



[Home](#) > [Publications](#) > [ABA Health eSource](#) > [2016-2017](#) > [Opioid Epidemic Special Edition](#) > [Naloxone: The Science and Laws Behind the Antidote](#)

Naloxone: The Science and Laws Behind the Antidote

Allison Muller, Acri Muller Consulting, Media, PA



It's hard to throw a stone without hitting a news story related to opioid use, opioid overdose, prescription pain relievers, or naloxone. These topics are of interest to toxicologists because of the serious dangers opioids can present and the existence of an antidote (and antidotes aren't all that common). These topics are also of interest to the non-medical community because of the growing public health concerns related to opioids and the availability of an opioid antidote beyond the hands of medical personnel.

Opioids are powerful drugs and both heroin and prescription opioids produce a euphoric "high." Prescription opioids can provide pain relief to the right patient, at the right dose, and at the right time. These scenarios do not always hold true, as prescriptions for opioid pain relievers and dosages of these drugs have steadily increased in recent years.¹ The use of heroin, an illicit opioid drug, is on the rise and so are deaths related to its use. The rising use of heroin may be due to the increased difficulty and expense of obtaining prescription opioids for abuse purposes. Reasons for this include the focus on prescription opioid abuse and the rescheduling of hydrocodone-containing products from a Schedule III controlled substance to the more restrictive Schedule II.²

Attorneys may find the science behind the antidote for opioid overdose, naloxone, to be of interest since it is a prescription drug becoming a life-saving antidote, no longer only in emergency rooms or in ambulances, but in the hands of the lay person. In addition, attorneys are following the changing legal landscape regarding naloxone.

This article provides a background of the basics of opioid drugs, the public health implications of the opioid-use epidemic, the science behind the antidote (naloxone), and the changing laws to reflect the shift of naloxone use from only emergency medicine personnel to also those in the general public who may be at risk for experiencing or witnessing an opioid overdose.

Opioids: What are They and What Do They Do?

Opiates are drugs derived from the opium poppy, such as morphine. Opioids are man-made drugs. The term opioid is now used to refer to both these families of drugs that bind to opioid receptors in the body.³ Opioids have legitimate medical uses⁴ (with the exception of Schedule I drugs like heroin) but are often turned to as drugs of abuse. The human body contains nerve cells in the brain, spinal cord, and other organs, called "opioid receptors." When opioids attach to these specific receptors in the brain, patients will experience pain relief, changes in mood, fatigue, strong feelings of elation or unease, slower breathing, constricted pupils, less movement in the gastrointestinal tract, and stimulation of sensors that control nausea and vomiting. The greater the amount of an opioid brought into the body, the more receptors in the brain become occupied, leading to an increase in the effects of an opioid. While patients may experience a greater degree of euphoria or pain relief, they may also start to feel undesired side effects at higher doses. These effects can manifest as headaches, itchiness, nausea and vomiting, dizziness, tiredness, constipation, urinary retention, pinpoint pupils, and trouble breathing.⁵

Opioid Toxicity: When It All Goes Wrong

Opioid overdose occurs when too many receptors in the brain are occupied by opioids, causing diminished or shallow breathing.⁶ Signs of an opioid overdose include snoring or choking sounds, slow breathing, unresponsiveness even when shaken, a slow pulse or low blood pressure, pale, clammy skin, and pinpoint pupils.⁷ There are many scenarios where users of opioid drugs are at risk for overdose: when users are prescribed a high dose, take more than their prescribed amount, have difficulty breaking down and eliminating the opioid, are using illicit drugs such as heroin, combine depressants (such as tranquilizers) with opioids, or use contaminated illicit drugs (as in the case of heroin intentionally or unintentionally cut with other drugs).⁸

The Opioid Epidemic

The number of overdose-related deaths due to prescription and illicit opioid abuse in the United States continues to at an alarming rate. Statistics are available from as recently as 2013 and are alarming. From 1999 to 2013, drug overdose deaths doubled in the United States. In fact, drug overdose has become the number one cause of unintentional deaths due to injury in the country since 2009, surpassing deaths due to homicides and motor vehicle accidents.⁹ Seventy-one percent of overdose deaths have been related to opioid use,¹⁰ with heroin overdoses quadrupling from 2002 to 2013.¹¹ More than 75 people die every day from heroin and prescription opioid pain medications.¹² Increased access to prescription narcotics is thought to be a contributing factor. The number of prescriptions for opioids increased four-fold from 1999 to 2014,¹³ with 259 million prescriptions written for opioids in 2012.¹⁴ The financial burden resulting from prescription opioid abuse is significant, costing an estimated total of \$55 billion annually in 2011 due to costs related to healthcare, criminal justice, and loss of workplace productivity.¹⁵ These startling statistics highlight the need for public health initiatives to address the epidemic of opioid overdose.¹⁶

Naloxone: An Antidote for Opioid Overdose

Opioid overdoses do not result in immediate death, whether the source of the opioid is a prescription opioid or heroin. Deaths due to opioid overdoses are largely preventable; it may take up to several hours for an opioid to interfere with breathing to the point that death results.¹⁷ However, the toxic effects of opioids should be reversed as soon as possible for best outcomes.

Naloxone is an opioid antagonist, approved by the Food and Drug Administration (FDA) in 1971 for reversing the potentially fatal effects of opioids: difficulty breathing and decreased consciousness.¹⁷ Because naloxone has a high level of attraction to the same receptors in the brain that opioids do, it breaks the attachment between opioids and these receptors and then attaches itself to the receptors.¹⁸ This reverses the effects of opioids, including both heroin and prescription opioids, but higher doses of naloxone may be required for certain types of opioids. In the case of an opioid overdose, any negative effects on breathing and consciousness are reversed, typically within a few minutes (depending on the route that naloxone is given). Naloxone's duration of action does not outlast that of opioids.²⁰ Therefore, immediate medical attention, and possibly repeated administration of naloxone, are necessary.²¹

Why is naloxone the only game in town for reversing opioid overdose? Some additional opioid antagonists do exist: naltrexone and methylnaltrexone. Although these drugs work like naloxone, there are some distinct differences. Naltrexone takes a longer time to start working: one – two hours when given by mouth (orally) or via injection into muscle (intramuscularly). Patients with an opioid overdose need an antidote that works within a few minutes. Also, naltrexone stays in the system for a longer time than naloxone (24 to 72 hours orally). It is, therefore, used for treatment of alcohol and opioid dependence rather than emergency settings of opioid overdose. Methylnaltrexone does not act on the opioid receptors in the brain and is not useful in mediating the effects of an opioid overdose. This opioid antagonist is used for constipation related to opioid use (a sometimes severe side effect, especially in patients using opioids for cancer pain) since it works on receptors in the gastrointestinal tract.

Naloxone does not get absorbed into the bloodstream if taken orally and is FDA-approved for administration intravenously (IV), intramuscularly (IM), intranasally (IN), and subcutaneously (SC). Intranasal naloxone has been proven to be as effective as IV and IM naloxone in reversing effects of opioid overdoses and has the advantages of being easy to use by lay responders and without the safety issues related to the use of needles.²²

Naloxone is relatively safe. If an opioid overdose is suspected, naloxone should be given. If a patient has actually not taken opioids (i.e., there is some other cause for the patient's symptoms) and naloxone is administered, there will be no pharmacological effect.²³ The most common side effects of naloxone may be attributed to opioid withdrawal: anxiety, visible shaking or shivering, sweating, nausea and vomiting, fever, runny nose, and an increase in blood pressure. Serious complications following naloxone administration are reportedly rare²⁴ and are more likely in patients suffering from underlying cardiac disease.²⁵

Naloxone: Laws Related to Its Use in the Community Setting

While deaths resulting from opioid overdoses can be prevented with the timely administration of naloxone, it is not always available to the first responder (often a lay person). Opioid overdose commonly occurs when the victim is at home with friends or family members, and time is of the essence when treating an opioid overdose.

There are challenges in the expansion of naloxone access to laypersons. Many state laws prohibit the prescription of drugs to a person other than who the drug would be administered to (i.e., third party prescriptions) or to a patient if the prescriber has not examined (i.e., standing-order prescriptions).²⁶ Friends or family of the victim may not call for medical assistance due to the fear of being incriminated for drug-related crimes. Furthermore, there are liability concerns about administering the medication as a bystander.²⁷

In light of the data surrounding opioid overdoses and the role of naloxone, all but three states (Kansas, Montana and Wyoming) have passed laws to encourage layperson naloxone access and use.²⁸ Amendments related to decreasing overdose fatalities have been met with little opposition.²⁹ While laws vary by state, naloxone access laws at least address one of the following barriers: general legality of naloxone prescribing and distribution; liability of a healthcare provider for providing naloxone; liability of a bystander for administering naloxone; and reluctance of bystanders to call for emergency responders.³⁰ State laws may then increase access to naloxone among lay persons via one or a combination of the following examples: by waiving the requirement that the prescriber and the person for whom the naloxone is intended for have a provider-patient relationship (therefore waiving the third party prescribing prohibition by allowing a prescriber to authorize a specific set of professionals who ordinarily do not have prescribing authority (paramedics, nurses, or pharmacists) to supply naloxone with a standing order from a prescriber, and/or by allowing pharmacists to directly prescribe naloxone without oversight by a licensed prescriber.³¹ Some states provide immunity to prescribers and/or bystanders through Good Samaritan laws (although immunity under the Good Samaritan Law does not protect a person for the sale of drugs, and immunity for possession of controlled substances and/or drug paraphernalia varies by state). Additionally, federal legislation, specifically the Comprehensive Addiction and Recovery Act of 2016 (P.L. 114-198), was passed on July 22, 2016 to provide states with resources and funding for opioid abuse prevention efforts, drug treatment programs, and naloxone access.³²

Changes in laws related to naloxone distribution and use are evolving and their impact on the rising number of deaths related to opioids continues to be followed. In 2001, New Mexico became the first state to change its laws to increase access to naloxone.³³ However, after 2010 there was a staggering increase in the number of states that amended their laws to improve access to naloxone.³⁴ Today, the majority of states have worked to pass laws to increase naloxone access and decrease liability risk related to the provision and use of naloxone.³⁵ There has been an expansion of states with some version of a Good Samaritan Law from four in 2010 to 36 states and the District of Columbia as of July 2016.³⁶

Impact of these Changes

The prescription requirement for naloxone and bystanders' lack of awareness of Good Samaritan Law provisions are barriers to naloxone access that persist. With the expanded access of naloxone comes the future analysis of the antidote's impact on opioid-related deaths. The challenge in determining naloxone's role in opioid overdose rates is that the use of naloxone by bystanders is often unreported. However, there are states like Maryland that utilize the services of their poison control center to evaluate the effectiveness of their overdose education and naloxone distribution programs.³⁷

Conclusion

Opioid overdoses are on the rise. However, there is an antidote that can prevent these fatalities: naloxone. Barriers are being broken down at the state level to make naloxone more accessible and to decrease associated liability with its provision and use in the non-healthcare setting. It is still too soon to determine if the increased availability of naloxone will ultimately reduce opioid fatalities, but this is an area that the healthcare and legal communities will continue to follow.

¹ Green TC, Doe-Simkins M, "Opioid overdose and naloxone: the antidote to an epidemic?" *Drug Alc*

² Brodrick JE, Brodrick CK, Adinoff B, "Legal regimes surrounding naloxone access: considerations for 128.

³ 21 US Code § 802 definitions, <https://www.law.cornell.edu/uscode/text/21/802>], accessed September

⁴ Legal prescription opioids include buprenorphine (Butrans®), meperidine (Demerol®), methadone hydrocodone (Vicodin®, Lortab®, Norco®), fentanyl (Aqtiq®, Duragesic®, Fentora®) and hydromorphone (Exalgo®).

opioids include the antidiarrheal drugs diphenoxylate (Lomotil®) and loperamide (Imodium®), but euphoric effects.

- 5 Calas T, Wilkin M, Oliphant C, "Naloxone: an opportunity for another chance," *J for Nurse Pract* 20:
6 *Id.*
7 *Id.*
8 *Id.*
9 *Supra* note 2.
10 *Supra* note 5.
11 *Id.*
12 Legal interventions to reduce overdose mortality: naloxone access and overdose Good Samaritan |
https://www.networkforphl.org/_asset/qz5pvn/network-naloxone-10-4.pdf, accessed September 6
13 Centers for Disease Control and Prevention: Injury Prevention and Control: Opioid overdose, <http://www.cdc.gov/vitd/toll-free>,
accessed September 17, 2016.
14 Centers for Disease Control and Prevention: Opioid pain killer prescribing, <http://www.cdc.gov/vitd/toll-free>
15 Hoback J, "Overdosed on opioids: a deadly opioid epidemic sweeping the country has lawmakers v
13.
16 Bailey AM, Wermeling DP, "Naloxone for opioid overdose prevention: pharmacists' role in communi
48(5):601-606.
17 Davis C, Webb D, Burris S, "Changing law from barrier to facilitator of opioid overdose prevention,
18 *Supra* note 5.
19 *Id.*
20 *Id.*
21 *Id.*
22 Kerr D, Kelly AM, Dietze P, Jolley D, Barger B, "Randomized controlled trial comparing the effective
for the treatment of suspected heroin overdose," *Addiction*, 2009, 104(12):2067-2074.
23 Burris S, Norland J, Edlin BR, "Legal aspects of providing naloxone to heroin users in the United St
24 *Supra* note 5.
25 *Supra* note 1.
26 State Legislation Overdose Prevention, January 2016,
http://www.drugpolicy.org/sites/default/files/Fact%20Sheet_State%20based%20Overdose%20Prevention.pdf,
accessed September 17, 2016.
27 *Supra* note 12.
28 *Id.*
29 *Supra* note 17.
30 Davis CS, Carr D, "Legal changes to increase access to naloxone for opioid overdose reversal in th
31 *Id.*
32 Comprehensive Addiction and Recovery Act (CARA), <http://www.cadca.org/comprehensive-addiction-recovery-act>

33 *Supra* note 30.

34 *Id.*

35 *Supra* note 12.

36 *Id.*

37 Doyon S, Benton C, Anderson BA, et al, "Incorporation of poison center services in a state-wide ov
J Addict, 2016, 25(4):301-306.