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Which Opioid Was Ingested?

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Metabolism can often complicate the interpretation of urine drug screen (UDS) results after opioid ingestion. It is not uncommon for a different drug to appear on the UDS result when compared to what was ingested. To avoid confusion when correlating results, it is good idea to get some background advice as to which medications may cause a positive (or even multiple positive) results.

Codeine, hydrocodone and oxycodone undergo Phase I metabolism in the human body via the cytochrome P450 pathways, utilizing mainly one or two enzymes - CYP2D6 (codeine and hydrocodone) and CYP3A4 (oxycodone).¹ Their respective major metabolites are morphine, hydromorphone and oxymorphone. It is important to note one of the challenges to correctly interpreting opioid-

positive analyses – that these metabolites are also controlled substances that may be prescribed for similar reasons. Furthermore, the metabolites also undergo enzymatic conjugation to glucuronide forms that enhances elimination from the body and must undergo a hydrolysis procedure during analysis to facilitate recovery of the drug from the urine.

Further complicating opioid urinalysis are minor metabolic pathways for codeine and hydrocodone. Codeine can metabolize to hydrocodone, generally amounting to less than ten percent of the codeine level found in the urine.² Similarly, morphine may metabolize to hydromorphone and that level is generally less than five percent of the morphine level found in the urine.³ One common post-urinalysis question may be, “My patient was prescribed oxycodone, why were they oxymorphone-only positive?”. From the reference above, oxycodone is metab-

olized to oxymorphone, but the latter is eliminated more slowly from the body. At the end of excretion, only oxymorphone may be present in the urine.

Heroin use is normally detected by heroin metabolite (6-acetylmorphine) accompanied by a large amount of morphine in the urine. In fact, morphine may be the only metabolite present as it is difficult to detect 6-acetylmorphine in the urine more than 12-24 hours after taking the drug. However, copious amounts of morphine in the urine may be accompanied by hydromorphone and only these two compounds may be present.

Please note; because of the interrelation of thebaine-based opioids in structure and metabolism, it is always prudent to obtain advice if the laboratory results don't correlate with expectations.

Drug Ingested	Major Urinalysis Products	May also be present
Codeine	Codeine, Morphine *	Hydrocodone (<10%)
Morphine	Morphine	Hydromorphone (<5%)
Hydrocodone	Hydrocodone and/or Hydromorphone	Hydromorphone (up to 100%)
Hydromorphone	Hydromorphone	Hydromorphone only
Oxycodone	Oxycodone and/or Oxymorphone	Oxymorphone (up to 100%)
Oxymorphone	Oxymorphone	Oxymorphone only
Heroin	6-Acetylmorphine **, Morphine	Hydromorphone (see Morphine)

*Morphine may be present but below the cutoff and therefore not reported.

**6-Acetylmorphine may not be detected.