

Q

Should I discharge a patient on Percocet (oxycodone/acetaminophen) for chronic back pain with unexpected oxymorphone detected in her urine drug screen?

A

The short answer is No. The question came to us from a clinician with a compliant chronic pain patient. Last year, the clinician began ordering urine drug tests. The patient's urine has repeatedly come back positive for oxymorphone as well as oxycodone. "She keeps denying

taking any other opioid besides the Percocet, but I find this hard to believe, especially since there is more oxymorphone than oxycodone in the urine," wrote the clinician.

Oxycodone Metabolism

Oxycodone is metabolized in the liver by Phase I and Phase II metabolism. Phase I metabolism occurs through the cytochrome P450 (CYP450) enzymes 3A4 and 2D6 to nor-oxycodone and oxymorphone, respectively (Figure). Oxymorphone is a minor metabolite, which represents less than 15% of the total administered dose, but certainly is an expected byproduct of oxycodone.¹ In fact, absence of oxymorphone would be more cause for concern because it may be indicative that oxycodone was placed directly into the urine specimen cup by a patient without ingesting the oxycodone.

Although oxymorphone has almost 3 times the half-life of oxycodone, it generally has a lower urine concentration than oxycodone and nor-oxycodone.² If oxymorphone levels are unusually elevated, it may indicate a number of confounding conditions, including:

- The patient is an ultra-rapid 2D6 metabolizer and/or a poor 3A4 metabolizer
- The patient is concomitantly receiving a potent 3A4 inhibiting drug (ie, erythromycin)
- The patient is using a natural product regularly such as grapefruit extract that inhibits 3A4 enzyme production.³

We should note also that for patients on codeine, morphine is expected in the urine, and for patients on hydrocodone, you will likely find hydromorphone in the urine. There are

some opioids that avoid CYP Phase I metabolism altogether; these include morphine, hydromorphone, levorphanol, oxymorphone, and pentadol.

Unexpected UDT Results

In the current climate of concern about abuse of opioids, prescribers are increasingly ordering urine drug tests (UDTs) for patients taking chronic opioids. This is a good thing, as these tests can show if patients are taking non-prescribed opioids, using illegal drugs, or not taking their prescribed opioids. We can't know if a drug is being diverted just because a UDT is negative, only that the patient isn't taking it.

However, ordering a UDT brings with it the responsibility of determining the cause of any unexpected result, such as finding an opioid in the urine that you have not prescribed. The current availability of prescribed oxymorphone (Opana) has resulted in an increasing number of oxycodone-treated patients being discharged unfairly because oxymorphone has

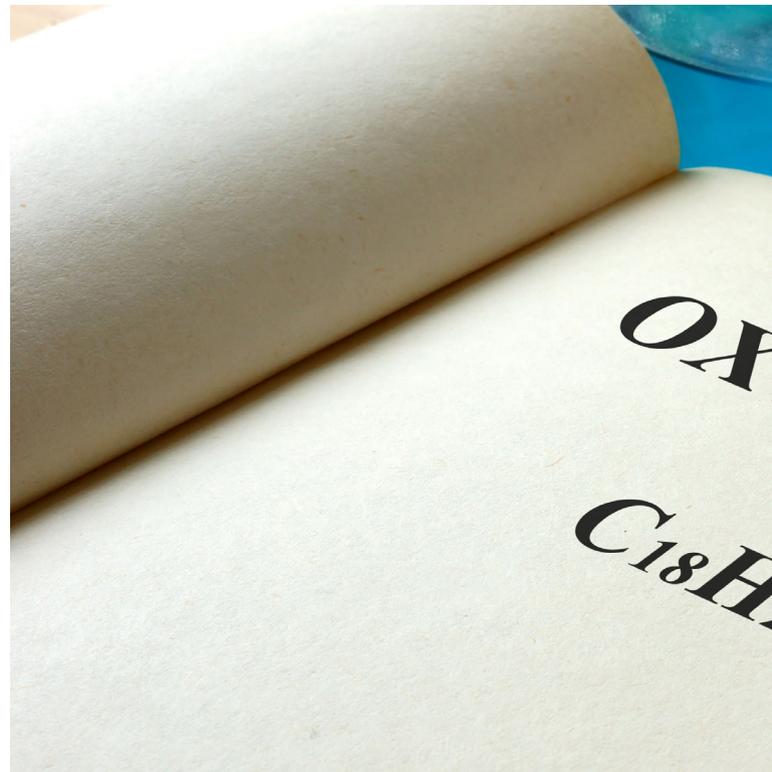
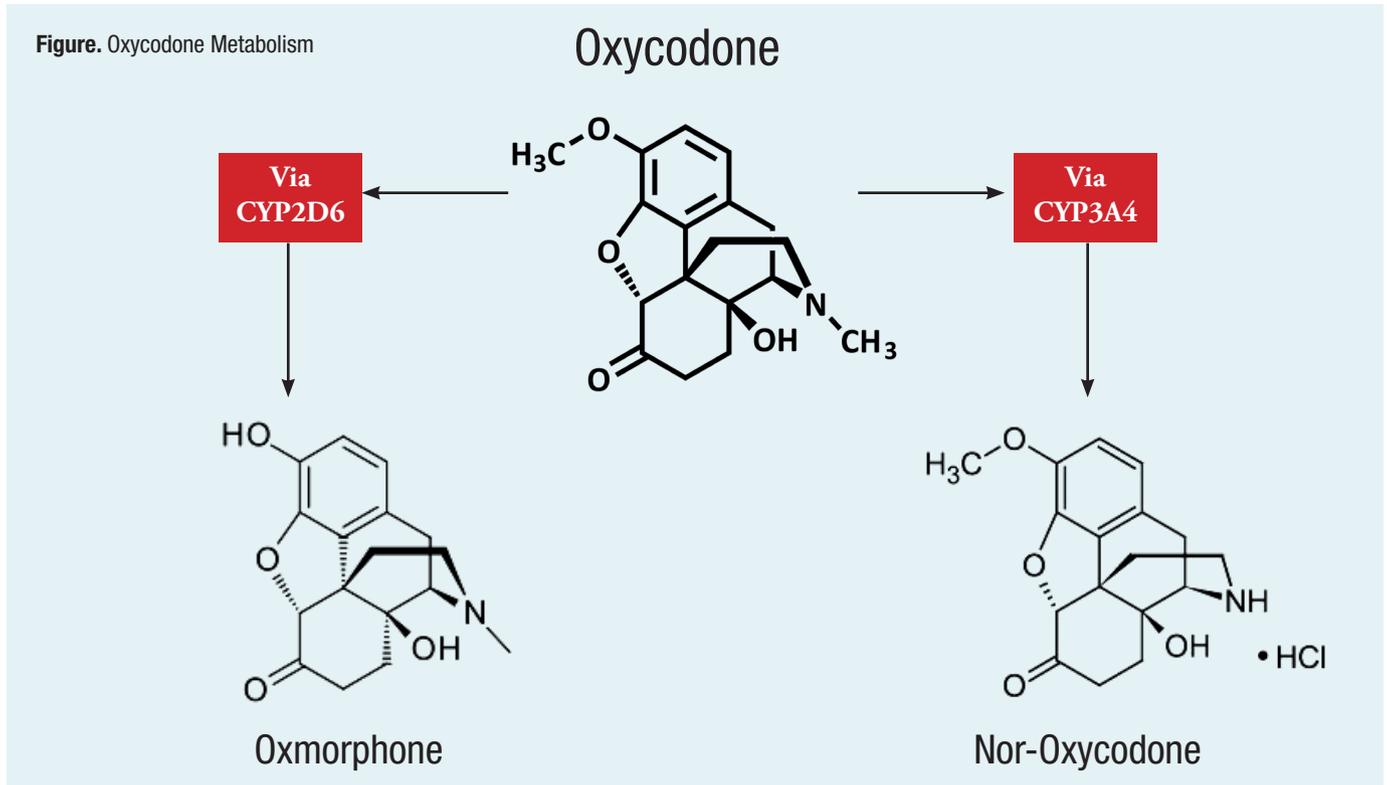


Figure. Oxycodone Metabolism



also been found in their urine. Such patients have inappropriately been labeled as drug abusers, and this stigma may make it difficult for them to find another physician willing to prescribe an opioid although they have done nothing wrong.

When you find a UDT result that you don't understand, you are ethically obligated to determine the cause before concluding that a patient has done wrong! Call the commercial laboratory and speak to a knowledgeable person there, ask a knowledgeable medical colleague or pharmacist, research it online, or consider a urine drug screen application such as Urintel.⁴ Patients deserve this.

Jennifer Schneider, MD, PhD

*Internal Medicine, Addiction Medicine, and Pain Management
Tucson, Arizona*

Jeffrey Fudin, BS, PharmD

*Clinical Pharmacy Specialist
Director, PGY2 Pain and Palliative Care Pharmacy Residency
Stratton VA Medical Center
Albany, New York*

References

- Schneider J, Miller A. Oxycodone to oxymorphone metabolism. *Pract Pain Manage.* 2007;7(7):71-73.
- Moeller KE, Lee KC, Kissack JC. Urine Drug Screening: Practical Guide for Clinicians. *Mayo Clin Proc.* 2008;83(1):66-76
- Vuilleumier PH, Stamer UM, Landau R. Pharmacogenomic considerations in opioid analgesia. *Pharmacogenomics Pers Med.* 2012;5:73-87.
- Fudin J. Interview: New App Helps Interpret Urine Drug Test Results. *Pract Pain Manage.* 2015;15(6):84-87.

