a clinically useful barometer of the effectiveness of

the current treatment plan, patient context is critical to the accurate interpretation of these urine tests and to the subsequent treatment plan revision.

Previously, we have presented data demonstrating urine buprenorphine (B) and NB levels for patients actively treated with buprenorphine for OUD in an academic addiction medicine clinic (Donroe et al., 2017). We identified urine B and NB concentrations suggestive of urine adulteration (Donroe et al., 2017).

Under-reporting illicit drug use is common among both teens and adults (Delaney-Black et al., 2010; Harrison et al., 1993). One study of 2349 college students at a single large university found that 4.0% had ever deliberately deceived a physician to conceal illicit drug use, to conceal diversion of prescribed medications, or both (Stogner et al., 2014). Another retrospective chart review study of 168 patients enrolled in a buprenorphine treatment program found that 8 patients (4.8%) had diluted and adulterated their urine sample with buprenorphine film submersion at least once (Suzuki et al., 2017). Self-disclosure of recent illicit drug use by patients is predicated on many factors,

---

including fear of a negative reaction from the provider, fear of real practical consequences (e.g. being discharged from the practice), perceived likelihood of "getting away with" urine adulteration, and the strength of the therapeutic relationship with the provider. Additionally, patients already engaged in treatment may be less likely to report ongoing cocaine or heroin use (51% and 67%, respectively) than patients at the start of their treatment (89% and 96%, respectively) (Hindin et al., 1994). These factors, and the specific methods used when asking patients to disclose recent substance use, strongly influence a patient's decision to self-disclose (Bowling, 2005).

We present three cases in which we recognized discordant urine B and NB levels, used the information to initiate a discussion with each patient, and adjusted the treatment plan to better meet the patients' needs. We describe an approach to addressing intentional adulteration of urine samples, in a way that we believe still adheres to the principles of harm-reduction (Marlatt et al., 2012), the centrality of the patient-provider relationship, and the acknowledgment that ongoing illicit drug use and subsequent dishonesty about disclosure is common among persons with substance use disorders.

## 2. Case descriptions

### 2.1. Case patient A

Patient A is a 52-year-old man with OUD and prior opioid overdose. After induction with buprenorphine, he was stabilized at a dose of 12 mg twice daily. His urine testing is shown in Table 1. A long history of discordant B and NB levels are noted and reflects our own learning curve with the interpretation of urine B and NB levels. After nearly 10 months of treatment in our clinic, a treatment team member raised the subject of discordant urine drug testing results with the patient, using non-judgmental language, and referred to the urine testing results as a problem in need of a collaborative solution (e.g. "The urine results

suggest that tampering has occurred, so together we need to figure out a plan to proceed"). The patient was advised to reflect on a solution and was left alone for several minutes. When the provider returned to the room, two options were discussed: 1) The patient could share why the test results revealed the pattern that they did, which would allow for a collaborative redesign of the treatment plan to better suit his needs, or 2) If he is unable to explain the findings, we would offer a supervised urine collection, and a 7-day supply of buprenorphine would be provided while awaiting the results of LC–MS/MS. He was also advised that if the latter option was chosen, and the supervised urine sample revealed findings inconsistent with recent results (e.g. more typical NB/B ratio and levels, indicating that recent samples had been diluted and adulterated with film submersion), we would transition the patient to a higher level of care with increased monitoring (i.e., methadone maintenance program or inpatient treatment program). If the supervised urine sample revealed results consistent with prior samples (i.e. widely discordant B and NB levels), then treatment would continue, and an alternative explanation would be sought (see Supplementary material Box 1 for a recommended approach).

When the provider returned to the patient's room, patient A disclosed diluting his urine countless times to mask continued intermittent heroin use. He further stated that he was only using heroin a few times per month, but that it had become commonplace for him to submerge a film in every urine sample, even if he had not recently used heroin. The treatment team increased the frequency of monitoring and he subsequently had several months of appropriate urine results, until he eventually began adulterating his urine again. After several attempts to revise the treatment plan, he was ultimately referred to a methadone treatment program.

### 2.2. Case patient B

Patient B is a 33-year-old man with opioid, benzodiazepine and

**Table 1**
Timelines of patient urine buprenorphine (B) and norbuprenorphine (NB) testing, starting with Week 1 of treatment. (For interpretation of the references to colour in this Table, the reader is referred to the web version of this article.)

| Patient A | | | | Patient B | | | | Patient C | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Weeks | B | NB | Comment | Weeks | B | NB | Comment | Weeks | B | NB | Comment |
| 1 | 0 | 6 | Opi + | 1 | 98 | 430 | MJA + | 1 | 11 | 45 | |
| 2 | 170 | 540 | Opi + | 2 | 130 | 1100 | MJA + | 2 | 13 | 51 | |
| 3 | >1000 | 250 | Opi + | 3 | 150 | 1100 | MJA +, Coc + | 3 | 50 | 64 | |
| 6 | >1000 | 120 | | 4 | 77 | 550 | MJA + | 5 | 8 | 7 | |
| 8 | >1000 | 120 | | 5 | 110 | 730 | MJA + | 8 | >1000 | 14 | |
| 10 | >1000 | 200 | Opi + | 7 | 46 | 430 | | 9 | >1000 | 33 | |
| 12 | >1000 | 150 | | 8 | 41 | 350 | | 10 | 0 | 0 | |
| 14 | >1000 | 190 | Opi +, Coc + | 12 | >1000 | 6 | | 15 | 550 | 5 | |
| 15 | >1000 | 240 | | 15 | >1000 | 6 | | 18 | >1000 | 19 | |
| | | | | 17 | >1000 | 11 | | 21 | >1000 | 3 | |
| | | | | 19 | >1000 | 6 | | 24 | >1000 | 5 | |
| | | | | 22 | >1000 | 9 | | 27 | 35 | 120 | |
| | | | | 26 | >1000 | 3 | | 30 | 12 | 140 | |
| 41 | >1000 | 50 | | 30 | >1000 | 2 | | 36 | >1000 | 12 | |
| 42 | 35 | 81 | | 34 | 48 | 120 | MJA +, Benz + | 40 | >1000 | 32 | |
| 47 | 0 | 0 | Opi + | 36 | 73 | 240 | MJA +, Benz + | 41 | >1000 | 19 | |
| 49 | 53 | 19 | Opi +, Coc + | 38 | 170 | 370 | MJA + | 47 | 190 | 170 | Coc + |
| 50 | 54 | 42 | Opi + | 40 | 110 | 110 | MJA +, Benz + | 48 | 370 | 54 | |
| 51 | 200 | 330 | Opi + | 42 | 21 | 45 | MJA +, Benz + | 49 | 74 | 71 | |
| 52 | 130 | 640 | Opi + | 44 | 240 | 120 | MJA +, Benz + | 50 | NT | NT | |
| 53 | >1000 | 14 | | 45 | 40 | 210 | MJA +, Benz +, Coc + | 51 | 24 | 59 | |
| 54 | >1000 | 10 | Opi + | 46 | 36 | 160 | MJA +, Benzo + | 52 | 39 | 86 | |
| 55 | 610 | 270 | | 48 | 220 | >1000 | MJA + | 56 | 77 | 10 | |
| 58 | 37 | 140 | | 49 | 160 | 170 | MJA + | 58 | 510 | 290 | |
| 59 | 67 | 200 | | 51 | 280 | 250 | MJA + | 59 | 180 | 130 | |
| 60 | 13 | 88 | | 53 | 240 | 160 | | 61 | 180 | 250 | |
| 61 | 45 | 110 | | 56 | 280 | 160 | | 65 | 29 | 37 | |
| 62 | 0 | 0 | Opi + | 59 | 310 | 140 | | 69 | 28 | 43 | |

Boxed week is week of initial is date of initial conversation re: discordant urine testing results. Grey shading is week patient endorsed urine adulteration. Blue shading is week of observed urine collection. MJA = marijuana. Coc = cocaine. Benz = benzodiazepine. Opi = opioids/opiates. NT = not tested.