

FENTANYL: MISUSE AND TOXICITY

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Topic Overview

Fentanyl, a synthetic opioid, is a primary contributor to the current opioid crisis in the United States. Statistics show that the use of fentanyl causes significant morbidity and mortality and is a burden on the healthcare system in the U.S. Treatment of a fentanyl overdose begins with a clinical assessment of a patient's airway, breathing, and circulation. Opioid overdose education and distribution of intranasal naloxone to laypersons, law enforcement officers, firefighters, and emergency service personnel are intended to promote recognition of opioid overdose and quick intervention.

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Target Audience: This educational activity is for pharmacists.

How to Earn Credit: From July 20, 2022, through July 20, 2025, participants must:

- 1) Read the “learning objectives” and “author and planning team disclosures;”
- 2) Study the section entitled “educational activity;” and
- 3) Complete the Post-test and Evaluation form. The Post-test will be graded automatically. Following successful completion of the Post-test with a score of 70% or higher, a statement of participation will be made available immediately. (No partial credit will be given.)

Learning Objectives: Upon completion of this educational activity, participants should be able to:

1. **Identify** the role of fentanyl in the opioid crisis
2. **Describe** the basic pharmacological profile, use and clinical outcomes of fentanyl
3. **Compare** the benefits and risks of fentanyl use
4. **Identify** treatments for opioid overdose

Disclosures

The following individuals were involved in the development of this activity: Susan DePasquale, MSN, PMHNP-BC, Amanda Mayer, PharmD, and Jeff Goldberg, PharmD. There are no financial relationships relevant to this activity to report or disclose by any of the individuals involved in the development of this activity.

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Introduction

The use of fentanyl and fentanyl analogs has increased significantly in the past ten years due to the influx of illegal forms of fentanyl. The consumption of these drugs is a primary contributor to the current opioid crisis in the United States. Illegally manufactured fentanyl is widely available on the street, and it is a relatively common adulterant in heroin. Unfortunately, some of the beneficial pharmacologic properties of fentanyl, such as the rapid onset of action, and its high potency relative to other opioids, also make it very dangerous when it is used inappropriately. Because of the relatively common occurrence of fentanyl use and the potential consequences of fentanyl intoxication, health clinicians need in-depth information about fentanyl.

Fentanyl Medical Uses

Fentanyl is a synthetic opioid. It is used to treat post-operative pain and medical conditions that are accompanied by severe pain.¹ Fentanyl has also been misused and has become a major driver of the ongoing opioid crisis.¹ Fentanyl was introduced in 1960 to replace morphine and other opioids for use in cardiac surgery due to its higher potency and fewer adverse cardiovascular effects, and less histamine release. Fentanyl is a highly lipophilic drug that allows it to cross the blood-brain barrier and produce analgesia and sedation readily.² The FDA approved transdermal fentanyl in 1990 for the treatment of chronic pain, generally in an outpatient setting. The transdermal patch allows for discreet, convenient, noninvasive, and generally safe opioid analgesia.³

Fentanyl and the Opioid Crisis

According to the Centers for Disease Control and Prevention (CDC), from 1999 to 2018, more than 232,000 people died in the United States from overdoses involving prescription opioids.⁴ Overdose deaths involving opioids (including prescription opioids, heroin, and synthetic opioids like fentanyl) have increased by more than eight times since 1999.⁵ In 2020, overdoses involving opioids killed nearly 69,000 people, with over 82% of those deaths

involving synthetic opioids. At this time, drug overdose is the leading cause of accidental death in the U.S., and the opioid epidemic is only getting worse.¹

Fentanyl is currently the primary driver of the opioid crisis. It is involved in many deaths from illicit drug use.⁶ It has been reported that over 150 people die each day from overdoses related to synthetic opioids like fentanyl.⁷ Fentanyl has been estimated to be 50-100 times stronger than morphine² and is classified as a Schedule II drug under the Controlled Substances Act.⁸

Statistics updated in 2019 on fentanyl use in the U.S., include the following chronology:^{1,7,9}

- 2013-2014: The number of confiscated fentanyl-containing drugs increased 436%.
- 2014-2015: Death rates from synthetic opioids like fentanyl increased 72.2%.
- 2015-2016: Death rates from synthetic opioids doubled.
- 2017-2018: Synthetic opioid death rates increased again by 10% and accounted for 67% of opioid-involved deaths by 2018.
- 2018: Fentanyl availability was high and increasing across most of the US; even more available than it had been the year before.
- July 2022: More recent data has not been officially published by the CDC. It should be noted that it is nearly impossible to tell if drugs not acquired at a pharmacy contain deadly levels of fentanyl. Fentanyl test strips that can give results within 5 minutes are available; however, even in the case of a negative test, caution should be taken, and street drugs should be avoided as a test strip may not detect more potent fentanyl-like drugs such as carfentanil.

The illicit manufacturing of fentanyl is the source of most of the fentanyl that is used as an adulterant in heroin and has a direct correlation with the rapid increase in overdose deaths.⁶ It is the cause of the great increase in deaths from a synthetic opioid overdose. Fentanyl analogs like acetylfentanyl, carfentanil, and furanylfentanyl are increasingly responsible for deaths from synthetic opioids, and although fentanyl is a highly potent medication, it pales

in comparison to carfentanyl, a fentanyl analog that has been estimated to be 10,000 times stronger than morphine.⁶ Illegally manufactured fentanyl has been found in counterfeit medications that have been passed off as prescription benzodiazepines and prescription oxycodone/acetaminophen tablets, and it has been sold as methylenedioxymethamphetamine (MDMA), also named *ecstasy*.⁶

The opioid crisis is a complex public health problem. One of the driving forces to combat the dramatic increase in opioid use, and particularly the use of fentanyl, has been an intense focus on decreasing the availability of opioids. Clinicians, suppliers, and pharmaceutical companies have been pressured to limit the amounts of opioids that reach the public.⁶ Law enforcement has made strong efforts to stop illegal manufacturing, prevent opioids from crossing the borders, and seize drugs from sellers and buyers. Unfortunately, this response does not address the root causes of drug misuse or the need for education, awareness, and treatment. Also, it ignores the human and economic realities of drug use. Without treatment, many opioid users will continue to use the drugs, so the demand for opioids will always be there. Furthermore, as long as there is a demand and potential for profit, lawbreaking individuals will find a way to sell opioids.⁶

As previously mentioned, illicit manufacturing is the primary source of most of the fentanyl that is misused. It is often used as an adulterant in heroin and illicit fentanyl and is primarily responsible for the rapid increase in overdose deaths in the United States.^{6,10} Opioid users typically do not know they are taking fentanyl. They simply use the product (drug) that is available to them on the illegal market. Sellers have a strong financial reason to adulterate heroin with fentanyl: they can add fentanyl to heroin they have diluted, so their product stretches further. Historically distributors reduced the purity of their heroin product by mixing or “cutting” it with caffeine, procaine, and lidocaine. This gave the distributor more product to sell but it also decreased the drug’s effectiveness. Adding fentanyl provided a greater potency to the heroin while giving the distributor more product to sell, thereby increasing the distributor’s profit.⁶

The DEA has reported that heroin and fentanyl markets remain mixed and that law enforcement and public health officials in certain regions have reported that “fentanyl is supplanting a significant portion of the pre-established heroin market.”⁶

Due to the fact that fentanyl is more potent than heroin, traffickers are able to mix small quantities of fentanyl with other diluents and drugs to market as heroin.⁶ The DEA has stated that the “increased presence of fentanyl in white powder heroin markets continues to result in higher rates of fentanyl-involved overdose deaths, straining law enforcement and public health resources in areas already afflicted with high levels of heroin-involved overdoses.”⁶ In 2021, the Drug Abuse Warning Network (DAWN) reported approximately 122,884 Emergency Department visits in the U.S., due to fentanyl.¹¹

The American Medical Association (AMA) issued a report in 2020 on the increases in opioid and other drug-related overdoses identified during the COVID pandemic.¹² The position of the AMA is that the combined challenges of the COVID-19 global pandemic and the opioid epidemic in the U.S., suggest that a highly complicated and deadly drug overdose epidemic exists. Mention is made by the AMA that a great concern exists due to the “increasing number of reports from national, state and local media suggesting increases in opioid- and other drug-related mortality, particularly from illicitly manufactured fentanyl and fentanyl analogs.”¹² The AMA reported that greater than 40 states showed increases in opioid-related mortality, as well as ongoing concerns for those with a mental illness or substance use disorder.¹²

The AMA raised the critical need to “remove barriers to evidence-based treatment for those with a substance use disorder as well as for harm reduction services, including sterile needle and syringe services and naloxone.”¹² Reference was made to the Substance Abuse and Mental Health Services Administration (SAMHSA) and Drug Enforcement Administration (DEA) in the U.S., relative to their increased flexibility to provide buprenorphine and methadone to patients who are diagnosed with an opioid use disorder and for those who are in need of medication for pain control.¹²

The COVID-19 pandemic in the United States introduced new risks to Americans impacted by substance use disorder, as well as a series of new challenges related to treatment and recovery. Drug overdose deaths continue to impact communities across the United States.¹

Fentanyl Overdose

The medical literature has focused mostly on the epidemiologic aspects of fentanyl overdoses, not on clinical presentation and treatment. This is understandable as the signs, symptoms, and medical care of patients who have overdosed with fentanyl are often the same as for other opioid drug overdoses; however, fentanyl overdose may have distinctive symptoms. For example, respiratory depression may be more profound with fentanyl toxicity than with other opioids.¹³ Chest wall rigidity can be present, and this may lead to a rapid onset of overdose death. This requires a clinician to make an early diagnosis and treatment in order to save the patient's life.¹³

Detection of Fentanyl Toxicity

Fentanyl is extremely potent, which means that even a small amount of the drug - "the equivalent of several grains of salt" — can result in death.¹³ The standard for drug toxicology or screening involves a urine sample, and the results are received promptly.¹⁴ However, these screens only detect the presence of five drugs and/or their metabolites, amphetamine, cocaine, marijuana, opioids (morphine and its metabolites and structurally similar drugs), and phencyclidine (PCP).¹⁴ Urine and serum tests remain the most commonly used tests for other misused substances by medical professionals.¹⁴ Fentanyl lacks the structural similarity to produce a positive test result on the opioid/opiate component of a standard immunoassay-based "urine drug screen"; therefore, liquid chromatography-mass spectrometry is the standard for measuring serum fentanyl concentrations.^{14,15} Rapid result drug screens that can detect fentanyl are available, but they are not in common use, and laboratory confirmation of fentanyl in blood or other biologic specimens cannot be done within a timeframe that is useful for anyone caring for a patient who has overdosed on fentanyl.¹³⁻¹⁵

Patient's History of Use

Being aware of the drug type and amount that a patient took is one of the fundamentals of caring for an overdosed patient, but people typically do not know they have taken fentanyl. Fentanyl is surreptitiously used to adulterate heroin and has been used to make counterfeit prescription medications. The effects of fentanyl intoxication are identical to intoxication with any opioid, making it difficult to differentiate.¹²

The Pattern of Fentanyl Misuse

Fentanyl may be inadvertently injected if it has been used to adulterate heroin, but there are other ways to misuse fentanyl that are specific to the drug that clinicians should know about.¹⁶ Perhaps the most important of these is the misuse of fentanyl patches. Patients may apply multiple patches, and if an opioid overdose is suspected, a complete examination of the patient's skin should be done.¹⁷ Reported ways of misuse also include inhalation of pyrolyzed transdermal devices, insertion of device rectally, and drinking water in which the transdermal device was steeped like a tea bag.¹⁸⁻²⁰

The original transdermal therapeutic system (TTS), also called reservoir transdermal device, has four functional layers and a protective peel strip. The four layers are the backing, fentanyl reservoir, adhesive, rate-controlling release membrane, and adhesive with a protective peel strip. The reservoir, which is the second layer of this system, accounts for much of the potential for misuse.²¹ The fluid state of the drug reservoir layer allows for the fentanyl to be extracted, and even after the 72-hour use period, every transdermal device still contains a significant quantity of fentanyl. Misuse of the fentanyl-containing gel extracted from the reservoir device through IV administration contributes to many fatalities due to fentanyl overdose.²²⁻²⁸

There is also a fentanyl transdermal system commonly called the matrix patch, which is newer and contains two functional layers and a protective peel strip. The fentanyl transdermal system does not have a fluid fentanyl

reservoir; however, some opioid misusers cut the matrix into desired sizes and place the fragment in their mouth for transmucosal absorption.²

Variations in skin thickness and degree of keratinization can alter Fentanyl's systemic bioavailability and account for interindividual variability in transdermal fentanyl absorption.^{29,30} If applied to broken skin, blood fentanyl concentrations can rise 5-fold. An increase in skin temperature enhances the absorption of transdermal fentanyl, and a 3° Celsius body temperature increase can raise the peak fentanyl blood concentrations by 25%.² Case reports of sources raising ambient temperatures such as hot tubs or heating blankets may lead to a fentanyl overdose.² The potential for toxicity is also raised when an overlay to hold a non-sticking transdermal device is applied to the patch and may be associated with altered fentanyl absorption.²

Used fentanyl patches require proper disposal after use— the FDA recommends folding the patch, sticky sides together, and flushing it down the toilet right away.² It is important to note that fentanyl can be absorbed through the skin, and all persons involved in the administration and disposal of fentanyl patches must use caution when handling the patches as unintentional exposure must be avoided.^{2,29-31} Pharmacists and technicians should be aware of proper administration and disposal techniques.

Pediatric Exposure to Fentanyl

Outside of therapeutic use in a monitored setting, pediatric exposure to fentanyl is very dangerous. Fentanyl toxicity in children - which may be encountered in an emergency department - tends to involve serious neurological and cardiovascular symptoms.³²⁻³⁴ Any child who has or may have been exposed to fentanyl should be evaluated in an emergency room setting immediately.

Oral prescription opioids are the cause of high rates of emergency hospitalizations due to poisoning in children under 6 years of age (2007 to 2011).³⁴ Children are often exposed to accidental opioid ingestion and to malicious or careless exposure to illegal drugs, frequently with fatal outcomes.³²⁻³⁴

Toxicity Reversal with Naloxone

There has been concern that standard doses of naloxone (discussed below) are insufficient for the reversal of fentanyl intoxication, but there is limited clinical experience that confirms this. Expert reviews do not recommend using higher than normal doses of naloxone for the reversal of fentanyl intoxication.³⁵⁻³⁷

Treatment of Fentanyl Overdose

The typical signs and symptoms of a fentanyl overdose are central nervous system depression (ranging from drowsiness to coma), respiratory depression, hypoventilation, respiratory arrest, hypotension, and miosis. Fentanyl overdose may also present with a characteristic “chest wall rigidity.”^{13,38,39}

Treatment should begin with an assessment of a patient’s airway, breathing, and circulation.³⁴⁻³⁷ Hypotension can be treated with intravenous (IV) fluids and supportive care. Hypothermia caused by prolonged immobility and/or exposure to the cold should be treated with standard care.⁴⁰ Respiratory depression and hypoventilation should be treated with supplemental oxygen (and endotracheal intubation if indicated). Naloxone should always be given if there is any suspicion of an opioid overdose.⁴⁰

Naloxone is an opioid antagonist that blocks opioids from binding to mu-opioid receptors and can displace opioids from mu-opioid receptors. Healthcare professionals should discuss the availability of naloxone with all patients who are prescribed opioids. Clinicians are encouraged to consider prescribing naloxone to patients who are at increased risk of opioid overdose.⁴¹ Most states have passed laws that allow pharmacists to dispense naloxone under a standing order, which takes the place of a prescription written by a provider. Some states also allow pharmacists to prescribe and sell naloxone to patients. It is important to keep up to date on naloxone dispensing laws and regulations by pharmacists in your current state of practice.⁴¹

Naloxone can be given by several different routes of administration for opioid overdose. Intravenous naloxone is the preferred route of administration, but the administration should not be delayed if the patient does not have IV access. If IV access is not possible (such as with an opioid overdose in the community), intramuscular and intranasal routes are preferred.^{42,43} The initial IV dose for an adult is 0.4 – 2 mg, which can be repeated every two to three minutes as needed for several doses.^{42,43} If it is known or suspected that a patient is opioid-dependent, a lower initial dose may be used (0.1 – 0.2 mg) to avoid precipitating withdrawal. Lower doses may also be used to reverse respiratory depression caused by the therapeutic use of an opioid.^{42,43}

After administering a dose, the clinician should observe the patient carefully for signs of reversal, such as an increased level of consciousness, increased respiratory rate, or improved ventilation. If a total of 10 mg is used and there is no significant clinical response, it is unlikely the patient is experiencing an opioid overdose.⁴² If a continuous infusion is needed, two-thirds of the effective dose should be administered every hour. For example, if 6 mg is the effective dose, the continuous infusion rate would be 4 mg/hour.^{42,43}

The intranasal dose of naloxone is generally one spray (4 mg) in one nostril. The dose can be repeated every 2 to 3 minutes, alternating nostrils. The injectable solution given intranasally using an atomization device may also be used. When using this method, the dose is 2 mg (1 mg per nostril) and repeated every three to five minutes.^{42,43}

On April 30, 2021, the U.S. Food and Drug Administration announced its approval of a product that provides a higher dose of naloxone hydrochloride in the form of a nasal spray for the treatment of an opioid overdose.⁴⁴ This product is marketed under the trade name KLOXXADO™.⁴⁴ This new product delivers 8 mg of naloxone intranasally.⁴⁴ The manufacturer provides dosing and delivery instructions for adult and pediatric patients.⁴⁵ One 8 mg dose of naloxone is sprayed into one nostril. If the desired response is not reached after 2 or 3 minutes, another dose may be administered in the other nostril,

alternating nostrils every 2 to 3 minutes until emergency medical help arrives.⁴⁵ The drug comes with two warnings of potentially serious adverse reactions: recurrent respiratory and CNS depression; and severe opioid withdrawal.⁴⁵ For infants and children ≤ 20 kg, the dose is 0.1 mg/kg to a maximum of 2 mg. For reversal of respiratory depression caused by therapeutic use of an opioid, the pediatric dose is 0.001 to 0.005 mg/kg, repeated every two to three minutes as needed.⁴⁶

Naloxone is primarily used to reverse the respiratory effects of opioid overdose. The goal of naloxone use in an opioid overdose is to restore adequate ventilation, not to bring the patient to a fully conscious state. Death from an opioid overdose is regarded as a result of the cardiopulmonary effects of opioids, not necessarily from the central nervous system (CNS) depression.⁴⁷ As mentioned above, fentanyl overdose may be characterized by chest wall rigidity.³⁸ In addition, "fentanyl metabolites are almost nonexistent in tissue from patients who died of a fentanyl overdose, suggesting rapid cardiopulmonary collapse."³⁸

There are no listed contraindications for naloxone, and the only significant adverse effect of naloxone is the precipitation of withdrawal in patients who are opioid users. Acute lung injury and ventricular fibrillation have been reported after administration of naloxone, but these reports are rare and the association between the drug and these complications is tenuous and has been questioned.⁴⁷

Physical Examination

A complete physical examination should be performed, checking for fentanyl patches and signs and symptoms of compartment syndrome.⁴⁸ A patient who has taken an overdose of fentanyl should be observed for several hours after the last dose of naloxone has been given.⁴⁸ If at that time, the patient is awake, alert, oriented, and has normal vital signs, discharge may be considered, provided the patient is going to a safe environment, and some arrangements have been made for follow-up care. If there is any suspicion

that the patient may have taken an overdose of methadone, an electrocardiogram should be done to look for QTc prolongation.⁴⁹

Education of Opioid Overdose Treatment

In response to the opioid crisis, a majority of U.S., states have implemented programs that provide opioid overdose education and distribution of intranasal naloxone to laypersons, law enforcement officers, firefighters, and emergency services personnel.^{41,50} These programs, which are intended to promote recognition of opioid overdose and quick antidotal therapy, have been proven to be effective, reversing opioid toxicity and reducing mortality rates from opioid overdose. Naloxone is recognized as a well-established medication that can reverse an opioid overdose and prevent death. Distribution of naloxone and training of varied segments of the public will benefit opioid users who are not in treatment and those using opioids for non-acute pain management.^{41,50}

Case Study: Fentanyl Transdermal for Chronic Pain

The following case study was located through a PubMed search in which the authors reported on a 70-year-old woman diagnosed with fentanyl patch toxicity.⁵¹ The authors reported that the patient had been started on a transdermal fentanyl patch for chronic back pain for approximately 10 years. Gradually, the patient accumulated 100 mcg fentanyl patches from prescription refills and then applied 14 patches combined with oral mirtazapine, tramadol, and morphine sulfate oral solution with an intention to suicide. The patient did not die; instead, she awakened to the telephone ringing after 24 hours of deep sleep. She expressed being in disbelief that her effort to die had failed.⁵¹

Psychiatry was consulted and the pain management team who had managed the patient's prior pain treatment took charge of her case. The patient had a history of chronic non-malignant back pain from severe lumbar scoliosis and osteoarthritis, for which she had received numerous treatments, including spinal decompression surgery and joint injections. She had also been

diagnosed with breast cancer and underwent chemotherapy and surgery. Chemotherapy was stopped due to side effects prior to the planned course of administration.⁵¹

Psychiatrically, she was diagnosed with generalized anxiety disorder, but not treated with standard treatment of serotonin reuptake inhibitors. Two months prior to her suicide attempt, the patient was started on mirtazapine 15 mg daily. Static risk factors for suicidality included comorbid chronic pain and a diagnosis of cancer.⁵¹

The authors reported that opioid analgesics were prescribed; transdermal buprenorphine was increased from 5 to 20 mcg and then changed to fentanyl patches. The fentanyl dosing was rapidly increased from 25 to 100 mcg over a period of 7 weeks. The patient developed side effects of drowsiness and nausea, and the patient was switched to modified-release oxycodone 10 mg twice a day. She missed scheduled appointments with an orthopedic surgeon and physiotherapist and eventually was restarted on fentanyl 100 mcg patches.⁵¹

The patient was also prescribed morphine sulfate solution and had two more prescriptions over several months following breast cancer treatment and surgery. Chronic back pain continued, and an extra fentanyl 50 mcg was prescribed in addition to the fentanyl 100 mcg patch.⁵¹

It was discovered that the patient's opioid prescription was running out every 3 days. Morphine sulfate was limited to 20 ml per day by pain clinic clinicians with consideration given to the fentanyl 100 mcg patch prescribed. When the patient intentionally overdosed with 14-100 mcg transdermal fentanyl patches, laboratory testing was performed in the emergency department with normal findings in the urea and electrolytes, liver function tests, and clotting results.⁵¹

The patient was discharged after being evaluated as low risk and referred to outpatient services for follow-up by a multidisciplinary health team of pain specialists and psychology services. Low-dose fentanyl patches were

continued along with duloxetine for mood instability with improved outcomes in the patient's mood symptoms and quality of life.⁵¹

Discussion

The authors reported that the patient had no evidence of insensitivity to opioids; however, she had an extensive pain history, which possibly explained her survival.⁵¹ No prior cases were found of people who survived deliberate self-poisoning with such a high dose of transdermal fentanyl. However, a literature search highlighted three other case reports of suicide by fentanyl patches in adults: "in a woman aged 42 years with eleven 100 mcg patches, an assisted suicide of a woman aged 46 years with 34 mixed dose patches, and suicide of a woman aged 78 years with ten 100 mcg patches. These cases are a testament to the lethality of the fentanyl dose presented here and how remarkable it was that the patient was able to survive."⁵¹

Summary

Fentanyl is a synthetic opioid that has long been used as an analgesic, most often to treat breakthrough cancer pain, chronic pain, and as an adjunct to anesthesia. It is available in multiple forms and is a potent opioid with potentially severe adverse effects. Even therapeutic use can cause serious central nervous system and respiratory system depression. Fentanyl should be used cautiously, especially in patients with known cardiovascular or respiratory diseases and in patients taking other CNS depressants (for example, benzodiazepines). Before prescribing or administering fentanyl, clinicians should carefully review a patient's medical history and drug profile.

The high potency and rapid onset of the effects of fentanyl make it an attractive drug to people who misuse opioids. Fentanyl is a major contributor to the opioid epidemic. The use of fentanyl and fentanyl analogs has increased dramatically in the U.S., and fentanyl has become one of the major causes of a fatal drug overdose. Efforts to control the supply of opioids and fentanyl have, in part, helped to make the drug even more sought after, because illegally manufactured fentanyl is much cheaper to produce than heroin.

Education, treatment, and the availability of naloxone to the lay public, law enforcement offices, and emergency personnel have been proven to be effective at reducing deaths from opioid overdoses. Despite these efforts, the use of fentanyl has been steadily increasing and may potentially worsen.

Interdisciplinary healthcare teams that include medical and psychiatric professionals are able to develop a comprehensive treatment plan for patients who misuse fentanyl. Case studies have shown that even in patients with a severe opioid use disorder, patients are able to recover and progress to an improved quality of life through proper treatment, careful monitoring, and follow-up.

Course Test

1. _____ is a fentanyl analog that has been estimated to be 10,000 times stronger than morphine.
 - a. Acetylfentanyl
 - b. Furanylfentanyl
 - c. Carfentanil
 - d. Oxycodone

2. Fentanyl crosses the blood-brain barrier and produces
 - a. hypertension.
 - b. psychosis.
 - c. analgesia.
 - d. anesthesia.

3. Illicitly manufactured fentanyl is the source of most of the fentanyl that is used as an adulterant in
 - a. heroin.
 - b. opioids.
 - c. ecstasy.
 - d. benzodiazepines.

4. The dosing and administration instructions for the 8 mg intranasal naloxone product KLOXXADO™ provides for
 - a. two 4 mg doses delivered simultaneously to each nostril.
 - b. a maximum dose of 4 mg for pediatric patients.
 - c. one 8 mg dose only until emergency help arrives.
 - d. one 8 mg dose in one nostril, then every 2 or 3 minutes thereafter as needed in alternating nostrils.

5. True or False: Fentanyl is extremely potent, which means that even a small amount of the drug can result in death.
 - a. True
 - b. False

6. A patient may misuse fentanyl patches by

- a. inserting rectally.
- b. inhalation of pyrolyzed transdermal devices.
- c. steeping in water like a tea bag.
- d. All of the above

7. Pediatric exposure to fentanyl is dangerous because

- a. fentanyl is a Schedule I drug.
- b. children tend to experience serious neurological and cardiovascular symptoms.
- c. because the reversal agent naloxone is contraindicated in children.
- d. All of the above

8. The typical signs and symptoms of a fentanyl overdose include

- a. respiratory depression.
- b. dilated pupils.
- c. hyperventilation.
- d. psychosis

9. The preferred route for the administration of naloxone to treat an opioid overdose is

- a. intramuscularly (IM).
- b. intravenously (IV).
- c. intranasally.
- d. by a nebulizer.

10. Naloxone is primarily used to reverse the _____ effects of opioid overdose.

- a. hypertensive
- b. hallucinogenic
- c. severe mood
- d. respiratory

- 11. Fentanyl is a synthetic opioid that is used to treat**
- a. severe mood disorders.
 - b. bradycardia.
 - c. post-operative pain.
 - d. pulmonary depression.
- 12. If a patient is not responding to normal doses of naloxone after a suspected opioid overdose,**
- a. the dose must be increased.
 - b. it is unlikely the patient has taken an opioid.
 - c. then naloxone is contraindicated for that patient.
 - d. buprenorphine should be coadministered immediately.
- 13. _____ can lead to a rapid onset of overdose death, requiring a clinician to make an early diagnosis and treatment in order to save the patient's life.**
- a. Chest wall rigidity
 - b. Hypertension
 - c. Tachycardia
 - d. Hyperventilation
- 14. Ironically, one of the driving forces of the dramatic increase in opioid use has been the**
- a. decline in alcohol misuse.
 - b. lack of medicinal opioids available on the market.
 - c. state prescription reporting systems.
 - d. effort to decrease the availability of opioids.
- 15. True or False: Once a patient receives an intranasal dose of naloxone, it should not be repeated.**
- a. True
 - b. False

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