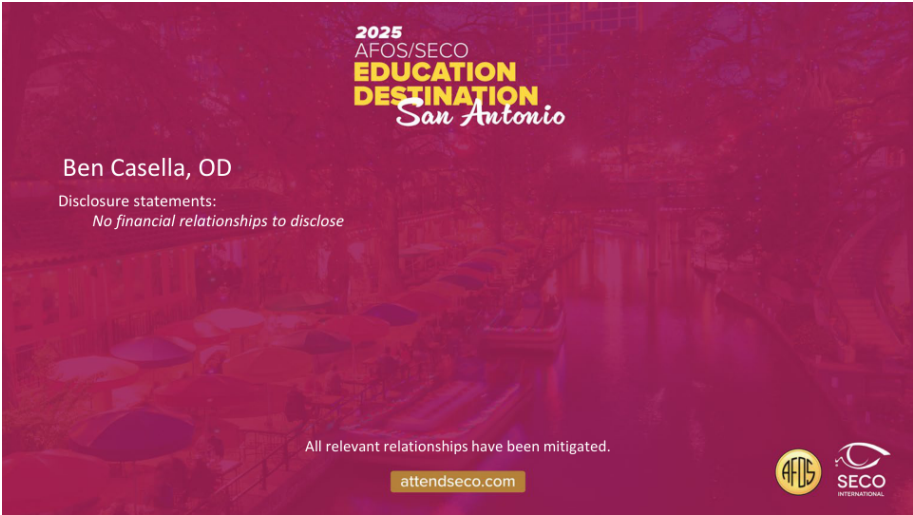


Slide 1



Slide 2



Slide 3

Opioids In Eyecare

Benjamin Casella, O.D., FAAO

Slide 4

Disclosures

- None

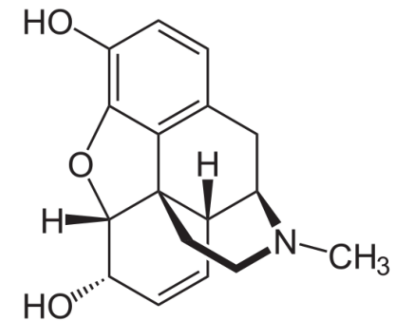
Slide 5

Why opioids?

- Indicated for severe acute pain
- Not intended for a lifetime of use
- Not intended for everyone
- Certainly have their place in healthcare

Slide 6

What are opioids?



Slide 7

What are opioids?

- Drugs that are derived from or mimic naturally occurring chemicals found in the opium poppy plant



Slide 8

- CNS has opioid receptors (in CNS, PNS, GI system) which opioid molecules bind to mimicking morphine
- Indicated mostly for severe pain / anesthesia
- Sometimes used for diarrhea and RLS
- Evidence points to opioids as perhaps no better than placebo for cough
- Side effects include euphoria, depressed respiration, and death

Slide 9

- “Opiate” refers to natural chemicals derived from opium, itself
 - Morphine
- “Opioid” includes synthetic chemicals, as well
 - Oxycodone
 - Fentanyl
 - Hydrocodone

Slide 10

- Opioids preferred for severe acute pain
 - Relatively quick onset
 - Peak around 2 hours
- Risks likely outweigh benefits for chronic pain not due to cancer
 - Recommendation is that caution be taken when Rxing opioids for such
 - Opioid prescription for chronic non-cancer pain is primarily what led to opioid epidemic

Slide 11

Changing Gears

What *is* pain?

Slide 12

Pain: Defined

- usually localized physical suffering associated with bodily disorder (such as a disease or an injury) *the pain of a twisted ankle*; also : a basic bodily sensation induced by a noxious stimulus, received by naked nerve endings, characterized by physical discomfort (such as pricking, throbbing, or aching), and typically leading to evasive action *the pain of bee stings*

Slide 13

The Nature of Pain

- *Acute* pain
 - Comes on suddenly, has a known cause, typically resolves within three months
- *Chronic* pain
 - Pain that persists with a degree of chronicity, typically beyond three months

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The Nature of Pain

- Nociceptive pain
 - Experience related to stimulation of sensory nerves
 - Immediate from a slap, hot object, broken bone, etc.

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The Nature of Pain

- Inflammatory pain
 - From tissue disruption and subsequent immune response
 - Hordeolum, etc.



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The Nature of Pain

- Neuropathy
 - Damaged or diseased nervous system
 - Fibromyalgia, etc.

The Nature of Pain

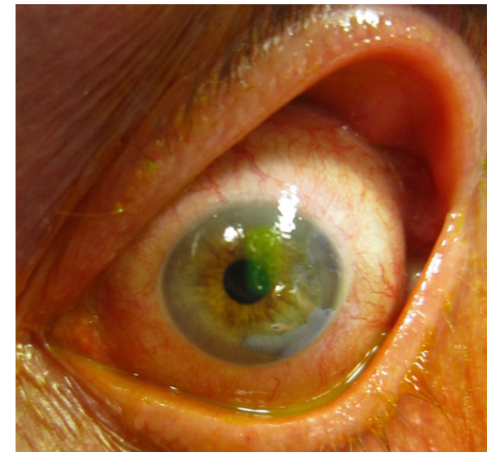
- There is even phantom pain
 - Pain where an amputated limb used to be, etc.
- Breakthrough pain
 - Sudden burst of pain that is beyond the control of a patient's customary pain medications
 - More common in cancer patients

Pain Is Necessary

- Pain experience can lead to better health
 - Pain tells us something is wrong
 - Think of a hot stove or a bug bite

Pain In or Around the Human Eye

- Cornea
 - Density of pain receptors is *hundreds* of times more compared to pain receptors of skin
 - Essential role in the function of the blink reflex
- *Why?*



Slide 21

Corneal Pain

- Abrasion, laceration, etc.
- Disrupts nerves / nerve endings
- Nociceptive pain

Slide 22

Intraocular Pain

- From inflammation or injury
- May also be neuropathic from proximal nerve damage

Slide 23

Retrobulbar Pain

- Typically from inflammation
- May be from infection or injury
- May be neuropathic
- Can be difficult to determine

Slide 24

Non-narcotic Analgesics

- Act on CNS to elevate pain threshold
- Acetaminophen
 - 325-500mg q4-6h
- Tramadol
 - 50-100mg q4-6h
 - Analog of narcotic molecule

Slide 25

Acetaminophen

- Exact mechanism unknown
- Usually safe in pediatric patients
- No cross-over sensitivity with aspirin/NSAIDS
- Antipyretic
- Little to no GI issues
- No effect on platelets
- Seems to be safe short-term in pregnant/nursing patients

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Acetaminophen

- Does have a ceiling effect
- Caution with hepatic disease
- May lead to liver toxicity
- Commonly Rx'd in combination with narcotic (more on this later)

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Narcotics

- Mechanism
 - Bind directly to opioid receptors mimicking morphine (take with food!)
- CNS effects (don't mix with alcohol)
- 5 schedules (Schedule II, III most common)

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Controlled Substance Schedules

- Five schedules
 - Based on several factors, such as...
 - Medicinal value
 - Addictive potential

Schedule I Controlled Substances

- No currently accepted medicinal use in U.S.
- Lack of safety for use under medical supervision
- Potential for abuse is high

Source: www.deadiversion.usdoj.gov

Schedule I Controlled Substances

- Examples:
 - Cannabis
 - Heroin
 - 3,4-methylenedioxymethamphetamine ("Ecstasy")
 - lysergic acid diethylamide (LSD)

Source: www.deadiversion.usdoj.gov

Schedule II Controlled Substances

- Accepted medicinal use in U.S.
- High potential for abuse, may lead to severe psychological/physical dependence
- 2/2N

Source: www.deadiversion.usdoj.gov

Schedule II Controlled Substances

- Examples of narcotics:
 - Oxycodone
 - Opium
 - Methadone
 - Hydrocodone
 - Codeine (more than 90mg per dosage unit)

Source: www.deadiversion.usdoj.gov

Schedule II Controlled Substances

- IIN (2N): stimulants (Rx'd mainly for ADHD, etc.)
 - Amphetamine
 - Methylphenidate
- Seen as non-narcotic

Source: www.deadiversion.usdoj.gov

Controlled Substances Act: Changed

- Effective October 6th, 2014
 - Hydrocodone moved from schedule III to schedule II
 - Legislation fought for and enacted in states for so-called “hydrocodone fix”, so that OD's may continue to provide the care their patients deserve

Schedule II Narcotics

- Vicodin
 - Hydrocodone with acetaminophen
 - 5/500mg, 7.5/750mg (ES), 10/650mg (HP)
 - q4-6h
- Lortab
 - Hydrocodone with acetaminophen
 - 2.5/500mg, 5/500mg, 7.5/500mg, 10/500mg
 - q4-6h

Schedule II Controlled Substances

- Cocaine is schedule II
 - Local anesthetic for some ENT surgeries
 - Any uses in eye care?
 - Still seen as highly addictive

Schedule III Controlled Substances

- Lower potential for abuse relative to Schedules I, II
- Still carry risk of psychological/physical dependence
 - “Low to moderate” physical dependence
 - “High” psychological dependence

Source: www.deadiversion.usdoj.gov

Schedule III Controlled Substances

- Schedule III Narcotics
 - Codeine (not more than 90mg per dosage unit)
 - Buprenorphine
- IIIN/3N
 - Non-narcotic
 - Benzphetamine
 - Anabolic steroids

Source: www.deadiversion.usdoj.gov

Schedule III Controlled Substances

- Tylenol 3
 - 30mg codeine / 300mg acetaminophen
 - q4-6h
 - Codeine frequently causes more nausea than other narcotics
 - Use seems to be decreasing

Codeine With Acetaminophen

- Have different mechanisms of action
 - Combination allows for enhanced pain control
- Codeine can also be combined with aspirin
 - Pain relief and anti-inflammatory effect

Schedule IV Controlled Substances

- Low potential for abuse relative to Schedule III
- Include several anti-anxiety and sedative medications
 - Alprazolam
 - Clonazepam
 - Lorazepam
 - Diazepam

Source: www.deadiversion.usdoj.gov

Schedule V Controlled Substances

- Low potential for abuse relative to Schedule IV
- Mainly medications with limited quantities of narcotics
 - Cough suppressants with no more than 200 mg of codeine per 100 ml or per 100 grams

Narcotics

- Have CNS effects
- Have respiratory effects
- Peak around 2 hours after initial dose
- For severe acute pain
- DO NOT have ceiling effect

Narcotics

- Make Rx “tamper-proof”
- Write out “ten”, etc.

Narcotics

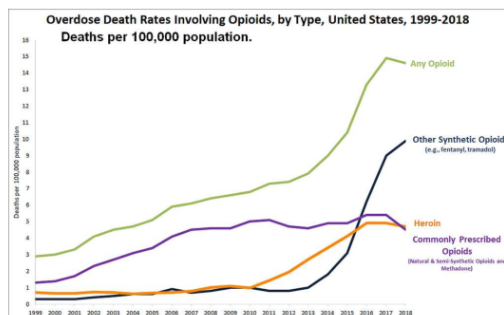
- Adverse effects include
 - Nausea / vomiting
 - Breathing difficulties
 - Euphoria
 - Constipation
 - Pruritis

Narcotics

- Contraindications
 - Hypersensitivity
 - Pregnant (nursing?)
 - COPD
 - Bronchial asthma
 - Caution with renal/hepatic dysfunction
 - Alcoholism
 - Use of other CNS agents

The opioid epidemic

- Still a significant issue in the U.S. and throughout the world



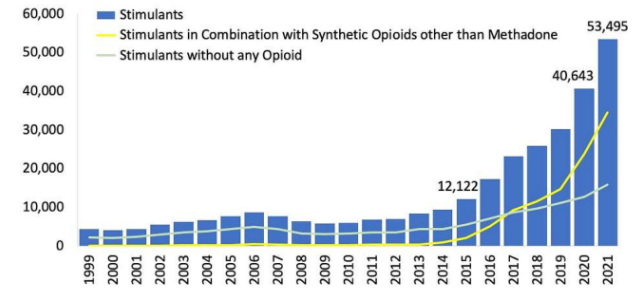
A Clear Problem in the U.S.

- Number of drug overdose deaths in 2016 = 5x 1999
- Over 700,000 deaths since 2000
- 2/3 of all drug overdose deaths in U.S. involve an opioid

Source: www.cdc.gov

- 108,000 people in the U.S. died from a drug overdose in 2022
 - 82,000 involved opioids
 - 76%
- 2022 overdose deaths were 10x what they were in 1999

Figure 6. National Overdose Deaths Involving Stimulants (Cocaine and Psychostimulants*), by Opioid Involvement, Number Among All Ages, 1999-2021

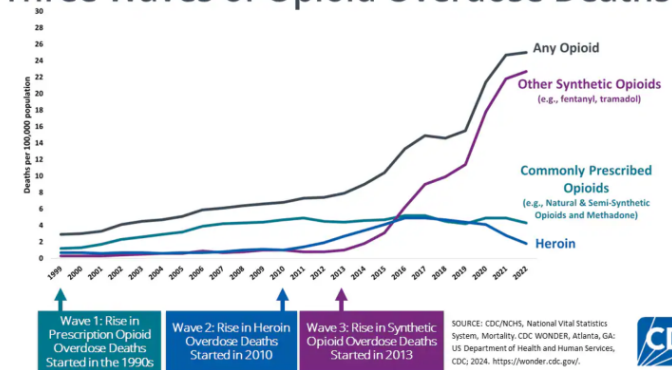


*Among deaths with drug overdose as the underlying cause, the psychostimulants with abuse potential (primarily methamphetamine) category was determined by the T43.6 ICD-10 multiple cause-of-death code. Abbreviated to *psychostimulants* in the bar chart above. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

From 2021 to 2022

- Synthetic opioid related deaths not involving methadone *increased* by 4%
 - Mainly from fentanyl
- Heroin related deaths *decreased* by 36%
- Deaths from prescription opioids *decreased* by 12%

Three Waves of Opioid Overdose Deaths



A Clear Problem

- From 1999-2010, amount of opioids sold (legally) increased four-fold
- However, amount of pain reported by Americans stayed relatively flat
- Opioid deaths *also* quadrupled

Source: www.cdc.gov

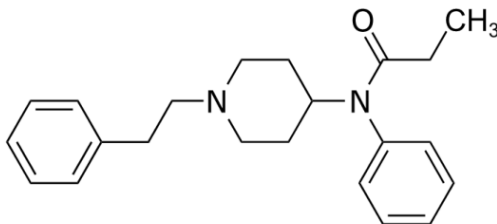
“Gateway” Drugs

- Heroin use has also increased in this same time period
- Approximately *three fourths* of new heroin users report using prescription opioids prior to trying heroin
- Heroin is currently cheaper and more available in U.S. than before

Source: www.cdc.gov

Fentanyl

- Synthetic opioid sometimes added to heroin
 - *With or without* the heroin user’s knowledge



A Clear Problem

- 2010-2016 saw a *five-fold* increase in heroin related deaths
- 2015: *9580* prescription synthetic opioid (besides methadone) related deaths
- 2016: number increased to *19,413* (fentanyl is a large contributor)

Source: www.cdc.gov

A Clear Problem

- 2013 – almost 250,000,000 prescriptions written in U.S. for opioids
- Alabama had highest rate; Hawaii the lowest
- What is the U.S. population???

Sudden Jump In Overdose Death Rates

2015-2016:

Washington D.C.: 108.6% increase

Florida: 56.3% increase

Maryland: 58.9% increase

New Jersey: 42.3% increase

Prescribing Rates

- 2012: 81.3 prescriptions dispensed per 100 persons in U.S.
- 2016: 66.5 prescriptions dispensed per 100 persons in U.S.
- 2016: ¼ of U.S. counties had enough opioid prescriptions for every resident

Who is more likely to die from overdose?

Who?

- Highest rates among ages 25-54
- Higher rates among males (but difference getting smaller)
- Higher among non-Hispanic whites compared to non-Hispanic blacks or Hispanics

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Detecting and Combating Abuse

- Again, it's about the journey
 - BOTH ways

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We Have Resources Available

- CDC Guideline for Prescribing Opioids for Chronic Pain
 - 224 people died per day in opioid-related overdoses in 2022
 - More prescribing guidance is needed for clinicians
 - When to initiate opioid therapy, when to discontinue, etc.

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CDC Guidelines

- How is progress assessed and reassessed?
- How and when is discontinuation considered, undertaken?
- How is the proper medication chosen (and what dose)?

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CDC Guidelines

- A team approach is necessary
 - The clinician and patient must work together when assessing risks and benefits of opioid use

CDC Guidelines

- CDC Recommendations
 - Twelve principle recommendations borne out of CDC Guideline

CDC Recommendations

- Opioids not first-line therapy
 - Non-pharmacologic therapy and non-opioid pharmacologic therapy preferred as first-line
 - Benefits must outweigh risks for opioid to be deemed necessary to alleviate pain
 - If opioid deemed necessary, combine with non-opioid medication as appropriate

CDC Recommendations

- Establish Goals
 - Prior to starting opioid therapy
 - Should be realistic and be used to assess treatment of pain and function of the patient
 - Should be used to help determine if benefits are still outweighing risks (i.e., is therapy improving pain?)

CDC Recommendations

- Risks / benefits should be discussed
 - Prior to starting opioid therapy
 - Known risks should be discussed
 - Benefits of opioid therapy should be realistic

CDC Recommendations

- Immediate-release opioids should be used when starting therapy
 - As opposed to opioids that are “extended-release” or “long-acting”
 - Immediate-release (or “short-acting”) opioids include formulations of codeine, hydrocodone, and oxycodone
 - Various immediate-release opioids are also available as extended-release

CDC Recommendations

- Prescribe lowest effective dose
 - Caution must be used with *any* dose
 - Reassess cost/benefit when raising dosage to >/ 50 MME/day
 - Avoid increasing to >/90 MME/day or carefully titrate to that level if necessary
 - MME = morphine milligram equivalents
 - Used as a metric to gauge abuse and overdose potential

CDC Recommendations

- Prescribe short duration of therapy for acute pain
 - Long-term use typically starts with treatment of acute pain
 - Prescribe no greater quantity than should be used for treatment of acute pain (using lowest effective dose and immediate-release opioids)
 - Three days or less often sufficient
 - More than one week of opioid therapy rarely needed for treatment of acute pain

CDC Recommendations

- Frequently re-evaluate benefits/harms
 - Important for treatment of chronic pain
 - Within 1-4 weeks of start of opioid therapy for chronic pain (or after increasing dosage)
 - Re-evaluate for continued therapy every three months (or more)
 - Work towards tapering or discontinuing opioid therapy if feasible

CDC Recommendations

- Use strategies to mitigate risk
 - Consider offering naloxone when higher risk of overdose is present (i.e., history of overdose, increased dosage, concurrent benzodiazepine use)

CDC Recommendations

- Review Prescription Drug Monitoring Program data
 - PDMP: statewide electronic database that tracks all prescriptions of controlled substances
 - Determine if a patient is receiving dosages that may increase risk of overdose
 - Review when starting opioid therapy for chronic pain and re-evaluate periodically

CDC Recommendations

- Urine drug testing
 - Recommended prior to starting opioid therapy for chronic pain
 - Consider at least annual testing to assess for opioid use and illicit drug use

CDC Recommendations

- Avoid concurrent opioid and benzodiazepine prescribing whenever possible
 - Benzodiazepine: sedative used often to treat anxiety, insomnia

CDC Recommendations

- Offer to treat opioid use disorder
 - Typically medication-based treatment (methadone, buprenorphine) combined with behavioral therapy

Recognizing Abuse

- Tolerance
 - Body's response to chronic use
 - Think about alcohol and nicotine
 - Physical dependence, more readily recognized if therapy stopped abruptly

Source: www.mayoclinic.org

Recognizing Abuse

- Addiction
 - May involve physical dependence
 - Continuous seeking out of a drug
 - Continuous abuse even though life is being made worse by abuse

Source: www.mayoclinic.org

When To Be Wary

- Signs and symptoms don't match
- Evidence of "doctor shopping"
- Careful history is always key (and never stops until the exam is over)

When To Be Wary

- Be engaging, not dismissive
- 53yo female with fiberglass in eye immediately asked me for opioid Rx
 - Had fiberglass inside eye
 - ER doctor was immediately dismissive after figuring out she was an addict (and subsequently missed the foreign body)

When To Be Wary

- Early / frequent calls for refills
- Patient seems to already know what dosage works and disputes Rx
- Symptoms of withdrawal present

Recognizing Withdrawal

- Muscle pain
- Increased lacrimation
- Increased sweating
- Anxiety / irritability
- Restlessness
- Increased heart rate

Recognizing Withdrawal

- Hypertension
- Diarrhea
- Nausea / vomiting
- Goosebumps / chills
- Dilated Pupils
- Shakiness

May be an urgency / emergency

Recognizing Overdose

- Depressed respiration
- Confusion / mood change
- Pupillary miosis
- Constipation (may be severe)
- Nausea / vomiting
- Lethargy
- Decreased skin color / blue skin from poor circulation

Recognizing Overdose

- Medical emergency
- Activate emergency medical care system
- Returning to proper respiration of utmost importance
- Increasing evidence supporting naloxone to treat overdose

Treatment for Overdose

- Naloxone
 - Becoming more common
 - Reverses chemical effects of opioids
- Some states beginning to distribute
- Some states: immunity laws in place - encourage people to seek help for themselves/others experiencing overdose

Treatment of Abuse

- People typically do not seek treatment for abuse by themselves
- Primary care providers positioned to detect and refer
- Opioid use disorder must be treated as a medical condition

Source: www.cdc.gov

Treatment of Abuse

- Proper care is multifactorial
 - Medical therapy with prescription drugs often necessary
 - Methadone, etc.
 - Mental health care is important
 - Behavioral therapy is important
 - Long-term therapy involves patient recognizing cravings and learning to cope

Resources



Resources

- U.S. Dept. of HHS
 - HHS Opioid Initiative www.hhs.gov/opioids/
 - Agency for Healthcare Research and Quality www.AHRQ.gov
 - Centers for Disease Control and Prevention www.cdc.gov
 - U.S. Food and Drug Administration www.fda.gov
 - Substance Abuse and Mental Health Services Admin. www.samhsa.gov