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Clinical Update

The Risk of Opioid Toxicity and Naloxone Use in Operational K9s

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ABSTRACT

The increasing use of opioids (e.g., fentanyl, carfentanil) for illicit drug manufacturing poses a potential life-threatening hazard to law enforcement officers and first responders (e.g., EMS, fire and rescue) who may unknowingly come into contact with these drugs during the course of their daily activities. Similarly, Operational canines (OpK9s) of all disciplines—detection (drug, explosive, accelerant), patrol, tracking, search and rescue, and others—are at risk for accidental illicit opioid exposure. The most serious adverse effect of opioid exposure is respiratory depression leading to slow, shallow breathing or complete cessation of voluntary breathing (respiratory arrest). Naloxone, an opioid antagonist, is the antidote for reversing the effects of an opioid overdose in both humans and OpK9s. This clinical update describes the potential risks associated with opioid exposure as well as the use of naloxone as it pertains to the OpK9.

KEYWORDS: *Operational K9; opioid; naloxone; intranasal; overdose; canine medicine*

Introduction

Opioid drugs may be considered a double-edged sword in the medical community; they provide both a tremendous benefit and a large risk to public health. Derived from the compound opium, opioid analgesics serve a staple in the medical and veterinary communities for managing acute and chronic pain as well as perioperative anesthesia.¹⁻³ Interestingly, evidence supporting their absolute benefit for chronic pain management has come into question.⁴ When taken or administered as prescribed by a medical professional, opioids are considered a relatively safe and warranted medical intervention. However, since their discovery, opioids have been misused as well as abused illicitly for recreational drug use.^{1,2,5} Illicitly, opioids are used for their psychoactive effects, causing intense euphoria and relief of tension and anxiety. Tolerance, physical dependence, and addiction are adverse events that may occur in people taking opioids, which often leads to drug abuse.^{1,6}

Today, opioid drug abuse represents one of the largest components of the illicit drug market worldwide.¹

In humans, the increasing misuse of and addiction to both prescription and nonprescription opioid drugs reached epidemic levels in America.^{7,8} As reported by the Centers for Disease Control and Prevention (CDC), the number of overdose deaths involving opioids (both prescription drugs and heroin) quadrupled since 1999, with more than 90 people dying daily.⁷⁻¹⁰ This opioid epidemic or crisis, as it is now termed,^{8,11} not only affects the health of the nation but also incurs a social and economic burden on society.^{7,12,13} The estimated “economic burden” of prescription opioid misuse in the United States is \$78.5 billion per year; this includes costs associated with healthcare, lost productivity, addiction treatment, and criminal justice involvement.¹²

Although heroin is the prototypical manufactured illicit opioid with which most of society is familiar, all types of prescription and nonprescription opioids (natural, semi-synthetic, and synthetic) are being manufactured and sold for illicit, recreational use.^{10,11,14} The diversion of pharmaceutical fentanyl and the clandestine manufacturing of illicit fentanyl and fentanyl-related substances (e.g., carfentanil, 4-fluorobutyrylfentanyl, furanylfentanyl, acrylfentanyl, 3-methylfentanyl, etc.) have dramatically increased during the past few years.^{10,14} These compounds are used in place of or to adulterate (“cut or mix with”) other illicit substances (e.g., heroin, methamphetamines, cocaine, etc.) as well as to produce counterfeit prescription tablets of other semisynthetic opioids (oxycodone, hydrocodone, and others).^{11,14} Carfentanil, one of the most potent commercially available synthetic opioids legally prescribed for sedating large zoo animals (e.g., elephants), has also entered the illicit drug market and poses a great danger to society.^{14,15} A myriad of novel synthetic opioids also continue to enter the illicit drug trade (e.g., W-series opioids, MT-45, AH-7921, U-47700), many of which have been associated with opioid-induced deaths in people.¹⁶⁻²¹

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The clandestine manufacturing and illicit trade and use of unregulated novel synthetic opioids represent a significant challenge to public health.²² Many of these novel synthetic opioids never reached the human market and, therefore, most of these drugs do not have any pharmacokinetic or pharmacodynamic data for use in humans.^{11,14,22} As such, the potency and potential adverse effects of these agents remain unknown.^{14,22} Analytical methods for detecting and monitoring these novel drugs also remain lacking.^{14,22} Standard immunoassay urine toxicology screening in the clinical setting does not detect synthetic opioids. US Food and Drug Administration (FDA)-approved opiate immunoassays do not cross-react with the synthetic opioids, and few clinical laboratories offer fentanyl testing in real time.¹⁴ Most often, the only way the use of one of these novel drugs is detected is from an experienced recreational drug user reporting that his or her present drug exposure was significantly different from previous accounts using the same “drug” and same amount.^{11,22} All of these facts together present a challenge to emergency medical services (EMS) providers as well as emergency physicians in regard to early detection of and provision of timely treatment for potential lethal opioid exposures.

History of Opioids and Terminology

Opium is the archetypal compound from which all medicinal and illicit opioid drugs are either derived from or synthesized to mimic.^{1,23} It is obtained by collecting and drying the milky juice or latex sap (aka poppy tears, *Lachryma papaveris*) that comes from the seed pods of the poppy plant *Papaver somniferum*.^{23,24} For centuries, opium has been used for its euphoric, analgesic, and antianxiety effects.^{1,5,24} The pharmacologically active principles of opium lie within the several naturally occurring alkaloids found within the opium latex.^{1,24} The major psychoactive alkaloids include morphine (approximately one-tenth the volume of the opium latex), codeine, and thebaine.^{23,24} The term *opiate* refers to all naturally occurring alkaloids obtained from the opium sap.²⁵

First used in the 1950s, the term *opioid*, originated from combining the words “opium” + “-oid” (Greek derivations: “opium” = *opioin* [poppy juice] + “-oid” = *eidōs* [form]).²⁶ Originally, *opioid* referred only to the semisynthetic and synthetic drugs manufactured to provide opium-like effects.^{25,27} As a modern-day term, *opioid* defines a class of drugs that are either directly derived from (e.g., opium alkaloids) or synthetically manufactured to act like opium by binding to opioid receptors in the body.^{25–27} In a broader sense, *opioid* applies to “any substance, endogenous or synthetic, peptidic or nonpeptidic, that produces morphine-like effects through action on opioid receptors.”^{9,25}

From the opium alkaloids, various semisynthetic and synthetic drugs with similar psychoactive properties have been manufactured or synthesized for medicinal and/or illicit recreational use.^{9,14,16,23} Semisynthetic and synthetic opioid drugs are compounds not found in nature. Semisynthetic drugs, such as hydromorphone, oxycodone, hydrocodone, and oxycodone, are produced by combining an opium alkaloid with a synthetic compound. Synthetic opioid drugs (e.g., fentanyl, fentanyl analogues, oxycodone, the U-series opioids, methadone, and others) possess opium-like effects but do not contain any opium; they are synthesized in a laboratory setting purely from chemicals.^{14,23} As mentioned, novel synthetic opioids

(e.g., W-series, U-series) represent the greatest threat to the rising opioid crisis.^{16–21}

Opioid Receptors and Comparative Potency

Three main opioid receptors exist in the body: mu (μ), kappa (κ), and delta (δ).²³ The psychoactive effects of opioids result from binding and activation of endogenous μ opioid receptors (MOPs) located primarily throughout the brain.^{1,23} Opioids that primarily bind to, activate, and cause a maximal functional response at the MOP are referred to as μ -agonists (e.g., morphine, fentanyl, carfentanil).^{1,14,23} As a whole, novel synthetic opioids are highly selective for the MOP receptor.¹⁴ MOP receptor activation leads to analgesia but also sedation, euphoria, respiratory depression, bradycardia, nausea, vomiting, and decreased gastrointestinal motility.²³

Potency is the amount (concentration or dose [mg/kg, μ g/kg]) of drug required to produce an effect of given intensity.²⁸ In comparison to the natural opiate morphine, the following are reported comparative potencies¹⁴:

- Heroin is 2 to 4 times as potent as morphine.¹⁴
- Fentanyl is about 50 to 100 times more potent than morphine and 30 to 50 times more potent than heroin.²⁸
- Carfentanil is 10,000 times more potent than morphine and about 100 times more potent than fentanyl.¹⁴

The potency and clinical effects of illicitly manufactured opioids encountered in the field may vary greatly depending on the purity of the manufactured opioid-related substances. Because many novel synthetic opioids have not been evaluated in people or canines, estimates of relative potency of these drugs are not completely known.

Clinical Signs of Opioid Toxicity in OpK9s

Opioid toxicity may include dose-related respiratory, central nervous system, and cardiovascular depression. The greatest adverse risk is severe respiratory depression leading to respiratory arrest, coma, and death. Canines tend to have a higher tolerance (less susceptible) for opioid-induced respiratory depression than do humans.^{28–30} Opioid-induced dysphoria (restlessness, howling, whining, panting) is a commonly reported side effect in canines and may serve as the first clinical indication of exposure.³¹ Opioid toxicity in canines is primarily manifested clinically by^{28–30}:

- Low heart rate (bradycardia)
- Low blood pressure (hypotension)
- Pinpoint pupils (miosis)
- Hypothermia
- Progressive respiratory depression (slow to absent breathing) and hypoventilation
- Altered mental status (continuum of mild sedation to comatose)

Routes and Formulations of Exposure

OpK9s are at particular risk for encountering illicit opioids during routine activities such as drug raids and search warrants. Drugs may be found lying out in the open (on a table or counter) or concealed in innocuous devices such as eye droppers and hair spray containers. Possible routes of **accidental**

exposure for OpK9s include *inhalation* (through the respiratory tract), *transdermal* (through the skin), *oral* (ingestion), and *oral transmucosal* (across the buccal membrane). Inhalation or respiratory exposure is the most likely exposure route, with transdermal exposure being the second most likely route.^{32–34}

Illicit opioids are found as powders, blotter paper, liquids, nasal sprays, and pills.^{10,33,34} During a raid or drug search, an OpK9 may accidentally bite and/or ingest whole bags of drugs that may rupture and induce a massive exposure³⁵; they may lap up opioid solutions resulting in oral and oral transmucosal (buccal) exposures; or they may inhale small amounts of powdered drug. A dry powder is the most likely and probably most hazardous form a first responder, and similarly an OpK9, may encounter in the field.^{33,34} Synthetic opioid powders have a particulate size ranging from 0.2 to 2.0 mm³⁴ and are easily aerosolized when disturbed (e.g., “burping” sealed containers, deploying flash bangs); therefore, powders present a high inhalation risk. When an OpK9 contaminated with an opioid powder “shakes” or brushes up against something, the powder residues are readily dispersed into the air. This presents a significant inhalational exposure hazard to the canine as well as any nearby personnel.

Factors Affecting Drug Absorption and Relative Exposure Risk

The specific drug involved (heroin versus fentanyl versus carfentanil), the drug formulation (e.g., powder, liquid, aerosol), amount, concentration, and route of drug exposure encountered determine the exposure risk.²⁸ Absorption across the nasal mucosa via inhalation is rapid and may result in high drug bioavailability depending on the drug formulation (e.g., powder versus spray mist).^{36–38}

Transdermal absorption requires direct skin contact of a large or highly concentrated and localized amount of drug for a long duration. Absorption of opioid powders transdermally tends not to present a significant exposure risk for OpK9s with intact, unbroken skin. In general, powders settle atop the OpK9’s hair coat, where a large proportion never actually comes into direct contact with the skin. Subsequently, the powder is either dispersed into the air when the OpK9 shakes or when the OpK9 brushes up against surrounding objects. In addition, canines do not possess functional eccrine sweat glands dispersed throughout their body like people³⁹; therefore, this potential pathway for transdermal drug absorption is not a significant risk in canines.

Absorption of a powder through the paw pads is also an unlikely route of significant exposure in canines. Paw pads are the thickest region of canine skin and are heavily keratinized, providing an effective barrier.³⁹ Although canines do possess eccrine sweat glands deep within the fat and fibrous tissues of their digital pads, these tightly coiled, tubular glands are only approximately 25 to 35 µm in diameter.³⁹ The small pore size of these eccrine glands, along with the minutely small proportion of the canines total body surface area, limits the exposure risk for transdermal drug absorption through the pads to that of a dry drug powder.

Most opioids have a very poor oral bioavailability (e.g., 15–17% for morphine, 33–50% for fentanyl) due to a process

called first-pass metabolism.^{40–42} As such, ingestion of a small amount of opioid tends to present a very low exposure risk for OpK9s. Oral transmucosal (OTM) or transbuccal absorption is possible in canines⁴³ but is affected by factors such as the pH and formulation of the drug as well as the dwell or contact time within the buccal pouch.⁴³ In canines, fentanyl has OTM bioavailabilities ranging from 20% to 50% depending on the pH of the solution.⁴³ Although several OTM fentanyl formulations are approved for use in humans, these products are not currently used extra-label in canines.²⁸

Opioid Exposure Risk in OpK9s

Due to the wide array of pharmaceutical and illicitly manufactured opioids available on the market, a large variation in the levels of toxicity for each drug exists for animals. The minimum lethal dose reported for morphine is 110mg/kg intravenous (IV) and 210mg/kg subcutaneous (SC).²⁹ For heroin, the minimum lethal dose is 25mg/kg SC.²⁹ At approximately 0.2mg/kg IV, heroin causes sedation and respiratory depression, whereas 0.58mg/kg IV led to increased duration of effects, respiratory difficulty, and aggressive behavior with clinical signs lasting up to 8 hours.⁴⁴

In conscious dogs, safety studies demonstrate that fentanyl has a wide margin of safety.^{28,30} Available scientific evidence and professional clinical experience support the fact that canines tend to have a higher tolerance (less susceptibility) for opioid-induced respiratory depression than do people.³⁰ IV doses up to 3mg/kg (approximately 600 times the recommended dose 0.005mg/kg) invoked minimal effects on the cardiovascular and respiratory systems.²⁸ A single dose of a transdermal fentanyl solution, administered at 3 to 5 times the recommended dose in canines, did not result in any fatality and caused minimal changes in respiratory rates, oxygen consumption, and blood gas analysis.³⁰ All dogs fully recovered from the transient narcotizing effects with only minimal supportive care and without naloxone reversal. In whole, the data collected from these studies indicate that respiratory depression (hypoventilation) is a safety aspect of limited concern following fentanyl administration to dogs.^{28,30} No data are currently available evaluating pharmacokinetics or the toxic or lethal dose of carfentanil or the other aforementioned novel synthetic opioids in canines (or humans).

To date, there are a few anecdotal reports of OpK9s becoming clinically effected by a “suspect” opioid exposure during law enforcement activities⁴⁵; the actual illicit agent (if any) involved were not absolutely confirmed. A review of 652 canine single-agent home exposures to fentanyl (ingestion of transdermal patches and lozenges) reported to the ASPCA Animal Poison Control Center (APCC) during 2009–2013 (personal communication with Dr Tina Wismer, APCC, 13 August 2017) revealed:

- Approximately 84% (548/652) displayed signs of exposure.
- Most common clinical signs included lethargy/sedation (60%), hypersalivation (drooling) (37%), hypothermia (24%), ataxia (24%), and bradycardia (20%).

The APCC also reports an increase in heroin exposures in canines with four exposures reported in 2012 and 22 exposures reported in 2016 (personal communication with Dr Tina Wismer, APCC, 13 August 2017). Reported clinical manifestations

of canines exposed to heroin were similar to fentanyl. Considering many field exposures in OpK9s undoubtedly go unreported to the animal poison helplines, the true epidemiology of out-of-hospital illicit opioid exposures in OpK9s remains uncertain.

A challenge facing handlers, first responders, and veterinary personnel is knowing exactly what drug(s), if any, the OpK9 may have been exposed to. Because opioids are mixed with other nonopioid illicit agents (e.g., cocaine, methamphetamines, and others),¹⁴ an OpK9 may develop clinical manifestations related to the other compounds in the mixture. These clinical signs may be atypical and opposing that of an opioid overdose (e.g., methamphetamine produces fast heart rates [tachycardia], high blood pressure [hypertension] agitation/aggression, increased body temperature [hyperthermia], and convulsions).⁴⁶ This uncertainty may detrimentally delay appropriate and timely treatment and personal protective actions.

Role of Naloxone in the Treatment of Opioid Toxicity

Naloxone is a standard drug carried by EMS providers and hospital emergency departments (human and veterinary) for treating accidental or intentional opioid overdoses. It is one component of a larger stabilization protocol for managing opioid toxicity (Table 1). Naloxone is a reversible competitive antagonist of μ , δ , and κ OP receptors. It has greater activity at the MOP than the δ and κ OPs.³² As a competitive antagonist, sufficient concentrations of naloxone are required to displace the already bound MOP agonists (e.g., morphine, fentanyl, carfentanil, and others) as well as prevent further agonist binding to the MOP.

The two definitive clinical indications for naloxone administration in people and OpK9s include^{14,32,46}:

- Altered mental status (markedly sedated to unresponsive)
- Very slow, absent, or gasping breathing (i.e., fewer than six to eight breathes per minute with shallow chest excursions)

Opioid exposure alone does not always warrant naloxone administration. In canines, opioid overdose is most often manifested only by excessive sedation, bradycardia, and hypothermia.³⁰ Although these cases do not always require naloxone, it may prove more prudent to administer naloxone as soon as signs of toxicity appear, particularly since naloxone has few to little adverse effects when administered in canines.³²

Recommended Naloxone Doses and Administration

The initial recommended IV, IM, and SC adult human dose in a known or suspected opioid overdose is 0.4 to 2mg; this may be repeated to a total dose of 10mg.⁴⁸ Intranasal (IN) dosing for humans is dependent on the product used (refer to link for “Naloxone Product Chart” listed under *Recommended Internet Resources*). Based on current available data, the following are recommendations for initial naloxone dosing in OpK9s:

- IV/IO: 0.01 to 0.04mg/kg (1–2mg per 25 kg)^{30,49}
- IM: 0.04 to 0.16mg/kg (2–4mg per 25 kg)³⁰
- IN: 2 to 4mg per 25 kg OpK9
- OTM (buccal pouch): Use IN dosing recommendations. Consider as a last resort if no other route is available (e.g., cannot establish IV/IO access and IM or IN [blocked nasal cavity, excess nasal discharge, etc.] administration unavailable).

Table 1 *Recommended Actions When Treating an Exposed OpK9*

<ul style="list-style-type: none"> • Activate EMS response system, perform a scene survey, and ensure scene safety: <ul style="list-style-type: none"> ◦ Avoid self-exposure to opioids and cross-contamination while handling the OpK9. ◦ Take appropriate personal protection actions and don PPE (nitrile gloves, N-95, dust mask, eye protection, paper coveralls, and shoe covers). • Support ABCs (establish patent airway, support ventilation, move into fresh air, provide oxygen supplementation as needed, initiate CPR if in cardiac arrest): <ul style="list-style-type: none"> ◦ If rescue breathing is warranted, AVOID mouth-to-snout. Instead, use a bag-valve-mask with a canine-specific face mask. ◦ OpK9s with no pulse may be in cardiac arrest or may have an undetected weak or slow pulse. Manage as cardiac arrest patients. See <i>Recommended Internet Resources</i> for veterinary CPR guidelines. • When feasible, thoroughly wash powder or agent off the OpK9’s hair coat and skin and out of his or her eyes and mouth: <ul style="list-style-type: none"> ◦ Avoid interventions that may enhance transdermal absorption (e.g., alcohol-based hand sanitizers, alcohol, and warm-to-hot water). ◦ After washing drug/agent off OpK9, take actions to dry and keep the OpK9 warm (e.g., cover with blanket, sheet, etc.). ◦ If washing the K9 is not feasible, consider wrapping the OpK9 in a sheet, blanket, or other similar material to mitigate dispersion of powder off the OpK9’s hair coat. • Administer naloxone (see dose recommendations listed earlier) when exposure is known or highly suspect and the OpK9 is displaying clinical signs such as: <ul style="list-style-type: none"> ◦ Unresponsive or altered mental status ◦ Slow or absent breathing or gasping breaths ◦ Slow (<50 bpm) heart/pulse rate and weak femoral pulse quality ◦ Weakness or staggering ◦ Pinpoint pupils ◦ Dysphoria (vocalizing, agitation, appearing frantic) may be an early indicator of exposure <p>NOTE: When in doubt, administer naloxone.</p> • Repeat naloxone as needed. Perform serial reassessments. • Seek immediate veterinary medical attention even if OpK9 positively responds to naloxone administration. Never leave an exposed OpK9 unattended as OpK9s have a high likelihood of experiencing renarcotization. <p>WARNING: After administering naloxone, expect the OpK9 to rapidly awake from their state of drug-induced stupor in which they may still be disoriented and be in a ‘protective/defensive’ mode.</p> <ul style="list-style-type: none"> • OpK9s may want to bite/attack anything in the immediate vicinity, to include the handler. • OpK9s should be properly restrained and/or have an open basket muzzle secured in place before or immediately after administering naloxone.

- Repeat doses: Administer additional doses of naloxone as needed based on clinical signs.

SPECIAL NOTE: Two or more doses of naloxone are likely required en route to the veterinary facility. Naloxone’s duration of action is often shorter than that of the illicit opioid encountered.^{30,32,47} Recurrence of clinical sign (renarcotization) is a high possibility, particularly when an OpK9 is exposed to a long-acting opioid or to a large amount of a short-acting opioid. Renarcotization is common with carfentanil exposures where it is reported that human carfentanil exposures require higher and more frequent naloxone dosing than that typically used for a routine fentanyl or heroin intoxication.^{15,50}

Safety Concerns With Naloxone Administration

Naloxone has a very wide margin of safety in canines.^{30,47} In canines that have not been exposed to an opioid, naloxone exerts no pharmacologic agonistic effect.^{48,51} As such, even with using the high-end recommended dose, naloxone is unlikely to result in any significant adverse effects. Although naloxone

will not reverse the effects of nonopioid drugs, it also causes no adverse effects when administered with other nonopioid drug exposures. For scent detection canines, it is currently unknown what short- or long-term effect, if any, IN naloxone has on canine olfaction. Considering its wide margin of safety and relative lack of adverse effects in the face of other illicit drugs, when in doubt, it is best to administer naloxone.

Recommended Route for Naloxone Administration in an OpK9

Naloxone is available as injectable, IN, and autoinjector products (see link for “Naloxone Product Chart” under *Recommended Internet Resources*). In people, naloxone is approved for IV, IM, and SC administration, with IV being the recommended route.⁴⁸ In canines, naloxone is recommended for IV, intraosseous (IO), IM, or SC administration.⁴⁹ Naloxone is only minimally absorbed when given orally due to first pass metabolism; therefore, per os (PO) remains an ineffective route of administration.^{32,49} In people, per rectum (PR) bioavailability is 15%, whereas OTM administration has shown to have a high bioavailability ($\geq 70\%$) in people and rats⁵²; no data evaluating PR or OTM naloxone in canines are currently available. IV and IO routes provide the fastest onset of action (1–2 minutes) with the greatest bioavailability (100%)⁴⁹; IM has an onset of action of approximately 5 to 10 minutes. Following a single dose (5-fold overdose) of transdermal fentanyl, IM naloxone at 0.04mg/kg and 0.16mg/kg were both effective at reversing clinical manifestations caused by the opioid-induced overdose with the 0.16mg/kg dose being most effective.³⁰ Subcutaneous administration is expected to have a slower onset of action as compared with IM.⁴⁹

IN naloxone has been successfully used to reverse opioid overdose in people with a very fast absorption rate.^{53–55} Because IN preparations eliminate the risk of contaminated needle stick and sharps hazard in people, many law enforcement officers and other first responders are now being equipped with IN naloxone products. Interestingly, biopharmaceutics and clinical pharmacokinetics relating to IN naloxone in people are sparse, controversial, and not completely known. One study reported a $\leq 4\%$ bioavailability for IN naloxone.⁵⁶ This study may be misleading as it used a potentially inferior delivery system and nonoptimal solution concentration.⁴⁸

Due to its demonstrated clinical effectiveness for treating opioid overdoses,^{53–55} availability among first responders, noninvasive intervention, and user-friendly technique, IN naloxone is an option for exposed OpK9s as well. Scientific evidence evaluating IN naloxone in canines is limited. The pharmacokinetics of IN naloxone have only been evaluated in one small study involving healthy canines in which the reported bioavailability of an 8mg/100 μ L nasal spray was 87.88%.³⁸ The University of Pennsylvania Working Dog Center is currently engaged in a Department of Homeland Security–funded study evaluating the pharmacokinetics/pharmacodynamics, safety, and clinical efficacy of a 4mg IN naloxone spray in canines.³

The method of administration, formulation used, and existing pathologic conditions may affect IN naloxone absorption. IN absorption and bioavailability are probably best enhanced

when naloxone is dispersed into the nasal cavity as a concentrated fine particulate spray (e.g., mist or aerosol).⁴⁸ This is best accomplished by either administering the naloxone injectable solution through a nasal atomization device^b (Teleflex, Morrisville, NC) or via a commercialized naloxone nasal spray device^a (Adapt Pharma, Inc., Radnor, PA). Simply squirting an injectable aqueous solution into the nasal cavity via a syringe results in loss of a significant portion of the drug due to drainage (run-off) into the nasopharynx or externally from the nasal cavity. Pathologic conditions (e.g., allergic rhinitis, epistaxis, physical obstructions, nasal trauma, alterations in nasal mucus production) and concurrent use of other IN medications or drugs (cocaine) that alter nasal physiology may significantly impair IN naloxone absorption and bioavailability.⁴⁸

Risk to Personnel Handling a Potentially Exposed and Contaminated OpK9

A contaminated OpK9 poses a significant threat for cross-contamination and self-exposure to OpK9 handlers and first responders. Personnel must take appropriate personal protective actions and don personal protective equipment (PPE) when handling an exposed OpK9. At minimum, individual PPE includes: nitrile gloves, N-95 dust masks, eye protection, and long sleeves; paper coveralls and shoe covers are additional items to have on hand. For further information regarding human personal protection measures, refer to guidelines provided by the US Drug Enforcement Administration and Interagency Board (see “*Recommended Internet Resources*”). Table 2 provides information that handlers and first responders should consider to help prepare for handling potential opioid exposures in canines.

Table 2 Preparation Measures for OpK9 Handlers and First Responders

<ol style="list-style-type: none">1. Have appropriate PPE on hand at all times (See <i>Recommended Internet Resources</i>).2. Perform an OpK9 Medical Threat Assessment before training events and real-world missions:<ol style="list-style-type: none">a. Identify local veterinary resources available in the area of operations.<ol style="list-style-type: none">ii. Hours of operationsiii. Staffing, medical and equipment resourcesiv. Establish line of communications and rapportb. Identify evacuation and transport routes.c. Identify logistical evacuation assets (vehicle, air ambulance, other).3. Receive training in the following:<ol style="list-style-type: none">a. Identifying opioid toxicity in K9s.b. Proper use and administration of naloxone.c. Basic K9 life support measures (e.g., rescue breathing with bag-valve-mask, chest compressions).4. Keep important veterinary contact information on hand:<ul style="list-style-type: none">o Primary veterinarian's or local 24/7 emergency veterinary hospital phone numbero ASPCA Animal Poison Control Center (APCC): 1-888-426-4435o Pet Poison Hotline (PPH): 1-855-764-7661 <p>NOTE: A nominal one-time fee may be charged when calling the APCC and PPH helplines.</p>

Summary

Operational K9s of all discipline (detection, apprehension, SAR) are at risk for illicit opioid exposure and subsequent toxicity. Considering their contribution as a force multiplier

^aNarcan®, Adapt Pharma, Inc. Radnor, PA. (<https://www.narcan.com/>)

^bMAD Nasal™ Intranasal Mucosal Atomization Device. Teleflex. Morrisville, NC. (<http://www.teleflex.com/usa/product-areas/anesthesia/atomization/mad-nasal-device/>)

and to the success of many civilian law enforcement, humanitarian, and military operations, it seems reasonable that OpK9 handlers, in particular, along with first responders understand how to appropriately recognize and treat opioid toxicity in canines. Of vital importance, personnel must understand the proper personal protective measures to take in order to protect themselves from unintentional opioid exposures when handling a contaminated OpK9. Naloxone is the treatment of choice in clinically affected OpK9s as it is in people.

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Author Contributions

L.P. and A.G. conceived the topic as well as researched and composed the clinical review. No funding was required. A.G. developed the first draft, L.P. revised the second draft. Both authors read and approved the final manuscript.

Disclosure

The authors have no financial or other conflicts of interest to disclose.

Recommended Internet Resources

US Drug Enforcement Administration. *Fentanyl—A Briefing Guide for First Responders*. <https://www.dea.gov/druginfo/fentanyl.shtml>

The Interagency Board. *Recommendations on Selection and Use of Personal Protective Equipment and Decontamination Products for First Responders against Exposure Hazards to Synthetic Opioids, Including Fentanyl and Fentanyl Analogues*. <https://www.interagencyboard.org/>

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