

OPIOIDS

From Lippincott

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PAIN MANAGEMENT: Alleviation of pain depends on the specific type of pain, nociceptive or neuropathic pain. For example, with mild to moderate arthritic pain (nociceptive pain), nonopioid analgesics such as NSAIDs are often effective. Neuropathic pain can be treated with opioids (some situations require higher doses) but responds best to anticonvulsants, tricyclic antidepressants, or serotonin/norepinephrine reuptake inhibitors. However, for severe or chronic malignant or nonmalignant pain, opioids are considered part of the treatment plan in select patients.

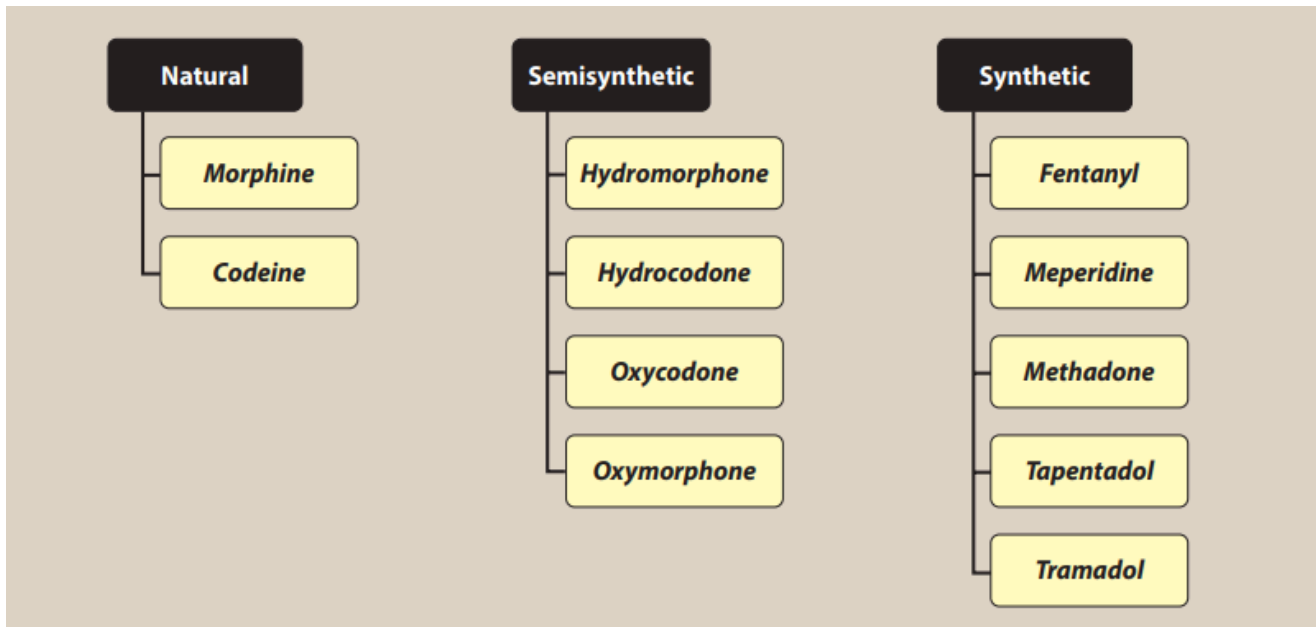
Opioids are natural, semisynthetic, or synthetic compounds that produce morphine-like effects.

All opioids act by binding to specific opioid receptors in the CNS to produce effects that mimic the action of endogenous peptide neurotransmitters (for example, endorphins, enkephalins, and dynorphins). Although the opioids have a broad range of effects, their primary use is to relieve intense pain, whether that pain results from surgery, injury, or chronic disease.

OPIOID RECEPTORS: The major effects of the opioids are mediated by three receptor families, which are commonly designated as μ (mu), κ (kappa), and δ (delta).

- The analgesic properties of the opioids are primarily mediated by the μ receptors that modulate responses to thermal, mechanical, and chemical nociception.
- The κ receptors in the dorsal horn also contribute to analgesia by modulating the response to chemical and thermal nociception.
- The enkephalins interact more selectively with δ receptors in the periphery.

All three opioid receptors are members of the G protein–coupled receptor family and **inhibit adenylyl cyclase**. They are also associated with ion channels, increasing postsynaptic K⁺ efflux (hyperpolarization) or reducing presynaptic Ca²⁺ influx, thus impeding neuronal firing and transmitter release



<p>STRONG AGONISTS</p> <p>Alfentanil Fentanyl Heroin Hydromorphone Levorphanol Mepiridine Methadone Morphine Oxycodone Oxymorphone Remifentanil Sufentanil</p>	<p>MIXED AGONIST-ANTAGONIST AND PARTIAL AGONISTS</p> <p>Buprenorphine Nalbuphine Pentazocine</p>	<p>MODERATE/ LOW AGONISTS</p> <p>Codeine</p>	<p>ANTAGONISTS</p> <p>Naloxone Naltrexone</p> <hr/> <p>OTHER ANALGESICS</p> <p>Tapentadol Tramadol</p>
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OPIOID AGONISTS

	MOA	THERAPEUTIC USES	ADVERSE EFFECTS	OTHER POINTS
MORPHINE	<p>-exert their major effects by interacting stereospecifically with opioid receptors on the membranes of certain cells in the CNS and other anatomic structures, such as the GI tract and the urinary bladder.</p> <p>-also acts at κ receptors in lamina I and II of the dorsal horn of the spinal cord. It decreases the release of substance P, which modulates pain perception in the spinal cord.</p>	<p>-Analgesia (relieve pain both by raising the pain threshold at the spinal cord level and, more importantly, by altering the brain's perception of pain)</p> <p>-Euphoria (may be caused by disinhibition of the dopamine-containing neurons of the ventral tegmental area)</p> <p>-antitussive (Depression of cough reflex)</p> <p>-relieves diarrhea by decreasing the motility and increasing the tone of the intestinal circular smooth muscle</p>	<p>-respiratory depression</p> <p>- Miosis (pinpoint pupils)</p> <p>- Emesis</p> <p>- constipation</p> <p>-With large doses, hypotension and bradycardia may occur</p> <p>-Morphine releases histamine from mast cells causing urticaria, sweating, and vasodilation.</p> <p>-Because it can cause bronchoconstriction, morphine should be used with caution in patients with asthma</p> <p>-Morphine increases growth hormone release and enhances prolactin secretion. It increases antidiuretic hormone and leads to urinary retention.</p> <p>-Elevation of intracranial pressure, particularly in head injury</p> <p>-e should be used with caution in patients with asthma, liver disease, or renal dysfunction.</p>	<p>-Because of respiratory depression and carbon dioxide retention, cerebral vessels dilate and increase cerebrospinal fluid pressure. Therefore, morphine is usually contraindicated in individuals with head trauma or severe brain injury.</p> <p>-Morphine may prolong the second stage of labor by transiently decreasing the strength, duration, and frequency of uterine contractions.</p> <p>-Morphine rapidly enters all body tissues, including the fetuses of pregnant women. It should not be used for analgesia during labor.</p> <p>- Infants born to addicted mothers show physical dependence on opioids and exhibit withdrawal symptoms if opioids are not administered.</p> <p>-Repeated use produces tolerance to the respiratory depressant, analgesic, euphoric, and sedative effects of morphine. However, tolerance usually does not develop to the pupil-constricting and constipating effects of the drug.</p> <p>-Withdrawal produces a series of autonomic, motor, and psychological responses that incapacitate the individual and cause serious symptoms, although it is rare that the effects cause death.</p> <p>-the depressant actions of morphine are</p>
			<p>Management of constipation associated with opioids:A non prescription laxative combination of</p>	

			the stool softener docusate with the stimulant laxative senna is useful to treat opioid-induced constipation	enhanced by phenothiazines, monoamine oxidase inhibitors (MAOIs), and tricyclic antidepressants
CODEINE	The analgesic actions of codeine are derived from its conversion to morphine by the CYP450 2D6 enzyme system	-used only for mild to moderate pain. -commonly used in combination with acetaminophen for management of pain -exhibits good antitussive activity at doses that do not cause analgesia.		
OXYCODONE and OXYMORPHONE	-Oxycodone is a semisynthetic derivative of morphine -Oxymorphone is a semisynthetic opioid analgesic.	-oral analgesic effect of oxycodone is approximately twice that of morphine -When oxymorphone is given parenterally it is approximately ten times more potent than morphine (oral formulation is about 3 times more potent than morphine)	-Abuse of the sustained-release preparation (ingestion of crushed tablets) has been implicated in many deaths	
HYDROMORPHONE and HYDROCODONE	Hydromorphone and hydrocodone are orally active, semisynthetic analogs of morphine and codeine, respectively.	-Hydromorphone is preferred over morphine in patients with renal dysfunction due to less accumulation of active metabolites - Hydrocodone is often combined with acetaminophen or ibuprofen to treat moderate to severe pain. It is also used as an antitussive		
FENTANYL		-has 100-fold the analgesic potency of morphine and is used for anesthesia	-The transdermal patch must be used with caution because death resulting from hypoventilation has	-has a rapid onset and short duration of action (15 to 30 minutes)

		<ul style="list-style-type: none"> -Fentanyl is combined with local anesthetics to provide epidural analgesia for labor and postoperative pain. -IV fentanyl is used in anesthesia for its analgesic and sedative effects. -The oral transmucosal preparation is used in the treatment of cancer patients with breakthrough pain who are tolerant to opioids. 	<p>been known to occur. Use is contraindicated in opioid-naïve patients, and patches should not be used in managing acute and postoperative pain.</p>	
SUFENTANIL, ALFENTANIL, REMIFENTANIL, CARFENTANIL	three synthetic opioid agonists related to fentanyl	mainly used for their analgesic and sedative properties during surgical procedures requiring anesthesia		
METHADONE	The actions of methadone are mediated by μ receptors. In addition, methadone is an antagonist of the N-methyl-d-aspartate (NMDA) receptor and a norepinephrine and serotonin reuptake inhibitor.	<ul style="list-style-type: none"> -Methadone induces less euphoria and has a longer duration of action -has efficacy in the treatment of both nociceptive and neuropathic pain. -used in the controlled withdrawal of dependent abusers from opioids and heroin. Oral methadone is administered as a substitute for the opioid of abuse, and the patient is then slowly weaned from methadone. 	<ul style="list-style-type: none"> -Methadone can produce physical dependence like that of morphine, but has less neurotoxicity than morphine due to the lack of active metabolites. - can prolong the QT interval and cause torsades de pointes, possibly by interacting with cardiac potassium channels. 	-The half-life of methadone ranges from 12 to 40 hours. It may extend up to 150 hours, although the actual duration of analgesia ranges from 4 to 8 hours. Consequently, the time frame it takes for an individual patient to reach steady state can vary dramatically, from 35 hours to 2 weeks. Upon repeated dosing, methadone can accumulate due to the long terminal half-life, thereby leading to toxicity.
MEPIRIDINE	acts primarily as a κ agonist, with some μ agonist	-used for acute pain	-has anticholinergic effects, resulting in an increased incidence of delirium as compared to other	-Due to the short duration of action and the potential for toxicity, meperidine should only be used for short-term (≤ 48

	activity also		opioids - Meperidine also has an active metabolite (normeperidine) that is renally excreted. Normeperidine has significant neurotoxic actions that can lead to delirium, hyperreflexia, myoclonus, and possibly seizures.	hours) management of pain. -Meperidine should not be used in elderly patients or those with renal insufficiency, hepatic insufficiency, preexisting respiratory compromise, or concomitant or recent administration of MAOIs. -Serotonin syndrome has also been reported in patients receiving both meperidine and SSRIs
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