Myocardial infarction (**MI**) or **acute myocardial infarction** (**AMI**), commonly known as a **heart attack**, occurs when blood flow stops to a part of the heart causing damage to the heart muscle. The most common symptom is chest pain or discomfort which may travel into the shoulder, arm, back, neck, or jaw. Often it is in the center or left side of the chest and lasts for more than a few minutes. The discomfort may occasionally feel like heartburn. Other symptoms may include shortness of breath, nausea, feeling faint, a cold sweat, or feeling tired. About 30% of people have atypical symptoms, with women more likely than men to present atypically. Among those over 75 years old, about 5% have had an MI with little or no history of symptoms. An MI may cause heart failure, an irregular heartbeat, or cardiac arrest.

Stroke, also known as **cerebrovascular accident** (**CVA**), **cerebrovascular insult** (**CVI**), or **brain attack**, is when poor blood flow to the brain results in cell death. There are two main types of stroke: ischemic, due to lack of blood flow, and hemorrhagic, due to bleeding. They result in part of the brain not functioning properly. Signs and symptoms of a stroke may include an inability to move or feel on one side of the body, problems understanding or speaking, feeling like the world is spinning, or loss of vision to one side among others. Signs and symptoms often appear soon after the stroke has occurred. If symptoms last less than one or two hours it is known as a transient ischemic attack (TIA). Hemorrhagic strokes may also be associated with a severe headache. The symptoms of a stroke can be permanent.[1]Long term complications may include pneumonia or loss of bladder control.

2. Paracetamol / acetaminophen

Paracetamol, also known as acetaminophen or APAP, is a medication used to treat pain and fever.[9] It is typically used for mild to moderate pain

Medical uses

- Fever
- Pain
- Osteoarthritis
- Low back pain
- Headaches
- Postoperative pain

Liver damage

Asthma

There is an association between paracetamol use and asthma but the evidence suggests that this likely reflects confounders[53] rather than a causal role. As of 2014, the American Academy of Pediatrics and the National Institute for Health and Care Excellence (NICE) continue to recommend paracetamol for pain and discomfort in children,[56][57][58][59][60][61] but some experts have recommended that paracetamol use by children with asthma, or at risk for asthma, should be avoided

Skin reactions[edit]

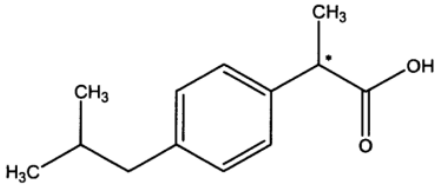
On August 2, 2013, the U.S. Food and Drug Administration (FDA) issued a new warning about paracetamol. It stated that the drug could cause rare, and possibly fatal, skin reactions, such as Stevens–Johnson syndrome and toxic epidermal necrolysis.

Paracetamol when taken recreationally with opioids may cause hearing loss

3. Ibuprofen

Ibuprofen, from **iso**-**but**-**phenyl**-**pro**panoic acid, is a nonsteroidal anti-inflammatory drug (NSAID) used for treating pain, fever, and inflammation. This includes **painful menstrual periods, migraines, and rheumatoid arthritis.**

About 60% of people improve with any given NSAID, and it is recommended that if one does not work then another should be tried. It may also be used to close a patent ductus arteriosus in a premature baby. It can be used by mouth or intravenously. It typically begins working within an hour.



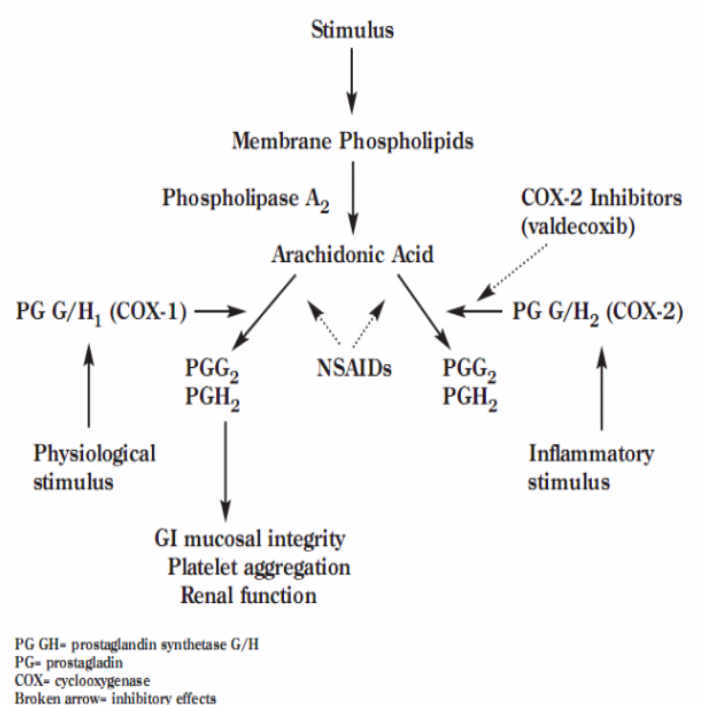
Ibuprofen

Discovery of Ibuprofen

Ibuprofen was discovered in 1961 by Stewart Adams and marketed as **Brufen**. It is available under a number of trade names, including **Advil**, **Motrin**, and **Nurofen**. It was first marketed in 1969 in the United Kingdom and in the United States in 1974. It is on the WHO Model List of Essential Medicines, the most important medications needed in a basic health system. It is available as a generic medication.

Mechanism of action of Ibuprofen

Nonsteroidal anti-inflammatory drugs such as ibuprofen work by inhibiting the COX enzymes, which convert arachidonic acid to prostaglandin H_2 (PGH_2). PGH_2, in turn, is converted by



PG GH= prostaglandin synthetase G/H
PG= prostagladin
COX= cyclooxygenase
Broken arrow= inhibitory effects

other enzymes to several other prostaglandins (which are mediators of pain, inflammation, and fever) and to thromboxane A_2 (which stimulates platelet aggregation, leading to the formation of blood clots).

The exact mechanism of action of ibuprofen is unknown. Ibuprofen is a nonselective inhibitor of cyclooxygenase, an enzyme involved in prostaglandin synthesis via the arachidonic acid pathway. Its pharmacological effects are believed to be due to inhibition of cyclooxygenase-2 (COX-2) which decreases the synthesis of prostaglandins involved in mediating inflammation, pain, fever, and swelling. Antipyretic effects may be due to action on the hypothalamus, resulting in an increased peripheral blood flow, vasodilation, and subsequent heat dissipation. Inhibition of COX-1 is thought to cause some of the side effects of ibuprofen including gastrointestinal ulceration. Ibuprofen is administered as a racemic mixture. The R-enantiomer undergoes extensive interconversion to the S-enantiomer *in vivo*. The S-enantiomer is believed to be the more pharmacologically active enantiomer.

Like aspirin and indometacin, ibuprofen is a nonselective COX inhibitor, in that it inhibits two isoforms of cyclooxygenase, COX-1 and COX-2. The analgesic,antipyretic, and anti-inflammatory activity of NSAIDs appears to operate mainly through inhibition of COX-2, whereas inhibition of COX-1 would be responsible for unwanted effects on the gastrointestinal tract.[36] However, the role of the individual COX isoforms in the analgesic, anti-inflammatory, and gastric damage effects of NSAIDs is uncertain and different compounds cause different degrees of analgesia and gastric damage.

Medical uses

Ibuprofen is used primarily for fever (including post immunisation fever), mild-to-moderate pain (including pain relief after surgery), painful menstruation, osteoarthritis, dental pain, headaches and pain from kidney stones. It is used for inflammatory diseases such as juvenile idiopathic arthritis and rheumatoid arthritis. It is also used for pericarditis and patent ductus arteriosus.

Side effects

Common side effects include heartburn and a rash. Compared to other NSAIDs it may have fewer side effects such as gastrointestinal bleeding. It increases the risk of heart failure, kidney failure, and liver failure. At low doses it does not appear to increase the risk of myocardial

infarction; however, at higher doses it may. It may result in worsened asthma. While it is unclear if it is safe in early pregnancy, it appears to be harmful in later pregnancy. Like other NSAIDs, it works by inhibiting the making of prostaglandins by decreasing the activity of the enzyme cyclooxygenase. Ibuprofen might be a weaker anti-inflammatory than other NSAIDs.

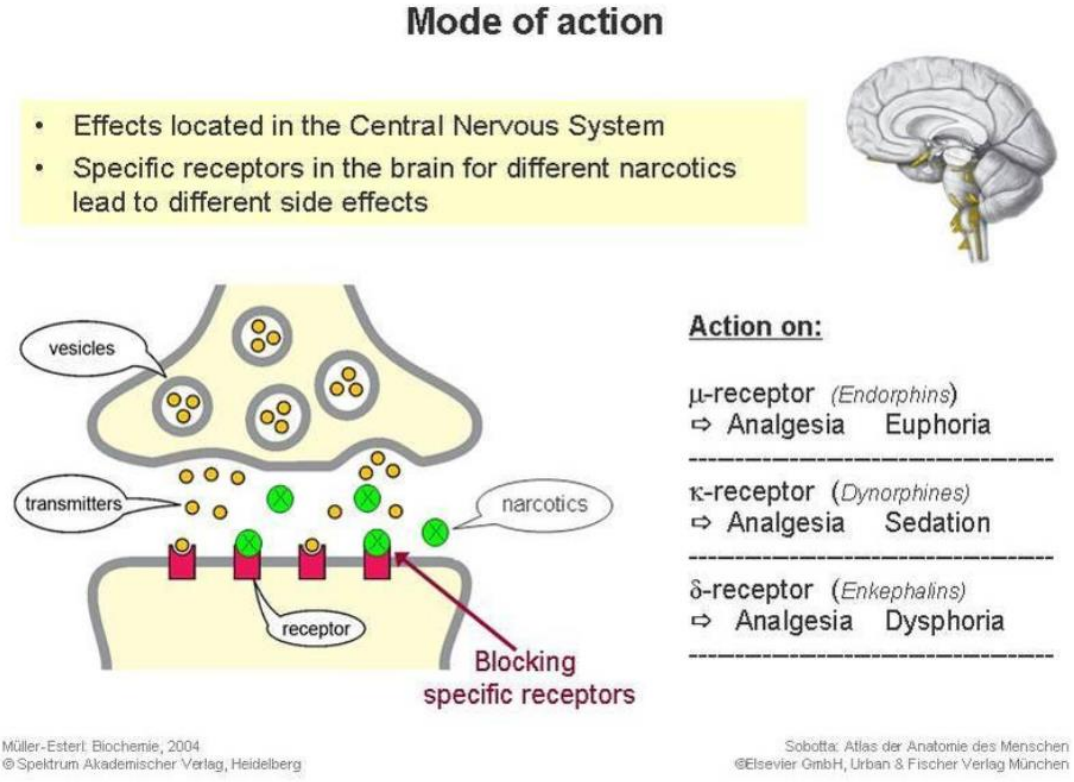
Miscarriage

A study of pregnant woman suggests those taking any type or amount of NSAIDs (including ibuprofen, diclofenac and naproxen) were 2.4 times more likely tomiscarry than those not taking the drugs.[33] However, an Israeli study found no increased risk of miscarriage in the group of mothers using NSAIDs.

STRONG ANALGESICS

OPIUM

Opium contains two main groups of alkaloids. Phenanthrenes such as morphine, codeine, and thebaine are the main psychoactive constituents. Isoquinolines such as papaverine and noscapine have no significant central nervous system effects, and are not regulated under the Controlled Substances Act. Morphine is the most prevalent and important alkaloid in opium, consisting of 10%–16% of the total, and is responsible for most of its harmful effects such as lung edema, respiratory difficulties, coma, or cardiac or respiratory collapse. Morphine binds to and activates mu opioid receptor in the brain, spinal cord, stomach and intestine. Regular use can lead to drug toleranceor physical dependence. Chronic opium addicts in 1906 China or modern-day Iran consume an average of eight grams of opium daily.



A narcotic is an addictive drug that reduces pain, induces sleep and may alter mood or behaviour. In medicine, an analgesic narcotic means opioid, which refers to all natural, semi-synthetic and synthetic substances that behave pharmacologically like morphine, the primary constituent of natural opium. The opioids are classified on the WADA List as narcotics. Pain killers (morphine, heroine, codeine) are, sometimes, used by athletes or competitors engaged in violent sports. Increased threshold for pain tolerance, adjusted by opioids application, allows a better sport performance. Opioids are drugs with great potential of physical and psychic dependence. Tolerance of the drugs develop quickly. The main biomedical effects of analgesic narcotics on central nervous system are euphoria, lethargy, apathy and inability to concentrate. Sudden withdrawal of opioid drugs, or application of opioid antagonists, causes a withdrawal syndrome in addicted persons. The opioid hunger is badly tolerated by addicted persons.

2. Heroine

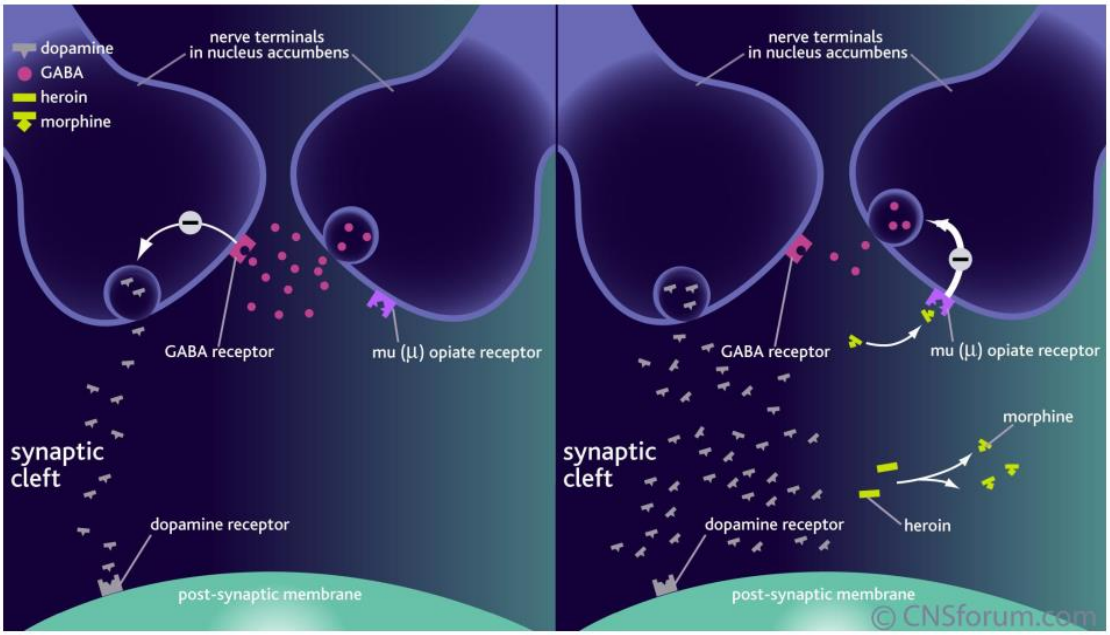
Heroin is an opioid painkiller and the **3,6-diacetyl ester** of morphine. Heroin is prescribed as an **analgesic, cough suppressant** and as an **antidiarrhoeal**. It is also used as a recreational drug for its euphoric effects. Frequent and regular administration is associated with tolerance and physical dependence. In some countries it is available for prescription to long-term users as a form of opioid replacement therapy alongside counseling.

It was originally synthesized by C. R. Alder Wright in 1874 by adding two acetyl groups to the molecule morphine, a natural product of the opium poppy. Internationally, heroin is controlled under Schedules I and IV of the Single Convention on Narcotic Drugs. It is generally illegal to manufacture, possess, or sell heroin without a license. In 2004, Afghanistan produced roughly 87% of the world supply in illicit raw opium. However, the production rate in Mexico rose six fold from 2007 to 2011, making Mexico the second largest opium producer in the world.

Administered **intravenously** by injection, heroin is two to four times more potent than morphine and is faster in its onset of action. Illicit heroin is sometimes available in a matte-white powder freebase form. Because of its lower boiling point, the freebase form of heroin is smokable.

What are the most common heroin withdrawal symptoms?

The mechanism of action of heroin at the mu (m) opiate receptors



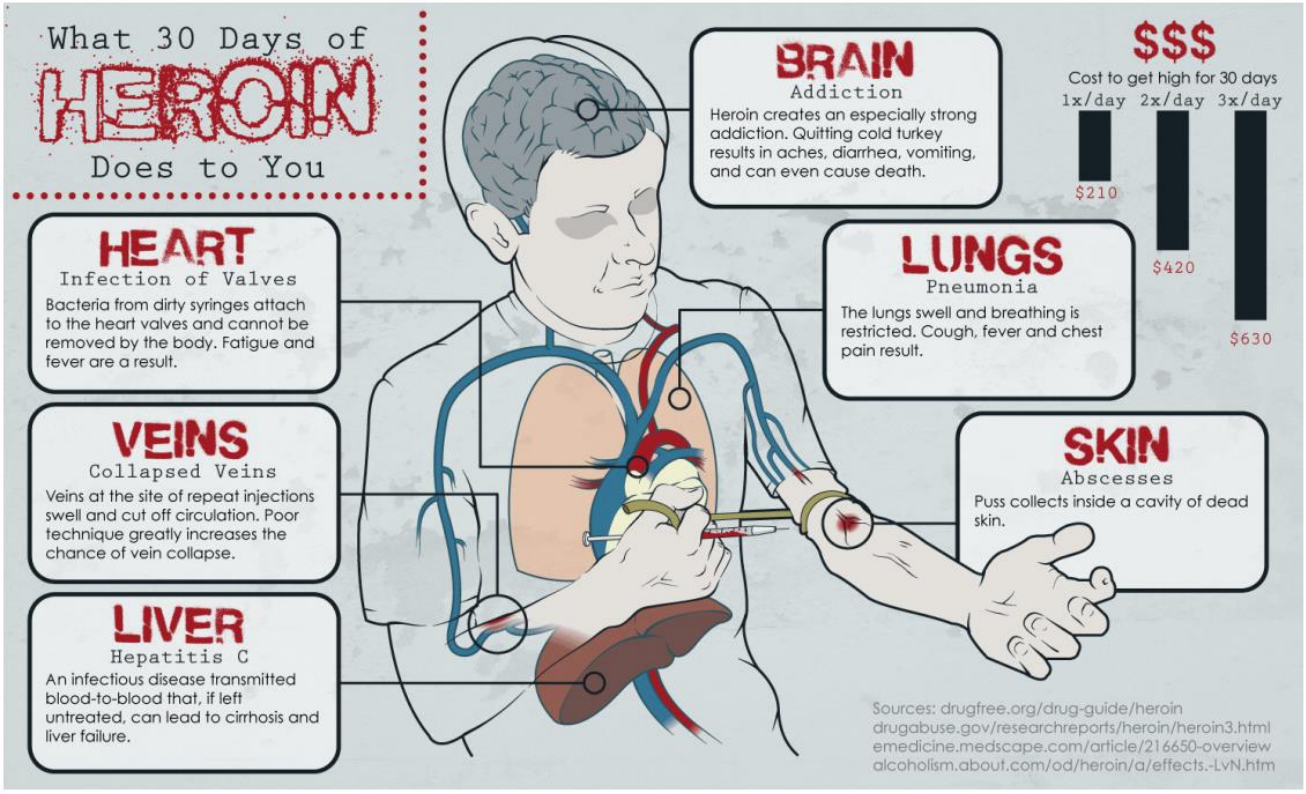
→ Heroine withdrawal can be utterly terrifying. Some recovering users have described the sensation as drowning under water or being deprived of oxygen! Even if an addict has the best intentions and is determined to throw off the addiction, the addict may just not be able to bear the symptoms.

- → Some have likened heroin withdrawal to a feeling of a never ending depression. Many people report that the anticipation of the symptoms is worse than the actual withdrawal itself. Often, people overcompensate for the harrowing effects of withdrawal by ingesting an even larger dose than before.
- → Symptoms begin to kick in within the first twelve hours and usually peak between the first and the third day. They begin to ease on the fifth day and most symptoms are gone within seven to ten days. After the psychical withdrawal symptoms have past it may take up to six months for the patient to fully recover from the emotional and psychological trauma.

Heroin modifies the action of dopamine in the nucleus accumbens and the ventral tegmental area of the brain – these areas form part of the brain's 'reward pathway'. Once crossing the blood-brain barrier, heroin is converted to morphine, which acts as a powerful agonist at the mu opioid receptors subtype. This binding inhibits the release of GABA from the nerve terminal, reducing the inhibitory effect of GABA on dopaminergic neurones. The increased activation of dopaminergic neurones and the release of dopamine into the synaptic results in sustained activation of the post-synaptic membrane. Continued activation of the dopaminergic reward pathway leads to the feelings of euphoria and the 'high' associated with heroin use. Morphine is a weak agonist at the opioid kappa and delta receptor subtypes and activation of these receptors has a weak activating effect on the dopaminergic reward pathway.

These are the tell-tale signs of heroin withdrawal:

- Anxiety
- Depression
- Profuse perspiration
- Muscle aches and cramps
- Loss of appetite
- Mood swings
- Nausea



- Vomiting
- Diarrhea
- Seizures (in some cases)

Some of the symptoms of heroin withdrawal are somewhat similar to a flue – but a lot more pronounced. Hence, the withdrawal phase is often referred to as a super flu! Note that unlike Alcohol or benzodiazepine (Xanex, Valium ect) the withdrawal symptoms of heroin is not life threatening. However, the unpleasant withdrawal symptoms may cause the patient to relapse and abuse higher doses of heroin or some other drug, which may result in a fatal overdose.

During withdrawal, users feel lonely and experience an inner compulsion to take heroin. In some extremely severe cases of addiction (either in terms of dosage or duration or both), the symptoms take months to subside – this condition is called post-acute withdrawal syndrome. What happens if a heroin addiction is not addressed? Nothing good happens! Over time, users build up a resistance to the drug. They begin to abuse it in progressively larger doses. Heroin can literally wreaks havoc in the human body.

The ill effects of the drug may include:

- Reduced sex drive and loss of sensation in the genitals. Inability to achieve orgasm
- Impotence in men and infertility in women
- Inability to focus
- Severe weakening of the body's immune system
- Loss of memory
- Inability to think coherently, loss of intellectual capacity
- Rotting of teeth and inflammation in the gums
- Inability to succeed in any aspects of life – be it social, professional, personal, emotional or spiritual.

- Extreme depression
- Insomnia
- Cold sweats
- Digestive issues – the most common being constipation
- Pustules on the face
- Respiratory problems – difficulty breathing.
- Loss of appetite

Seriously, this list can extend into multiple pages! Heroin addiction can cause a person to lose absolutely everything – friends, parents, family, job, money. Users may even lie or steal in order to get their fix; they lose their self-respect and feel that their life becomes totally meaningless. Some people are of the opinion that you should try everything in life at least once – well, that certainly does not apply to heroin and other drugs.

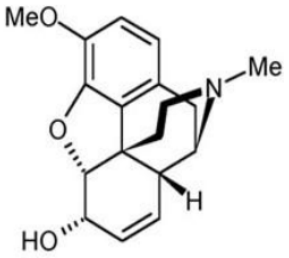
Is there hope for a heroin abuser?

1. Definitely, even though the withdrawal phase is nasty, the addiction is certainly beatable! Each year, thousands of people manage to shake off their addiction and return to a fulfilling life.
2. **Methadone** treatment is probably the most commonly prescribed treatment for heroin addiction. Many people will instead use a combination over the counter drugs, supplements and/or herbal remedies to help manage and get through heroin withdrawals. Some examples would be the Thomas Recipe or natural supplement products such as **Elimidrol or CalmSupport** .
3. If you or a loved one is addicted to heroin and would like help. Seeing a doctor or medical professional in combination of counseling and having a support group will greatly increase a persons chances of success.

Note

Euphoria (semantically opposite of dysphoria) is medically recognized as a mental and emotional condition in which a person experiences intense feelings of well-being, elation, happiness, excitement and joy.

3. Codeine



Codeine, also known as **3-methylmorphine**, is an opiate used to treat pain, as a cough medicine, and fordiarrhea. It is typically used for mild to moderate degrees of pain. Greater benefit may occur when combined withparacetamol (acetaminophen) or aspirin. Evidence for use for cough is poor.

In Europe it is not recommended as a cough medicine in those under twelve years of age. It is taken by mouth. It typically starts working after half an hour with maximum effect at two hours. Effects last for about four to six hours.

Common side effects include vomiting, constipation, itchiness, and lightheadedness. Serious side effects may include a decreased effort to breathe and addiction. It is unclear if its use in pregnancy is safe. Care should be used during breast feeding as it may result in opiate toxicity in the baby. Codeine works following being broken down by the liver into morphine. How quickly this occurs depends on a person's genetics.

Codeine was discovered in 1832. In 2013 about 361,000 kilograms of codeine were produced while 249,000 kilograms were used. This makes it the most commonly taken opiate. It is on the WHO Model List of Essential Medicines, the most important medication needed in a basic health system. The wholesale cost is between 0.04 and 0.29 USD per dose as of 2014. In the United States it costs about one dollar a dose. Codeine occurs naturally and makes up about 2% of opium.

Formulations

Codeine is marketed as both a single-ingredient drug and in combination preparations with paracetamol (as co-codamol: *e.g.,* brands Paracod, Panadeine, and the Tylenol-with-codeine series, including Tylenol 3 and 1,2,4); with aspirin (as co-codaprin); or with ibuprofen (as Nurofen Plus). These combinations provide greater pain relief than either agent alone (drug synergy).

Codeine is also commonly marketed in products containing codeine with other pain killers or muscle relaxers, as well as codeine mixed with phenacetin (Emprazil With Codeine No. 1, 2, 3, 4 and 5), naproxen, indomethacin, diclofenac, and others, as well as more complex mixtures, including such mixtures as aspirin + paracetamol + codeine ± caffeine ± antihistamines and other agents, such as those mentioned above.

Codeine-only products can be obtained with a prescription as a time release tablet (*e.g.,* Codeine Contin 100 mg and Perduretas 50 mg). Codeine is also marketed in cough syrups with zero to a half-dozen other active ingredients, and a linctus (*e.g.,* Paveral) for all of the uses for which codeine is indicated.

Injectable codeine is available for subcutaneous or intramuscular injection only; intravenous injection is contraindicated as this can result in non-immune mast-cell degranulation and resulting anaphylactoid reaction. Codeine suppositories are also marketed in some countries.

Medical uses

Codeine is used to treat mild to moderate pain and to relieve cough. Codeine is also used to treat diarrhea and diarrhea-predominant irritable bowel syndrome, although loperamide (which is available OTC for milder diarrhea),diphenoxylate, paregoric or even laudanum (also known as *Tincture of Opium*) are more frequently used to treat severe diarrhea.

It is weak evidence that it is useful in cancer pain but it is associated with increased side effects.

Adverse effects

Common adverse effects associated with the use of codeine include drowsiness and constipation. Less common are itching, nausea, vomiting, dry mouth, miosis, orthostatic hypotension, urinary retention, euphoria, dysphoria, and coughing. Rare adverse effects include anaphylaxis, seizure, acute pancreatitis, and respiratory depression. As with all opiates, longer-term effects can vary, but can include diminished libido, apathy, and memory loss. Some people may also have an allergic reaction to codeine, such as the swelling of skin and rashes.

Codeine and morphine, as well as opium, were used for control of diabetes until relatively recently, and still are in rare cases in some countries, and the hypoglycemic effect of codeine, although usually weaker than that of morphine, diamorphine, or hydromorphone, can lead to cravings for sugar.

Tolerance to many of the effects of codeine develops with prolonged use, including to its therapeutic effects. The rate at which this occurs develops at different rates for different effects, with tolerance to the constipation-inducing effects developing particularly slowly for instance.

A potentially serious adverse drug reaction, as with other opioids, is respiratory depression. This depression is dose-related and is a mechanism for the potentially fatal consequences of overdose. As codeine is metabolized to morphine, morphine can be passed through breast milk in potentially lethal amounts, fatally depressing the respiration of a breastfed baby. In August 2012, the United States Federal Drug Administration issued a warning about deaths in pediatric patients < 6 years old after ingesting "normal" doses of paracetamol with codeine after tonsillectomy.

Some patients are very effective converters of codeine to its active form, morphine, resulting in lethal blood levels. The FDA presently is recommending very cautious use of Codeine in young tonsillectomy patients: use the drug in the lowest amount that can control the pain, use "as needed" and not "around the clock", and seek immediate medical attention if a child on codeine exhibits excessive sedation or abnormally noisy breathing.

Withdrawal and dependence

As with other opiate-based pain killers, chronic use of codeine can cause physical dependence. When physical dependence has developed, withdrawal symptoms may occur if a person suddenly stops the medication. Withdrawal symptoms include: drug craving, runny nose, yawning, sweating, insomnia, weakness, stomach cramps, nausea, vomiting, diarrhea, muscle spasms, chills, irritability, and pain. To minimize withdrawal symptoms, long-term users should gradually reduce their codeine medication under the supervision of a healthcare professional.

Codeine is metabolized to codeine-6-glucuronide (C6G) by uridine diphosphate glucuronosyl transferase UGT2B7, and, since only about 5% of codeine is metabolized by cytochrome P450 CYP2D6, the current evidence is that C6G is the primary active compound.[20] Claims about the supposed "ceiling effect" of codeine doses are based on the assumption that high doses of codeine saturate CYP2D6, preventing further conversion of codeine to morphine, however it is now known that C6G is the main metabolite responsible for codeine's analgesia.

There is also no evidence that CYP2D6 inhibition is useful in treating codeine dependence, though the metabolism of codeine to morphine (and hence further metabolism to glucuronide morphine conjugates) does have an effect on the abuse potential of codeine. However, CYP2D6 has been implicated in the toxicity and death of neonates when codeine is administered to lactating mothers, particularly those with increased 2D6 activity ("ultra-rapid" metabolizers).

Generic name (INN)	Physicochemistry	Mechanism of action	Routes of administration	Pharmacokinetics	Indications	Major safety concerns
Non steroidal anti-inflammatory drugs						
Aspirin	Comes in free form, aluminium and lysine salt forms; fairly insoluble in water (1 in 300); highly soluble (1 in 5) in alcohol; degrades on contact with air. Salicylate.	Irreversibly inhibitsCOX-1 and COX-2; hence inhibiting prostaglandin synthesis.	PO, IM, IV, rectal	Bioavailability = 80–100%; protein binding = 25–95% (inversely dependent on plasma concentration); half life = 2–3 hours, 15–30 hours (higher doses); excretion = 80–100%.[26]	Blood thining; mild-to-moderate pain; fever; rheumatic fever; migraine; rheumatoid arthritis; Kawasaki's disease	GI bleeds; ulcers; reye syndrome; nephrotoxicity; blood dyscrasias (rarely); Stevens-Johnson syndrome(uncommon/rare)
COX-2 Selective inhibitors						
Celecoxib	Comes in free form; practically insoluble in water, fairly soluble in organic solvents. Degrades on contact with light and moisture.Sulfonamide.	Selective COX-2 inhibitor.	PO.	Protein binding = 97%; hepatic metabolism, mostly via CYP2C9; faeces (57%), urine (27%).	Rheumatoid arthritis; osteoarthritis; ankylosing spondylitis; pain due to dysmenorrhoea or injury.	As per non-selective NSAIDs. More prone to causing thrombotic events than most of them, however, except diclofenac.
Opioids						
Morphine Skeleton						
Codeine	Comes in free form, hydrochloride salt, sulfate salt and phosphate salts;	Metabolised to morphine, which activates	PO, IM, IV.	Extensive hepatic metabolism, mostly viaCYP2D6,	Mild-moderate pain, often in combination with paracetamol or ibuprofen.	Constipation, dependence, sedation, itching,

	soluble in boiling water (free form), freely soluble in ethanol (free form), soluble/freely soluble in water (salt forms); sensitive to degradation by light. Methoxy analogue of morphine.	the opioid receptors.		to morphine; half-life = 3–4 hours; excretion = urine (86%).[76]		nausea, vomiting and respiratory depression.
Morphinans						
Butorphanol	Comes in tartrate salt form; sparingly soluble in water, insoluble in most organic solvents; degrades upon contact with air and at temperatures outside the range of 15°C and 30°C.	Kappa opioid receptor agonist; mu opioid receptor partial agonist.	IM, IV, intranasal.	Bioavailability = 60–70% (intranasal); protein binding = 80%; volume of distribution = 487 L; hepatic metabolism, mostly via hydroxylation; excretion = urine (mostly); half-life = 4.6 hours.	Moderate-severe pain, including labour pain.	As above, but with a higher propensity for causing hallucinations and delusions. Respiratory depression is subject to ceiling effect.
Benzomorphans						
Dezocine	No data available.	Mixed opioid agonist-antagonist.	IM, IV.	Volume of distribution = 9–12 L/kg; half-life = 2.2–2.7 hours.	Moderate-severe pain.	As above.
Phenylpiperidines						
Anileridine	Comes in free, hydrochloride and phosphate forms;	Mu opioid receptor agonist.	IM, IV.	No data.	Moderate-severe pain.	As per other opioids.

	fairly insoluble in water, soluble in ethanol, ether and chloroform; degrades upon contact with air and light.					
Open chain opioid						
Dextromoramide	Comes in tartrate salt and free forms; soluble in water (tartrate salt).	IM, IV, PO, rectal.	No data available.	Severe pain.	As per other opioids.	As per other opioids.
Anilidopiperidines						
Alfentanil	Comes in hydrochloride salt form; freely soluble in ethanol, water, methanol; degrades upon contact with air and light.	Mu opioid.	Epidural, IM, IV, intrathecally.	Protein binding = 90%; volume of distribution = small; half-life = 1–2 hours; hepatic metabolism, mostly viaCYP3A4; excretion = urine.	Procedural aenasthesia.	As per other opioids. Very sedating.