Course # 145

SECO2026
THE EDUCATION DESTINATION™

Opioids in Eye Care

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Disclosure statements:

No financial relationships with ineligible companies to disclose.

All relevant relationships have been mitigated.

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Opioids In Eyecare

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Disclosures

- None

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Why opioids?

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

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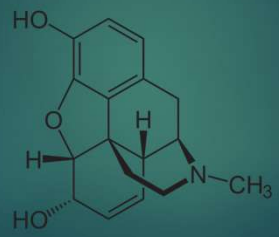
What are opioids?



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What are opioids?

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

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- 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

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

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- 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

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Changing Gears

What *is* pain?

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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*

www.merriam-webster.com/dictionary/pain

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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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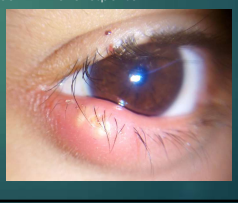
The Nature of Pain

- 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.

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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

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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

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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?*

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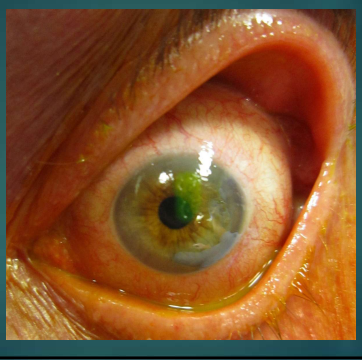

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Corneal Pain

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

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Intraocular Pain

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

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Retrobulbar Pain

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

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Non-narcotic Analgesics

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

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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

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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

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Schedule I Controlled Substances

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

Source: www.deadiversion.usdoj.gov

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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

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Schedule II Controlled Substances

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

Source: www.deadiversion.usdoj.gov

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Schedule II Controlled Substances

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

Source: www.deadiversion.usdoj.gov

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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

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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

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Schedule II Controlled Substances

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

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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

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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

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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

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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

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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

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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

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Narcotics

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

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Narcotics

- Make Rx "tamper-proof"
- Write out "ten", etc.

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Narcotics

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

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Narcotics

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

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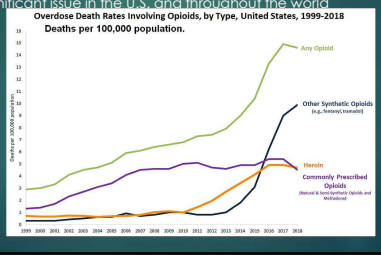
The opioid epidemic

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



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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

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- 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

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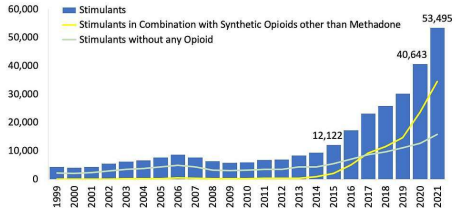
Figure 6. National Overdose Deaths Involving Stimulants (Cocaine and Psychostimulants*), by Opioid Involvement, Number Among All Ages, 1999-2021



*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.

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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%

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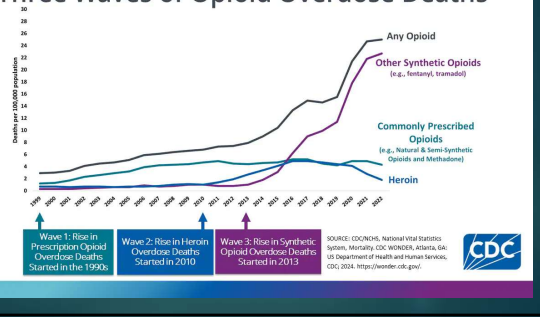
Three Waves of Opioid Overdose Deaths



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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

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"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

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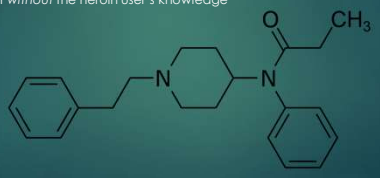
Fentanyl

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



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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

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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???

Source: www.cdc.gov

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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

Source: www.cdc.gov

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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

Source: www.cdc.gov

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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
  - 224people 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

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CDC Guidelines

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

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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

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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?)

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CDC Recommendations

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

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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

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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

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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

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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

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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)

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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

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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

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CDC Recommendations

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

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CDC Recommendations

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

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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

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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

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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)

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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)

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When To Be Wary

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

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Recognizing Withdrawal

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

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Recognizing Withdrawal

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

May be an urgency / emergency

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Recognizing Overdose

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

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Recognizing Overdose

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

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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

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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

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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

Source: www.cdc.gov

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Resources

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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

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