Opioid

Use

Misuse

Abuse

Steven Boggs, MD, MBA, FASA Professor and Interim Chair Department of Anesthesiology UTHSC





Lecture Objectives:



- History of opioid use
- Magnitude of the current opioid epidemic in the US
- Evolutionary understanding of "why" opioids are so enthralling
- What we can do as providers to minimize the risk of misuse and abuse in our patients
- Regulatory issues

Disclosures:







Early History of Opiates

1200 BC

Homer called *papaver somniferum* a "wondrous substance." Those who consume it do not shed a tear all day long, even if their mother or father dies, even if a brother or beloved son is killed before their own eyes. **3400 BC – 300 AD**

The Mesopotamians, the Sumerians, the Assyrians and then the Egyptians used the opium poppy **460 BC**

The Greek, Hippocrates, used for internal diseases and diseases of women.

330 BC

The Macedonian, Alexander the Great, spread opium through Europe, Persia and India.

220 AD

The Chinese surgeon Hua To of the Three Kingdoms used opium with Cannabis for patients before major surgery. **1527 AD**

Paracelsus (Swiss) developed tincture of opium, which he called *laudanum*, from the Latin verb, "to praise."

1680

Thomas Sydenham (British) introduced Sydenham's Laudanum, containing opium, sherry and herbs.

1700- 1900

Chinese had rampant opium addiction. The British and French forced continued opium trade on the Chinese to maintain their balance of trade, including two opium wars. 1772

Thomas Jefferson plants poppies at Monticello 1806

Friedrich Sertürner isolates morphine from opium. He names it after the Greek God of dreams, Morpheus.

1800-1850

Coleridge, Byron, Shelly, Keats, Baudelaire and Walter Scott and other Romantic poets struggled with opium addiction

1821

Thomas De Quincey published, "Confessions of an English Opium Eater."

1853

Hypodermic needle invented.

Synthetics Emerge, as does Regulation

1875-1900

>200,000 Americans addicted to opioids after the Civil War, called the "Soldier's Disease. Veterans and then their wives and female relatives became addicted.

1870

In industrializing Britain, working families spent up to 10% of their income on opium.

1886

William Stewart Halsted was admitted to the Butler Sanatorium for his cocaine addiction. He was discharged addicted to morphine as a treatment and would take 200 mg a day until his death in 1922, 36 years later.

1898

Bayer[®] develops heroin, a non-addictive opiate. Heroin from the German word, *Heroisch* or heroic. St. James Society began campaign to give free heroin samples to morphine addicts trying to give up habit.

1909

Congress passed the Opium Exclusion Act, barring importation of opium for smoking. Considered the first shot in the "War on Drugs."

1914

Harrison Narcotics Tax Act required physician and pharmacist registration and de facto prohibition of opiates. **1916**

A few years after Bayer[®] stopped the mass production of heroin, German scientists synthesized oxycodone in hopes it would cause less dependence.

1925

Robinson identifies the structure of morphine. Kabay receives patent for industrial extraction of morphine from poppy plant.

1938

Passage of the Food, Drug and Cosmetic Act gave authority to the US FDA for all drugs.

1952

Total synthesis of morphine.

1966

Lenny Bruce died of overdose of morphine. *"I'll die young, but it's like kissing God."*

Scientific knowledge explodes, as does Demand

1969

World Health Organization (WHO) abandoned belief that medical use of morphine inevitably led to dependence.

1970

Controlled Substance Act – began to consolidate all regulated medications under federal law into five separate schedules. Schedule I meds cannot be prescribed.

1973

Discovery of the opioid receptor. Drug Enforcement Administration formed and Nixon declares the "War on Drugs."

1975

Hughes and Kosterlitz discover enkephalins.

1976

Li and Chung discover β -endorphin. **1981**

Doctors still very reluctant to prescribe opioids. A is discovered. Vicodin[®] became generic. 1984

Cocaine regularly used by 4 - 5 million people compared to 500,000 heroin addicts.

1985

Indecal government replaces welfare payments for disability payments which cover opioids for pain.
A bottle with a \$3 – copay can bring in \$10K on the streets.
1987

DEA raids Monticello and rips out poppy plants **1990's**

The VA System and Joint Commission considered pain to be undertreated and develops the concept of "Pain as the

1992

Fifth Vital Sign."

Kieffer and Evans accomplish molecular cloning of the opioid receptor.

1997

Zadina discovers endomorphines.

Current Data

Most commonly prescribed opioids oxycodone and hydrocodone are also the most commonly involved opioids in overdose deaths.

	Prescription-	Opioid	Opioid-
	Related	Prescription	Related
	Death	Written	Death
1980	3,500		
2000	16,615	164 million	
2010		234 million	
2013			16,235
2014	18,893		
2015			33,091
2016			65,000

2007 – 2012

760 million hydrocodone & oxycodone pills delivered to West Virginia with 1.8 million residents

That is approximately 82 pills/resident/year

Present:

- USA consumes:
 - 99% of world's hydrocodone
 - 81% of world's oxycodone
 - 80% of the world's supply of narcotics
 - USA is 4.4% of the world's population
 - USA uses >> 20 x that of world average
- 8% of opioid-naïve patients who receive an opioid prescription become chronic users
- Surprisingly, no improvement in patient overall pain scores

Hah JM, Bateman BT, Ratliff J, Curtin C, Sun E. Chronic Opioid Use After Surgery: Implications for Perioperative Management in the Face of the Opioid Epidemic. A & A (2017); 125:5, pages 1733-40.

This letter and article helped launch the opioid epidemic

(1986, Pain) 171 Pain, 25 (1986) 171-186 \bullet Elsevier Chronic Use of Opioid Analgesics in Non-Malignant Pain: Report of 38 Cases \bullet Russell K. Portenoy and Kathleen M. Foley ightarrowPain Service, Department of Neurology, Memorial Sloan-Kettering Cancer Center, and Department of Neurology, Cornell University Medical College, New York, NY 10021 (U.S.A.) (Received 10 June 1985, accepted 28 October 1985)

Vol. 302 No. 2

Only 38 Patients! \bullet

- Retrospective
- Observational

CORRESPONDENCE

- 6-years of observation
- 1% 5% of patients had abuse problems

Summary

Thirty-eight patients maintained on opioid were retrospectively evaluated to determine efficacy of this therapy. Oxycodone was used levorphanol by 5; others were treated with pentazocine, or some combination of these dru four or more years at the time of evaluation, w 7 years. Two-thirds required less than 20 mon took more than 40 mg/day. Patients occas and/or hospitalization for exacerbation of pai baseline afterward. Twenty-four patients desc adequate relief of pain, while 14 reported inadsurgical procedure for pain management whil gains in employment or social function could opioid therapy. No toxicity was reported and only 2 patients, both with a history of prior dr characteristics, including data from the 16 Pe patients, the Minnesota Multiphasic Persona psychiatric evaluation in 6, failed to disclose capable of explaining the success of long-te opioid maintenance therapy can be a safe, salu the options of surgery or no treatment in those nant pain and no history of drug abuse.

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

January 10,1980

N Engl J Med 1980; 302:123

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients' who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,2 Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare inmedical patients with no history of addiction.

JANE PORTER HERSHEL JICK, M.D. **Boston Collaborative Drug** Surveillance Program Boston University Medical Center Waltham, MA 02154

1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.

17,000 L remission tral-nerv trathecal both). De ine (70 m meter ca

three to

-cell le

ever, bec

up, the p

this poin

lymphob

induction

lished po

plantatic

the time

lished cr

The study analyzed:

- Hospitalized patients \bullet
- Small doses of opioids \bullet
- Controlled setting \bullet
- Acute pain \bullet
- Not given long-term opioid \bullet prescriptions which they'd be free to administer at home

National Overdose Deaths Prescription Opiates (left) and Heroin (right)





Tennessee Fatal Overdose Data



Source: https://www.tn.gov/health/health-program-areas/pdo/pdo/data-dashboard.html

Total U.S. drug deaths



Since **1999**, over **735,865** Americans have died. This is more than died during the 1918-1919 Influenza Pandemic National Center for Health Statistics, Centers for Disease Control and Prevention



https://www.cdc.gov/nchs/data/databriefs/db294.pdf



https://www. cdc.gov/nchs /data/hus/20 16/027.pdf

Drug Overdose Rates by Race and Urban versus Rural Location



Urban counties are those classified by the N.C.H.S. as large central metropolitan areas. Rural counties are those classified as nonmetropolitan or as small metropolitan areas.

https://www.cdc.gov/nchs/data/hus/2016/027.pdf



https://www.cdc.gov/nchs/data/databriefs/db294.pdf

Some states have more opioid prescriptions per person than others.





Sources of Prescription Opioids Among Past-Year Non-Medical Users^a

^a Obtained from the US National Survey on Drug Use and Health, 2008 through 2011.⁵
 ^b Estimate is statistically significantly different from that for highest-frequency users (200-365 days) (P<.05).
 ^c Includes written fake prescriptions and those opioids stolen from a physician's office, clinic, hospital, or pharmacy; purchases on the Internet; and obtained some other way.

SOURCE: Jones C, Paulozzi L, Mack K. Sources of prescription opioid pain relievers by frequency of past-year nonmedical use: United States, 2008–2011. JAMA Int Med 2014; 174(5):802-803.

Estimated Number of New Hepatitis B and Hepatitis C Infections in the United States, by Year.





Science Behind Opioids

Antibodies to MOR and DOR receptors in Zebra fish



Int J Mol Sci. 2018 Jan 2;19(1). pii: E14. doi: 10.3390/ijms19010014.





The Human G-protein Coupled Receptors (GPCR) superfamily. Human GPCRs are targeted by over 50% of marketed drugs.





 δ opioid receptor OPRD1

Brunton LL, Hilal-Dandan R, Knollmann BC. Molecular Mechanisms of Drug Action. *Goodman & Gilman's:* The Pharmacological Basis of Therapeutics, 13e; 2017

Source: Laurence L. Brunton, Randa Hilal-Dandan, Bjorn C. Knolimann: Goodman & Gilman's: The Pharmacological Basis of Therapeutics, Thirteenth Edition: Copyright @ McGraw-Hill Education. All rights reserved



Benarroch EE:

Endogenous opioid systems: current concepts and clinical correlations.

Neurology. (2012) 79: 807-814



Delta (δ) Analgesia (spinal and supraspinal) Release of Growth Hormone (GH) Affective Behavior

Present in limbic system



Actions of Drugs of Abuse on Ventral Tegmental Area and Nucleus Accumbens





TRENDS in Pharmacological Sciences

et al.

Neuropathic and

down regulate

dopaminergic

transmission

Trends in

Pharmacological

299-305

Clinical Issues:





Acute and Chronic Effects of Opiate Receptor Activation

1. Desensitization:

- After activation, acute tolerance occurs specific for receptor
- Time course parallel to that of the clearance of agonist
- Uncoupling from Greceptor/internalization of receptor

2. Tolerance:

- Decrease in effectiveness with repeated agonist administration
- Right shift of dose-response curve
- μ receptor:
 - rapid tolerance to euphoria
 - moderate tolerance to sedation
 - no tolerance for miosis

- 3. Dependence:
 - Withdrawal if cessation of drug or antagonist administered
 - Increased somatomotor and autonomic outflow
- 4. Addiction:
 - Behavioral pattern characterized by compulsive use of drug
 - Aversion to withdrawal may be major factor
 - Drug dependence is not synonymous with addiction
 - i.e. cancer patients are frequently tolerant to high doses of opiates and are not considered addicted

Table 1.	Definitions Related to Use and Misuse of Opioid Analgesics
Term	Definition
Misuse	Use of a medication (for a medical purpose) other than as directed or indicated, whether willful or unintentional, and whether harm results or not
Abuse	Any use of an illegal drug or the intentional self-administration of a medication for a nonmedical purpose such as altering one's state of consciousness, for example, getting high
Addiction	A primary, chronic disease involving brain reward, motivation, memory, and related circuitry that can lead to relapse and progressive development, and that is potentially fatal if left untreated; markers include craving and continued use despite adverse outcomes
Tolerance	A state of adaptation in which exposure to the drug results in diminution of its effects over time
Physical dep	pendence Engenders abstinence syndrome when the drug is abruptly stopped

Katz NP, Adams EH, Chilcoat H, et al.Challenges in the development of prescription opioid abuse-deterrent formulations.Clin J. Pain. 2007; 23: 648-660.

Table 2. Criteria^a for Opioid-Use Disorders From the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

- 1. Opioid taken in larger amounts or over a longer period than intended
- 2. Persistent desire or unsuccessful efforts to cut down or control opioid use
- 3. A lot of time spent obtaining, using, or recovering from the effects of the opioid
- 4. Craving or a strong desire to use opioids
- 5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home
- 6. Continued use despite persistent or recurring social or interpersonal problems caused or exacerbated by opioid use
- 7. Stopping or reducing important social, occupational, or recreational activities due to opioid use
- 8. Recurrent use of opioids in physically hazardous situations
- 9. Continued use despite knowledge of having persistent or recurrent physical or psychological problems cause or worsened by opioid use
- 10. Tolerance as defined by either a need for markedly increased amounts to achieve intoxication or desired effect or by markedly diminished effect with continued use of the same amount (does not apply when used appropriately under medical supervision)
- 11. Withdrawal manifesting as either characteristic syndrome or the substance is used to avoid withdrawal (Does not apply when used appropriately under medical supervision)

Data were derived from Saunders.16

^aA minimum of <u>2–3 criteria is required for a mild substance-use</u> disorder diagnosis, while <u>4–5 is moderate</u>, and <u>6–7 is severe</u>. Opioid-use disorder is specified instead of substance-use disorder, if opioids are the drug of abuse.

Saunders JB. Substance use and addictions and the new ASAM definition of addiction.

J. Psychoactive Drugs. 2012; 44:1-4.

*Criteria from American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition,. Washington, DC, American Psychiatric Association page 541.

Risk Factors for **Opioid Use** Disorder (OUD)

- Pain:
 - Non-functional status due to pain
 - Exaggeration of pain
 - Unclear etiology of pain
- Substance abuse
 - Personal History
 - History of Substance Abuse Treatment
 - Family History
- Psychological:
 - Stress
 - Trauma
 - Disease
 - Mood Swings

- Young age:
 - Under 18
 - Preadolescent sexual abuse
 - Childhood adversity
- Smoking
- History of legal problems
- Poor social support

Webster LR. Risk Factors for Opioid-Use Disorder and Overdose. Anesth Analg 2017;125:1741–8

Opioid-Induced Respiratory Depression (OIRD) Ondine's Curse

Strong Predictors

- SUD diagnosis in previous 6 months^{*}
- Bipolar disorder or schizophrenia
- Cerebrovascular disease
- Renal disease
- Heart failure
- Nonmalignant pancreatic disease
- Concurrent benzodiazepine or antidepressant prescription

*(single strongest predictor)



Moderate Predictors

- Recurrent headache
- Chronic pulmonary disease
- Sleep apnea
- Extended-release and longacting opioid formulations
- Daily MED (morphine equivalence dose) ≥ 100 mg

Table 6. CIP-Based RIOSORD

Question	Points for "Yes"
	Response
In the past 6 mo, has the patient had a health care visit (outpatient, inpatient, or ED) involving any of the following health conditions? ^b Substance-use disorder (abuse or dependence)? (this includes alcohol, amphetamines, antidepressants, cannabis, cocaine, hallucinogens, opioids, and sedatives/anxiolytics)	25
Bipolar disorder or schizophrenia?	10
Stroke or other cerebrovascular disease?	9
Kidney disease with clinically significant renal impairment?	8
Heart failure?	7
Nonmalignant pancreatic disease (eg, acute or chronic pancreatitis)?	7
Chronic pulmonary disease (eg, emphysema, chronic bronchitis, asthma, pneumoconiosis, asbestosis)?	5
Recurrent headache (eg, migraine)	5
Does the patient consume:	N
Fentanyl?	13
Morphine?	11
Methadone?	10
Hydromorphone?	7
An extended-release or long-acting formulation of any prescription opioid?	5
A prescription benzodiazepine?	9
A prescription antidepressant?	8
Is the patient's current maximum prescribed opioid dose 100 mg morphine equivalents per day? (include all prescription opioids consumed on a regular basis)	7
Total point score (maximum = 146)	= 48

Zedler BK, Saunders WB, Joyce AR, Vick CC, Murrelle EL. Validation of a screening risk index for serious prescription opioid-induced respiratory depression or overdose in a US Commercial Health Plan Claims Database. Pain Med. 2017 Mar 6

Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression (RIOSORD)

Table 7. CIP-based RIOSORD: Probability by Risk Class of Experiencing Serious Opioid-Induced Respiratory Depression				
Risk Index Score ^a	Average Predicted OIRD Probability in Next 6 mo (95% CI), %			
0–4	1.9 (1.9–1.9)			
5–7	4.8 (4.8-4.9)			
8–9	6.8 (6.8-6.8)			
10–17	15.1 (15.1–15.3)			
18–25	29.8 (29.7–30.0)			
26–41	55.1 (54.8–55.4)			
≥42	83.4 (83.2–83.7)			

Zedler BK, Saunders WB, Joyce AR, Vick CC, Murrelle EL. Validation of a screening risk index for serious prescription opioid-induced respiratory depression or overdose in a US Commercial Health Plan Claims Database. Pain Med. 2017 Mar 6

Overdose **Mortality** Related to Opioids

- Comorbid mental and medical disorders
- Medications:
 - ✓ Substance abuse history [prescription, illicit drugs and alcohol]
 - ✓ High opioid dose (particularly with benzodiazepines)
 - ✓ Methadone use
 - ✓Antidepressant coprescribing
 - ✓ Polysubstance abuse
 - ✓Opioid naivety

- Middle age
- Heart or pulmonary complications (respiratory infections, asthma)
- Sleep apnea
- Pain intensity (elevated, low, moderate, severe)
- Unemployment
- Recent release from prison

Opioid Use After Surgery

Medical Risks of Opiates After Surgery

- Immunosuppression
- Endocrinopathy
- Hyperalgesia despite increasing doses
- Sedation
- Delirium
- Ileus
- Respiratory depression
- In 200,005 patients for elective surgery ¹:
 - ✓ 8.8% were using opiates before surgery
 - ✓ Preoperative use associated with:
 - Longer hospital stay
 - Higher 30-day readmission rate
 - Increased expenditures at 90, 180, 365 days

¹Waljee JF et al. Ann Surg. 2017; 265: 715-721

Chronic Use After Surgery

- Opiates prescribed after surgery may trigger longterm use - whether or not the patient has been exposed in the past.
- 60% of patients receiving 90 days of continuous opioid therapy are on opioid therapy 1 year later.
- Highest risk for:
 - ✓ Total knee replacement
 - \checkmark Total hip replacement
 - ✓ Open and lap cholecystectomy
 - \checkmark Simple mastectomy
 - ✓ C-section
- Other factors:
 - ✓ Male
 - ✓ Age > 50
 - ✓ Preoperative use of benzodiazepines, antidepressants, alcohol
 - ✓ Drug abuse history

Hah JM et al. A & A. 2017; 125: 1733-1740

What Patients Can Do To Maximize Safety for Themselves and Others With Opiates

Soffin EM, Waldman SA, Stack RJ, Liguori GA.

An Evidence-Based Approach to the Prescription Opioid Epidemic in Orthopedic Surgery.

Anesthesia and Analagesia. 2017; 125 (5) 1074-1712.

WHAT YOU CAN DO TO STAY SAFE:

- USE: Take your medications only as directed by your doctor. DO NOT share your medications with anyone.
 DO NOT mix opioid medications with alcohol.
- STORE: Store your prescriptions securely in their original containers. Keep them out of sight and out of children's reach, preferably in a locked cabinet or high shelf.
- DISPOSE: Dispose of medications immediately after your pain has resolved. Unused medications are best disposed of at a take back facility or pharmacy. For public disposal locations: <u>https://apps.deadiversion.usdoi.gov/pubdispsearch/spring/main?execution=e1s1</u>

MISUSE AND OVERDOSE RISKS:

- Prescription drugs may be just as dangerous as illegal drugs if they are misused
- Misusing your medications may have serious consequences, including confusion, weakness, nausea, vomiting ,and suppressed breathing to the point of death. If you think you have taken more medication than was prescribed, or you have any of these symptoms, go immediately to an emergency room.
- · Misusing your medications may also lead to addiction: take your medications ONLY as prescribed.
- As you recover from surgery, your opioid use should decrease. If severe pain persists or your opioid requirements increase, please notify your surgeon

FOR YOUR SAFETY, WE DO NOT ROUTINELY:

- Prescribe long-acting opioids, except in special circumstances
- Prescribe more than a short course of short-acting opioids
- Refill lost, stolen, or destroyed prescriptions

ADDITIONAL RESOURCES:

- National Institute on Drug Abuse: <u>http://www.drugabuse.gov</u>
- Substance Abuse & Mental Health Services Administration: <u>http://oas.samhsa.gov/prescription.htm</u>
- FDA recommendations: <u>http://www.fda.gov/Drugs/ResourcesForYou/default.htm</u>

Criteria and Process to **Identify Patients Requiring Preoperative Evaluation by** a Pain Management and/or Addiction Specialist **Prior to Surgery**

Soffin EM, Waldman SA, Stack RJ, Liguori GA.

An Evidence-Based Approach to the Prescription Opioid Epidemic in Orthopedic Surgery.

> Anesthesia and Analagesia. 2017; 125 (5) 1074-1712.

 Do you take pain medications? Dosage? How often? •How long have you been taking pain medication? Why? •Do you use illegal drugs? If yes, what? If no, have you ever? Ask Every •Do you drink alcohol? If you, how much, and how often? •Have you ever been in detox for drugs and/or alcohol?

Patient

Identify

Verify

Refer

 Opioid tolerance by CDC or FDA criteria 3,32 Current substance abuse disorder, including illicit drug use Current/history of buprenorphine, methadone, suboxone or Subutex use Intrathecal pump

 Primary prescriber and doses of controlled substances Check I-STOP (New York State) or state PDMP

 Pain Management Specialist Addiction Specialist

Signs of Potential Prescription Drug Misuse or Abuse

Obtaining prescriptions from multiple sources and locations

Use of illegal drugs or controlled substances not prescribed for the patient

Resistance to changing medications despite deterioration in function or significant side effects

Concurrent alcohol abuse / substance use disorder

Repeated episodes of:

- requests for early refills of controlled substances
- prescription loss or theft
- increasing dose without prescriber instruction

Foraging prescriptions for opioids

Soffin EM, Waldman SA, Stack RJ, Liguori GA. An Evidence-Based Approach to the Prescription Opioid Epidemic in Orthopedic Surgery. Anesthesia and Analagesia. 2017; 125 (5) 1074-1712.

Aggressive demands for opioids

SERVICE: JOINT ARTHROPLASTY

POLICY STATEMENT/PURPOSE: Promote judicious prescribing practices; encourage prescribers to employ conservative opioid prescribing practices to enhance patient safety and minimize risks of overuse & diversion

CONTENTAPPLIES TO: Post-operative inpatient & ambulatory patients with no history of opioid dependency (chronic opioid treatment with daily use > 6 months).

PRINCIPLES OF PRESCRIBING OPIOIDS AT DISCHARGE:

- Generally, we recommend that you prescribe only one (1) short-acting opioid. In situations where you prescribe two (2) short-acting opioids, the combined number of pills should not exceed the recommended maximum to prescribe (below).
- Do not prescribe long-acting opioids.
- Consider discontinuing or decreasing benzodiazepines (e.g. Valium, Xanax) with concurrent use of opioids. Consult with attending surgeon/medical doctor or pain management specialist if patient will take benzodiazepines and opioids due to increased respiratory risks.
- Do not pre-prescribe opioids for a patient's discharge needs prior to the procedure.

PROCEDURE	OPIOID	DOSE ROUTE FREQUENCY	DURATION	MAXIMUM	MULTIMODAL AGENTS	ALTERNATIVE (** do not prescribe acetaminophen with any other acetaminophen-containing medication)
Total Hip Arthroplasty	oxycodone 5mg hydromorphone 2mg	 1-2 tablets Oral Every 3-4 hours as needed 	2 weeks supply	90 tablets	 acetaminophen 1000mg 3-4x daily meloxicam 15mg daily, 15 tabs 	 oxycodone/acetaminophen 5/325 mg hydrocodone/acetaminophen 5/325 mg
Total Knee Arthroplasty	oxycodone 5mg hydromorphone 2mg	 1-2 tablets Oral Every 3-4 hours as needed 	2 weeks supply	120 tablets	 acetaminophen 1000mg 3-4x daily meloxicam 15mg 1x daily, 15 tabs 	 oxycodone/acetaminophen 5/325 mg hydrocodone/acetaminophen 5/325 mg

RECOMMENDED PRESCRIBING BY PROCEDURE:

Soffin EM, Waldman SA, Stack RJ, Liguori GA.

An Evidence-Based Approach to the Prescription Opioid Epidemic in Orthopedic Surgery.

Anesthesia and Analagesia. 2017; 125 (5) 1074-1712.

FDA Response to the Opioid Crisis

Issue

Balancing individual need and societal risk.

Patients require access to safe and effective pain medication, but both individuals and society must be protected from the effects of opioid misuse.

Meeting the need for timely action. The evolving meat or opioid abuse requires a flexible interim approach while the full policy framework is in development.

Reviewing labeling and postmarketing surveillance requirements. Current labeling requirements include detailed instructions, and manufacturers are required to conduct postmarketing safety surveillance and research studies, but these measures may need to be reevaluated.

Prioritizing abuse-deterrent formulations and overdose treatments. Abuse-deterrent opioid formulations have the potential to reduce misuse of opioid medications, and broader access to naloxone may help mitigate harm

from opioid overdose.

FDA Response

The FDA will consult with partners including the National Academy of Medicine to craft a framework for opioid review, approval, and monitoring that balances individual needs for pain control with the risk of addiction, as well as the broader public health consequences of opioid abuse and misuse.

The FDA Science Board will convene in March to advise on the role of pharmaceuticals in pain management, development of alternative pain medications, and postmarketing surveillance activities. Multiple other actions will also occur over the next several months, including an evaluation of the existing Risk Evaluation and Mitigation Strategy (REMS) requirements for extended-release/long-acting (EK/LA) oploids. An advisory committee will consider this review and offer advice regarding possible expansion of the scope and content of prescriber education and whether to expand the REMS program to include immediate-release opioids, potentially increasing the number of prescribers receiving training on pain management and safe prescribing.

The FDA will revise postmarketing requirements, expanding the requirements for drug companies to generate postmarketing data on long-term impact of ER/LA opioid use to provide better evidence on the serious risks of misuse and abuse associated with long-term opioid use, predictors of opioid addiction, and other important issues.

The FDA will continue to support abuse-deterrent formulations and, with guidance from an advisory committee, explore and encourage development of more effective abuse-deterrent features. The FDA will also prioritize issuance of draft guidance on generic abusedeterrent opioids and will consider ways to make naloxone more widely available, including as an over-the-counter medication. In addition, new non-abuse-deterrent formulations submitted for FDA approval will also be reviewed by an advisory committee.

Issue

Addressing the lack of nonopioid alternatives for

cations for chronic pain have recently been approved for the market, more alternatives are needed, including nonpharmacologic treatments.

Creating clear guidelines for opioid use. The cur-

- continue unless prescribing physicians have a clear understanding of appropriate use and management.
- Managing pain in children. Use of opioid medications in children with severe and chronic pain conditions requires special consideration, and physicians need information that helps them prescribe such medications safely and effectively, while protecting minors who lack mature decision-making capabilities.
- **Developing a better evidence base.** Despite ongoing efforts, the evidence base to guide the use of opioid medications, particularly in the setting of long-term use, is substantially lacking.

The FDA is working closely with industry and the National Institutes of Health to develop alternative medications without the addictive properties of opioids. Nonpharmacologic approaches to pain treatment have also been identified as an urgent priority.

FDA Response

- The FDA is supporting the CDC's guideline for prescribing opioids for chronic pain control. The FDA also supports the Surgeon General's efforts to engage the clinical community in curbing inappropriate prescribing and proactively treating opioid addiction, while reinforcing evidence-based pain management approaches that spare the use of opioids.
- An FDA Pediatric Advisory Committee will address the use of opioid medications in children, including the development of high-quality evidence to guide treatment, and provide input on the policies for adding new pediatric opioid labeling under the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act before any new labeling is approved.
- Health and Human Services agencies and the FDA program for mandated industry-funded studies are developing a coordinated plan for conducting research that will provide evidence to guide opioid use, elucidate the biologic phenomenon of pain, and consider new and alternative approaches to pain prevention and management.

Califf RM, Woodcock J, Ostroff S. A Proactive Response to Prescription Opioid Abuse. April 14, 2016 N Engl J Med 2016; 374:1480-1485 DOI: 10.1056/NEJMsr1601307

Molecular Targets for Pain Management: More than Just Mu

While alternatives exist to mu opioid monotherapy, the quest to develop ideal alternatives and adjuvants continues. In this issue, Knezevic et al¹ review targeted pain therapeutics.



IARS InfoGraphic

Wanderer JP, Nathan N.

November 2017 Volume 125 Number 5 Pg. 1427

Figure. Prevalence of Unused Opioids Prescribed After Surgery



Prescription Opioid Analgesics Commonly Unused After Surgery: A Systematic Review.

JAMA Surg. 2017;152(11):1066-1071. doi:10.1001/jamasurg.2017.0831 Published online August 2, 2017.

Michigan Opioid Prescribing Engagement Network

OUR WORK SAFE DRUG DISPOSAL~ UPDATES RESOURCES~ ABOUT~ **Q** GIVE NOW



Opioid Preventative Strategy

Michigan OPEN was founded to develop a preventative approach to the opiold epidemic in the state of Michigan through a focus on acute care prescribing (surgery, dentistry, emergency medicine, and trauma). Addressing opiold prescribing during the acute care period among those patients not using opiolds has the greatest potential to reduce the number of new chronic opiold users and minimize unintended distribution of prescription opiolds into communities.



Opioid Disposal Information and Resources

Why should I dispose of my opioids?

We recommend disposing of your unused opioids as soon as you finish taking it. 91 people die each day in the US from opioid-related overdoses – that is more than the number of people killed in car accidents or by guns. Opioids are often involved in accidental poisonings and intentional misuse.

- · Every 10 minutes a child visits the emergency room for medication poisoning
- 12.5 million people age 12 and older misused opioids in the last year
- Three in five teens say prescription pain medication is easy to get from their parents' medicine cabinet

How do I dispose of my opioids?

Approved opioid collectors, primarily pharmacies and law enforcement agencies, and special take-back events are the safest way of disposing unneeded medications. While flushing your unused opioids is preferable to keeping them in your home, we recommend safe disposal at an approved opioid collector.

You can find an approved opioid collector near you on our Opioid Disposal Map.

If you cannot get to a drive or an authorized opioid collector, you can safely dispose pills in your household trash

Step 1: Remove medicine from original container and mix (do not crush) with an unpalatable substance such as kitty litter or used coffee grounds.

Step 2: Place mixture in a sealed bag or container.

Step 3: Throw sealed bag or container in household trash.

Step 4: Scratch out personal information on prescription label and dispose original medicine container.

http://michigan-open.org/

Abuse-Deterrent Formulations in the USA

Table 1. Extended-release opioid analgesics with a US FDA abuse-deterrent formulation label or under FDA review (as of December 2016).

ADER-IMT: Abuse-deterrent, extended-release injection-molded tablets; ADF: abuse-deterrent formulation; ER: extended-release; FDA: Food and

Drug Administration.

		Year		
Drug brand name	ADF approach	approved	_	
FDA approved			_	
Morphine products				
Embeda [®]	Agonist/Antagonist combination	2014		
MorphaBond™	Physical and chemical barriers	2015 •	Targiniq ER	
Oxycodone products ^a		•	Embeda	
OxyContin [®]	Physical and chemical barriers	2013	Hysingla ER	
Xtampza ER®	Physical and chemical barriers	2016 •	MorphaBond ER	
Troxyca ER®	Agonist/Antagonist	2016 *	Xtampza ER	
	combination		Troxyca ER	
Hydrocodone product				
Hysingla [®] ER	Physical and chemical barriers	2014 •	Arymo ER	
Under FDA review		•	Vantrela ER	
Morphine product			BoyyBond	
Morphine-ADER-IMT (ARYMO™ ER)	Physical and chemical barriers		похувона	
Hydrocodone product				
CEP-33237 (Vantrela [™] ER)	Physical and chemical barriers			
^a Targiniq ER is approved but not currently commercially available in the United States.				

Table 2. Mechanisms of abuse deterrence.

Mechanism	Characteristics
Physical/chemical barriers (may not deter all of these)	Prevent chewing, crushing, cutting, grating, or grinding (physical barrier)
	common solvents (chemical barrier)
Agonist/antagonist combinations Aversion	Addition of a sequestered or non- sequestered opioid antagonist
Delivery system	unpleasant effect after manipulation, after administration by alternate routes (e.g. mucous membrane irritant), or if used at doses higher than those indicated Long-acting injectable or depot formulations
Prodrugs or new molecular entities	Require chemical or enzymatic transformation <i>in vivo</i> to active drug; may
Combination of technologies	pharmacokinetic properties that lower abuse potential Contain ≥2 of the other defined technologies
Novel approaches	Technologies that are not characterized by one of the defined categories (e.g. technology that provides protection against multiple-pill overdose)

Lynn R. Webster, John Markman, Edward J. Cone & Gwendolyn Niebler (2017)

Current and future development of extended-release, abuse-deterrent opioid formulations in the United States,

Postgraduate Medicine, 129:1, 102-110, DOI: 10.1080/00325481.2017.1268902

Immunity for Calling 911 or Seeking Emergency Medical Assistance – Good Samaritan Laws

To encourage people to seek out medical attention for an overdose or for follow-up care after naloxone has been administered, 40 states and the District of Columbia have enacted some form of a Good Samaritan or 911 drug immunity law. These laws generally provide immunity from arrest, charge or prosecution for certain controlled substance possession and paraphernalia offenses when a person who is either experiencing an opiate-related overdose or observing one calls 911 for assistance or seeks medical attention. State laws are also increasingly providing immunity from violations of pretrial, probation or parole conditions and violations of protection or restraining orders.



Naloxone Rescue

How to identify an opioid overdose:

Look for these common signs:

- The person won't wake up even
 if you shake them or say their name
- Breathing slows or even stops
- Lips and fingernails turn blue or gray
- · Skin gets pale, clammy

In case of overdose:

- 1 Call 911 and give naloxone If no reaction in 3 minutes, give second naloxone dose
- 2 Do rescue breathing or chest compressions Follow 911 dispatcher instructions

3 After naloxone

Stay with person for at least 3 hours or until help arrives

How to give naloxone:

There are 3 ways to give naloxone. Follow the instructions for the type you have.

Nasal spray naloxone



6 If no reaction in 3 minutes, give second dose.



Injectable naloxone

Auto-injector

The naloxone auto-injector is FDA approved for use by anyone in the community. It contains a speaker that provides instructions to inject naloxone into the outer thigh, through clothing if needed.



TDH Opioid Outbreak Strategic Map





Public Chapter 1033

Pain Management Clinics transitions from Certificate System to Licensure System:

- Medical director holds license -Non-transferable
- Only a pain specialist is eligible to be medical director
- > 50% of patients being treated for pain qualifies as a pain clinic and must be registered
- No pharmacy
- Clinic can be suspended based on specific violation
 - No new patients
 - Monitored
- Went into effect on July 1, 2017



Controlled Substance Monitoring Database (CSMD): Do all Healthcare Providers have to Register?

"If you provide direct care and prescribe controlled substances to patients in Tennessee for <u>more than 15 days per year</u> or you are a dispenser in practice providing direct care to patients in Tennessee for more than 15 days per year, you are required to register with the Tennessee Controlled Substance Monitoring Database."

https://www.tncsmd.com/TNNewRegistra tion.aspx





TCA 63-1-402 Continuing Education





 On or after July 1, 2014, all shall be required to complete a minimum of two (2) hours of continuing education related to controlled substance prescribing biennially to count toward the licensees' mandatory continuing education.

TCA 63-1-402 Continuing Education



 The continuing education <u>must</u> include instruction in the department's treatment guidelines on opioids, benzodiazepines, barbiturates, and carisoprodol, and may include such other topics as medicine addiction, risk management tools, and other topics as approved by the respective licensing boards.





Steven Boggs, MD, MBA, FASA

sboggs6@uthsc.edu