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FACTS ON OPIOIDS

In the Beginning, There Were Peptides

Why does any drug have an effect on the brain and behavior? The simple answer is that our body manufactures endogenous peptides (e.g., endorphins, enkephalins and dynorphins) that are natural euphoriants and pain relievers released during childbirth, strenuous exercise, some types of stress and periods of blissful relaxation. These feel-good chemicals work through special receptors. Drugs such as morphine, oxycodone, fentanyl, etc., activate the same receptors.

Then There Were Opiates

Opiates are drugs derived from opium. Raw opium is a natural opioid found as the exudate from the poppy plant. This sticky substance contains morphine, codeine and other chemicals. Opium has been smoked for thousands of years, during which time it was heralded to treat a range of disorders. Morphine is the primary psychoactive component of opium and the prototypical opioid against which the analgesic (pain relieving) potency of other opioids is judged.

The widespread use of opium led to research to isolate the active components in this drug, namely, morphine (named after the Greek god of dreams, Morpheus) and codeine, and the development and synthesis of other formulations of these molecules. Morphine offered unprecedented medical advantages in surgery and in medical and homeopathic pain relief.

By 1898, chemists at Bayer Laboratories found that changing the morphine molecule created a new drug, diacetylmorphine. Once in the blood, diacetylmorphine easily passes through the blood brain barrier, where it is quickly metabolized to morphine. Diacetylmorphine is also known as heroin. The analgesic effectiveness of opiate-related drugs such as morphine is second to none in treating pain. Another effect is sleepiness or a euphoric dreamlike state. To the observer, users often appear in a stupor or nodding off (hence the term "on the nod") during the onset of action.

Early laws (Harrison Narcotic Act of 1914) designed to control a burgeoning opiate problem used the now outdated term, narcotic. For many decades this term was erroneously applied to non-opiate related drugs (including cocaine and cannabinoids). The term opioid is now more accurate.

Evolution of Opioids

Today, the term opioid includes all compounds with morphine-like activity or that interact with opioid receptors throughout the body. These include opioids that are present naturally (e.g., endorphins, enkephalins and dynorphins), opiates (morphine, codeine), semi-synthetics (heroin, oxycodone, oxycontin) and synthetic opioids (e.g., methadone, buprenorphine, fentanyl). These opioids act as molecular *agonists* to activate specific receptors in nerve cells in the brain and elsewhere to produce their effects. Opioid *antagonists* such as naltrexone and naloxone (Narcan) occupy opioid receptors thereby blocking or reversing the action of opiate agonists. Naloxone nasal sprays or injections are used to treat opioid overdoses. The sooner they are administered, the more favorable the outcome. Naloxone kits are often made available to community members at no cost. Contact your local county drug prevention agency for more information.

Morphine shortages during World War II, led German scientists to develop a substitute drug, Dolophine, now commonly known as methadone. Methadone effectively treats pain and because it is water soluble, it can be taken orally. Although methadone is addicting, it is also used to treat heroin addiction because it can be administered orally in a clinic, thereby reducing health risks (HIV, AIDS) from needle sharing and clinical administration reduces criminal activity involved in purchasing street drugs. Buprenorphine (Suboxone, Subutex), another synthetic opioid, is a partial receptor agonist, which limits its euphoric effect, thereby making it

more beneficial than methadone in treating addiction. The search for more effective analgesics led to newer semi-synthetic opioids such as oxycodone, hydrocodone, and purely synthetic opioids like fentanyl. These drugs are widely prescribed, highly abused, addictive and more dangerous than heroin or morphine. Carfentanyl, is a molecular analogue of fentanyl sometimes used to spike heroin or other drugs or as a counterfeit drug. Because it is so much more potent than other opioids, the users' unanticipated reaction is all too often fatal.

Effects of Opioids

- Decreased pulse
- Decreased temperature
- Decreased respiration
- Slowed reflexes
- Slow, low raspy slurred speech
- Nausea (new users)
- Impaired memory and attention
- Vertigo (dizziness)
- Sleepy, lethargic
- Constricted pupils
  (*about* 1/8th inch or 3 mm)

Tolerance, Addiction and Withdrawal

Tolerance to opioid euphoria and analgesia develops rapidly so that higher doses are needed to achieve the desired clinical or other effects. Chronic use also results in severe withdrawal if drug taking is interrupted. Although not usually life threatening, withdrawal from opioids is extremely unpleasant.

How Do Opioids Kill?

Abuse and deaths from these highly potent drugs has reached epidemic proportions in the US. In recent years, deaths from opioid overdoses have exceeded deaths from drunk driving. The widespread availability, ease of use, and the high potency of many semi- and totally synthetic opioids contribute to this epidemic.

Opioids cause death by directly acting on receptors in brain areas that control consciousness, respiration and heart rate. As a central nervous system depressant, high doses of opioids can "*turn off*" respiratory areas in the brain and cause cardiac arrhythmias and heart attacks. If dose determines the poison, newer opioids are truly dangerous. Fentanyl, for example, is about 30-40 times stronger than heroin (by weight) and about 80-100 times more potent than morphine, highly lipid (fat) soluble and quickly enters the brain to produce a very rapid onset. Fentanyl and carfentanyl have been sold as, or in, other opioids to unsuspecting users. Carfentanyl is 100 times more potent than fentanyl, 10,000 times more potent than morphine, and can be absorbed through the skin. These opioids create a particularly high risk for overdose deaths.

How Much Opioid Use Is "Lethal"?

Street drugs may be spiked (contain other drugs) making them potentially deadlier than a single dose of any one drug. Thus, the lethal dose for many street opioids is not known, until after the fact. Even so, concentrations of various opioids detected after death do not allow any estimate of a safe or lethal dose.

Signs of Opioid Overdose

Of the many effects of opioids, some observable signs strongly indicate an overdose. If someone displays any of the following signs and you suspect drug use, this is likely a drug overdose.

- Vomiting
- Passed out, not responsive
- Stuporous or difficult to awaken
- Slow, shallow breathing
- Blue lips

What You Should Do?

Don't let the person "sleep it off". If they don't respond or have *any* other signs, call 911 and report a possible drug overdose. Administer Narcan, if available and as instructed.

Selected References:

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