

## Opiates and opioids: What a difference a name makes

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We often note the conflation of the words *opiate* and *opioid* in the medical literature. Surprisingly, we occasionally note it in the pages of this journal. In some articles, *opiate* is used consistently—but incorrectly—throughout the text. In other articles, *opiate* and *opioid* appear to be used interchangeably—and incorrectly—throughout the text, sometimes even within the same sentence. At times, *opioid* in the authors' primary source metamorphoses to *opiate* in the text of their manuscript. Our impression is that many authors consider these words as equivalents. In actuality, they have distinct meanings, and these meanings have clinical importance.

*Opiates*, in the most correct sense, refer specifically to substances extracted from the milky latex of ripening pods of the opium poppy, *Papaverum somniferum*. Important opiate alkaloids can be divided into two major classes. Phenanthrenes comprise analgesics and their precursors that bind to opioid receptors in the nervous system. They include morphine and codeine as well as thebaine, an alkaloid without intrinsic analgesic properties, but which serves as an intermediate in the *in vivo* biosynthesis of morphine and codeine. Thebaine is also an important precursor for the industrial manufacture of semisynthetic pure opioid receptor agonists (eg, oxycodone, oxymorphone), opioid receptor agonists/antagonists (eg, buprenorphine, nalbuphine), and pure opioid receptor antagonists (eg, naloxone, naltrexone). Benzylisoquinolones comprise substances that show no affinity for opioid receptors. They include, for example, papaverine, used therapeutically as a smooth muscle relaxant, and noscapine, an antitussive and currently the object of preclinical research as an antineoplastic agent.

*Opioids*, a broader category of drugs, encompass substances of widely disparate chemical structures, which nevertheless share some degree of agonist activity at one or more of the body's opioid receptors. Thus, opioids comprise (some) opiates and their semisynthetic derivatives, entirely synthetic compounds (eg, the fentanils, meperidine, methadone), and a variety of peptides known as endogenous opioids (eg, enkephalins, endorphins, dynorphin).

This distinction is not academic quibbling. In the field of clinical urine drug testing, evidence indicates that conflation of *opiate* and *opioid* may contribute to serious errors in the application and interpretation of opiate screening immunoassays. For example, Von Seggern et al.<sup>1</sup> reported the case of a patient prescribed OxyContin® (oxycodone), whose urine drug screen was negative for opiates. They accused the patient of selling his medication and, despite the patient's protestations of innocence, dismissed him from their practice. The patient's family found a toxicologist who suggested that this opioid might not be detectable by the screening assay. Subsequent testing of the original specimen by gas chromatography/mass spectroscopy confirmed the presence of oxycodone in the patient's urine. One of us (GMR) recently consulted on a patient with dual-diagnosis pain and opioid abuse. Review of his hospital records revealed a previous involuntary admission for witnessed ingestion of a large number of Lorcet® (hydrocodone and acetaminophen) tablets in a presumed suicide attempt. The hospitalist, in his discharge summary, wrote, "The patient denies that he took any Lorcets. In fact, his urine drug screen was negative for opiates, which confirms the fact that this information was erroneous." In actual fact, the opiate screening assay at our institution is not designed to detect hydrocodone.

The first case resulted in a false accusation of opioid misuse; the second case resulted in a false vindication of opioid misuse. It should be emphasized that neither case represents a false-negative opiate drug screen; the assays performed precisely as they were designed to perform. Rather, these are examples of how physicians can misinterpret true-negative opiate drug screens because they fail to understand that most prescription opioid analgesics are not, in fact, opiates, and may not cross react with common opiate screening assays. Although some opioids may cross-react with antibodies designed to detect morphine and codeine, and thereby produce positive opiate screening results, not all opioids will be detected at typical therapeutic—or even toxic—concentrations.

Emerging evidence indicates that cases such as these are not uncommon. Levy et al.<sup>2</sup> found that only 14 percent

of physicians who order urine drug screens were aware that oxycodone is not detectable by many opiate screening immunoassays. Our own work, published in the previous issue of this journal, confirms and extends the findings of Levy.<sup>3</sup> We found, for example, that nearly half of physicians who utilize urine drug testing are unaware that Dilaudid® (hydromorphone) may not be detected by some opiate screening assays. Physicians' lack of knowledge in this area has potentially serious consequences for patients. Participants in our study indicated that they would respond to these negative opiate screens by tapering and discontinuing opioid therapy (10 percent), notification of law enforcement (10 percent), or referral for addiction treatment (3 percent).

Certainly, terminology is not the only problem here; there is clearly a widespread lack of education in the area of clinical urine drug testing. But to some degree, faulty word choice begets fuzzy thinking, and fuzzy thinking begets flawed practice. This issue of word choice is implicitly understood by the *Journal of Opioid Management*. We believe that this publication, which is dedicated to the proper use of opioids, should also advocate for the use of proper nomenclature regarding this valuable class of drugs.

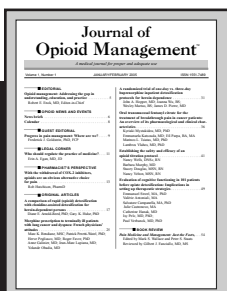
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