Classification: Narcotics, analgesics

Background: Opiates have been used for thousands of years for treatment of pain and remain the primary drugs used in pain management. Opium, which is derived from the unripe seeds of the poppy plant, Papaver somniferum, is the source of the naturally occurring opiates codeine and morphine. The term “opiates” refers to codeine and morphine, which occur naturally, and to the semisynthetic compounds hydrocodone, hydromorphone, oxycodone, oxymorphone and heroin, which are derived from codeine and morphine. The term “opioids” refers to compounds that act on the opioid receptors. Methadone, buprenorphine, meperidine, tramadol and fentanyl are opioids, not opiates. Morphine is the prototypical opiate to which all other opiates and opioids are compared.

Poppy Seeds: Poppy seeds contain enough codeine and morphine so that their consumption can result in both morphine and codeine detected in the urine. Poppy seed consumption always results in a morphine level less than 2,000 ng/mL, whereas heroin use results in much higher levels of morphine. The morphine/codeine ratio is similar following both heroin and poppy seed use (the morphine level is about 5 to 10 times the codeine level); thus an interpretation problem arises unless 6-acetylmorphine (6-AM) is detected in the same specimen. The federal government raised the mandatory cutoff level for opiates in workplace drug testing from 300 to 2,000 ng/mL in December 1998 to avoid the need to interpret many ambiguous test results.

Example
1. Morphine (Mor) and Codeine (Cod) present
   a. Codeine  Morphine  
   b. Morphine > 10,000 and Mor/Cod  10:1  
   c. Morphine < 10,000 and Mor/Cod  10:1
2. Only Morphine present
   a. Morphine > 10,000
   b. Morphine < 2,000

Detection in Urine: 2–5 days

Physiological Effects: Analgesia (pain relief), respiratory depression, constipation. Long-time use leads to dependence and tolerance such that a dramatic increase in dose is necessary for the same analgesic effect. Tolerance begins after the initial dose but is usually significant only after the second week of chronic use. A 35-fold increase in dose may be necessary for the same effect. Withdrawal symptoms may begin 6–8 hours after the last dose and reach a peak at 36–72 hours.
Toxicity: Respiratory depression/failure is the greatest risk associated with opiate abuse, aside from the risk of infection associated with illicit intravenous drug use.

Psychological Effects: Sedation, euphoria, mental clouding

Cutoff Levels:
- Immunoassay screen test: 2000 (or 300) ng/mL
- LC-MS/MS confirmation test: 2000 (or 300) ng/mL
- LC-MS/MS confirmation test: 10 ng/mL

Other Opiates: Oxymorphone (Numorphan), levorphanol (Dromoran), butorphanol (Stadol), nalbuphine (Nubain), and buprenorphine (Buprenex) are classified as narcotics. Dextromethorphan is not a narcotic and is used as an antitussive. Naltrexone (Trexan) and naloxone block the narcotic effects of heroin and other opiates.

Nonopiate Narcotics: Propoxyphene (Darvon), meperidine (Demerol) and methadone all exhibit narcotic analgesic properties similar to opiates. Although these drugs are sometimes classified as opiates, they do not share the same opiate chemical structure and therefore are classified separately for testing purposes.

Summary: The high potential for dependence and tolerance is the hallmark of the opiates. Although heroin is best known for its addictive properties, people also become dependent upon prescription drugs containing codeine, morphine, hydrocodone and oxycodone.

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**HEROIN**

Legally Obtained As: NO LEGAL SOURCE

Appearance: Powder or Rock

Mode of Use: Injection or nasal insufflation (snorting) (up to 200 mg daily)

Metabolism: In the body, heroin readily crosses the blood/brain barrier and is rapidly converted to 6-acetylmorphine (within a few minutes). 6-AM is further metabolized to morphine (within hours).

Heroin usually contains codeine because it is manufactured from opium, which contains morphine and codeine at a ratio of approximately 10 to 1. Heroin is rapidly metabolized in the body, first to 6-AM and then finally to morphine. Heroin, the parent drug, is so rarely detected in the urine following heroin use that laboratories do not normally test for it. 6-AM is a unique metabolite of heroin and its presence is unambiguous evidence of heroin use. However, it is usually only detected in the first 12 hours following heroin use. When the morphine level is less than 2,000 ng/mL, performing the test for 6-AM could be futile. However, the absence of 6-AM does not rule out heroin use.

Specific Issues: Following either heroin use or poppy seed consumption, morphine and codeine are detected in the urine, with the morphine level approximately 10 times the codeine level. However, poppy seed consumption alone rarely results in a morphine level greater than 2,000 ng/mL. When the codeine level is greater than ~1/2 the morphine level, the source is probably codeine use. When only morphine is detected, the source is probably pharmaceutical morphine.

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**CODEINE**

Legally Obtained As: Tylenol-3, methylmorphine, Robitussin-AC, some nonprescription cough syrups (in limited states), combined with many other prescription drugs

Mode of Use: Oral

Metabolism: The principle metabolites of codeine are morphine, norcodeine and, to a small extent, hydrocodone. All three are excreted in the urine. Codeine is normally present in the urine at levels greater than morphine. However, in the last 6–12 hours of the elimination process, as the levels drop toward zero, the morphine level can surpass the codeine level, complicating the interpretation of the urine drug test results.
### HYDROCODONE

**Legally Obtained As:** Vicodin, Lortab, Anexia, Panacet, dihydrocodeine, and combined with other prescription drugs.  
**Mode of Use:** Oral  
**Metabolism:** The principle metabolite of hydrocodone is hydromorphone. Both are excreted in the urine. The detection time window is 3–4 days following use.

### HYDROMORPHONE

**Legally Obtained As:** Dilaudid, dihydromorphinone  
**Mode of Use:** Oral, injection or as suppositories  
**Metabolism:** Hydromorphone is excreted in the urine principally as the parent drug and its glucuronide conjugate. The detection time window is 3–4 days following use.

### OXYCODONE

**Background:** The milky residue collected from the opium poppy plant (opium) is the natural material from which opiate compounds are extracted or synthesized. Oxycodone is a semisynthetic opiate derived from opium. Oxycodone, like other opiates, is characterized by its analgesic properties and the tendency for users to form a physical dependency and develop tolerance with extended use. It is a commonly prescribed analgesic taken orally, frequently in combination with acetaminophen or aspirin. OxyContin, the time-release form of oxycodone, is supplied in 80-mg doses and is often called “hillbilly heroin.” When the pills are crushed, the contents can be snorted or dissolved in water and injected. Its use as a club drug is reportedly on the increase.  
**Legally Obtained as:** Percocet, Roxicet, OxyContin, Tylox  
**Street names:** Oxy; OC; hillbilly heroin  
**Detection in Urine:** 1–3 days  
**Physiological Effects:** Analgesia (pain relief), respiratory depression, constipation. Long-time use leads to dependence and tolerance such that a dramatic increase in dose is necessary for the same analgesic effect. Tolerance begins after the initial dose but is usually significant only after the second week of chronic use. A 35-fold increase in dose may be necessary for the same effect. Withdrawal symptoms may begin 6–8 hours after the last dose and reach a peak at 36–72 hours.  
**Toxicity:** Respiratory depression/failure is the greatest risk associated with opiate abuse, aside from the risk of infection associated with illicit intravenous drug use.  
**Psychological Effects:** Sedation, euphoria, mental clouding  
**Cutoff Levels:**  
- Immunoassay screen test: 300 ng/mL  
- LC-MS/MS confirmation test: 300 ng/mL  
**Mode of Use:** Oral, crushed and snorted or dissolved and injected  
**Metabolism:** Oxycodone is excreted in the urine principally as the parent drug, its glucuronide conjugate, and its metabolite, oxymorphone. The detection time window is 1–3 days following use.