Morphine Myths: Important Tools for End of Life

Katheryn J. Lauer, MD/MPH
Virginia Mason Yakima Memorial Compass Care
Hospice & Palliative Medicine

Objectives

- Understanding the cultural context of opiates
- Demystifying the use of opiates in end-of-life care
- Understanding opiate use for ancillary effects
- Treatment of undesired effects of opiates

A Brief History of Opiates

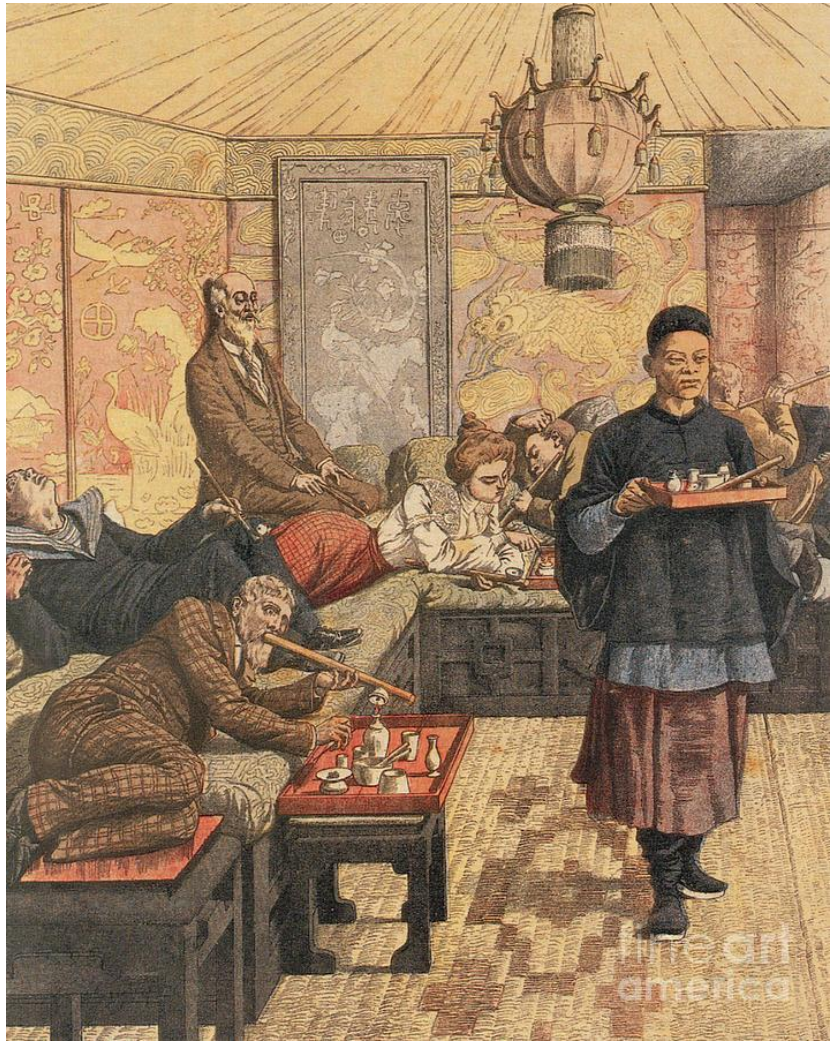
- Derivative of the opium poppy (*Papaver somniferum*)

- First documented medical use of opium on Sumerian clay tablets (3400 BCE)

A Brief History of Opiates

- Opium began being widely traded in the 1800s for recreational use

- Morphine was first created in 1803 as an extract from opium resin



A Brief History of Opiates

- Heroin first distilled from morphine in 1874

- Abuse potential of heroin recognized in 1924 and made a controlled substance

Regulation of Opiates

- DEA Drug Schedules
  - five categories
  - based on acceptable medical use
  - takes into account abuse/dependency potential

Regulation of Opiates

- Schedule I- no currently accepted medical use and high abuse potential (heroin)

Regulation of Opiates

- Schedule I- no currently accepted medical use and high abuse potential (heroin)
- Schedule II- high potential for abuse or dependency, but accepted medical use (most opiates)

Regulation of Opiates

- Schedule I- no currently accepted medical use and high abuse potential (heroin)
- Schedule II- high potential for abuse or dependency, but accepted medical use (most opiates)
- Schedule III-V- lower abuse potential, accepted medical use (low dose formulations of opiates)

A Brief History of Opiates

- Ongoing development of opium derivatives
  - morphine/MS Contin
  - oxycodone/Oxycontin
  - Fentanyl (Duragesic)
  - Hydromorphone (Dilaudid)
  - Methadone

A Brief History of Opiates

- Ongoing development of opium derivatives
  - Codeine/hydrocodone (Vicodin/Norco)
  - Meperidine (Demerol)
  - Tramadol (Ultram)

The Opioid Crisis (20th Century)

- In first half of 20th century, pain was considered an existential problem
- Complaints of pain were considered hysterical complaints
- Abuse of heroin led to regulation and increased fear of use of opiates

The Opioid Crisis (1980s)

- Until 1980s, official recommendation was for cancer patients to avoid or wean opiates until their “life could be measured in weeks”
- Studies into the 1990s suggest a fear and avoidance of opiates for any reason by physicians, due to abuse potential

The Opioid Crisis (1980s)

- WHO in 1986 reported under-treatment of post-operative and cancer pain
- Suggested opiates as a valid and effective means to treat

World Health Organization

The Opioid Crisis (1990s)

- Studies reported that use of opiates for pain is “unlikely to result in addiction”
- Encouraged use of opiates for acute pain (injuries/illnesses)

The Opioid Crisis (1990s)

- Studies reported that use of opiates for pain is “unlikely to result in addiction”
- Encouraged use of opiates for acute pain (injuries/illnesses)

...And chronic pain

The Opioid Crisis (1990s)

- In 1995, the American Pain Society introduced pain as “the fifth vital sign” with help from….
  - The Joint Commission
  - Veterans Administration
  - Pharmaceutical companies

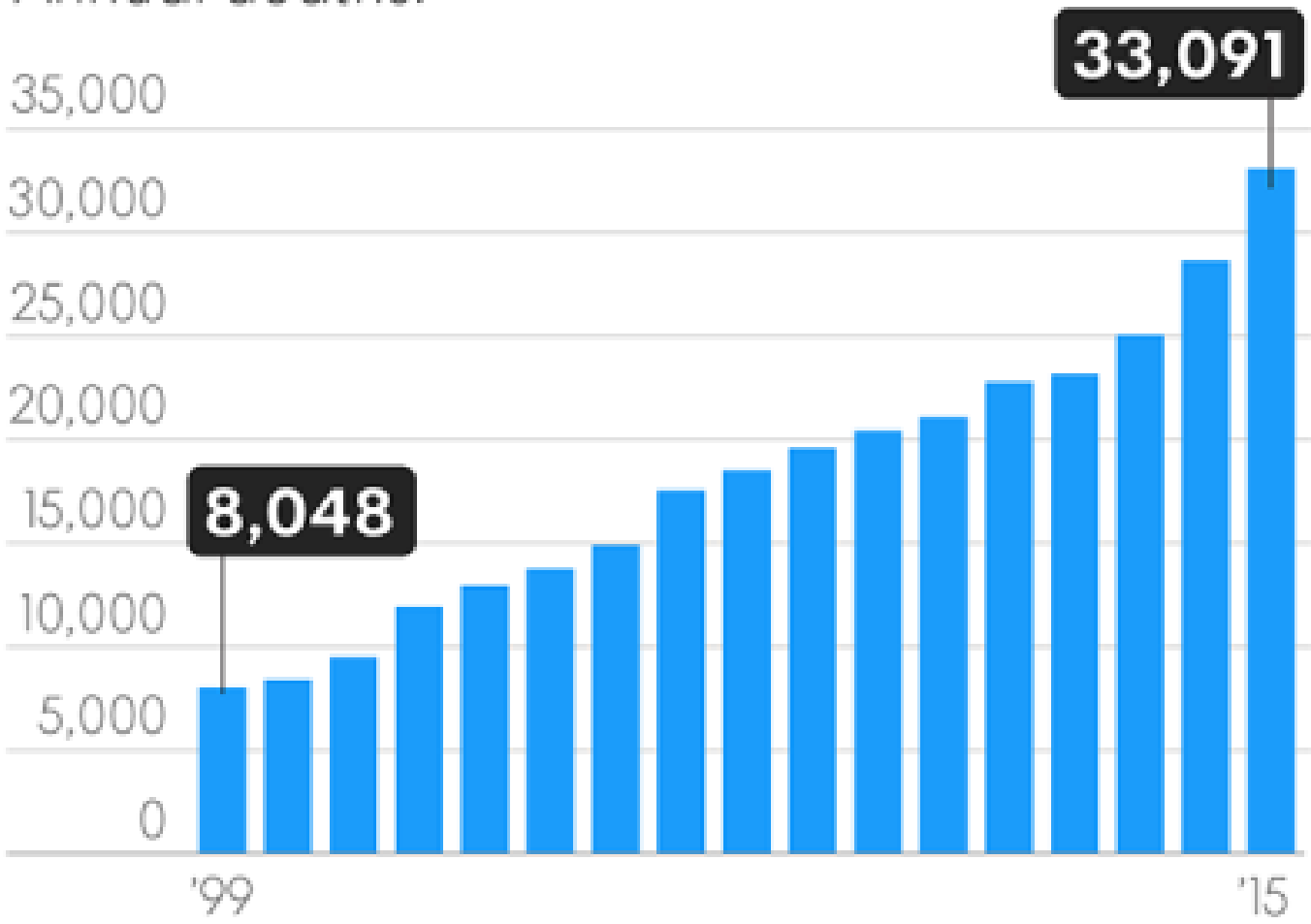
- Not treating any reported pain was labeled as “inhumane”

The Opioid Crisis (2000s)

- Massive increase in prescriptions for opiates for all indications
- Increase in abuse, dependence, addiction and deaths from overdose
- Management of chronic pain did not improve
- Labeled a public health emergency by the CDC in 2017

MORE DEATHS FROM OPIOID ABUSE

American deaths from overdoses of opioid drugs increased 311% from 1999 to 2015.
Annual deaths:



SOURCE National Institute on Drug Abuse
George Petras, USA TODAY

USA TODAY

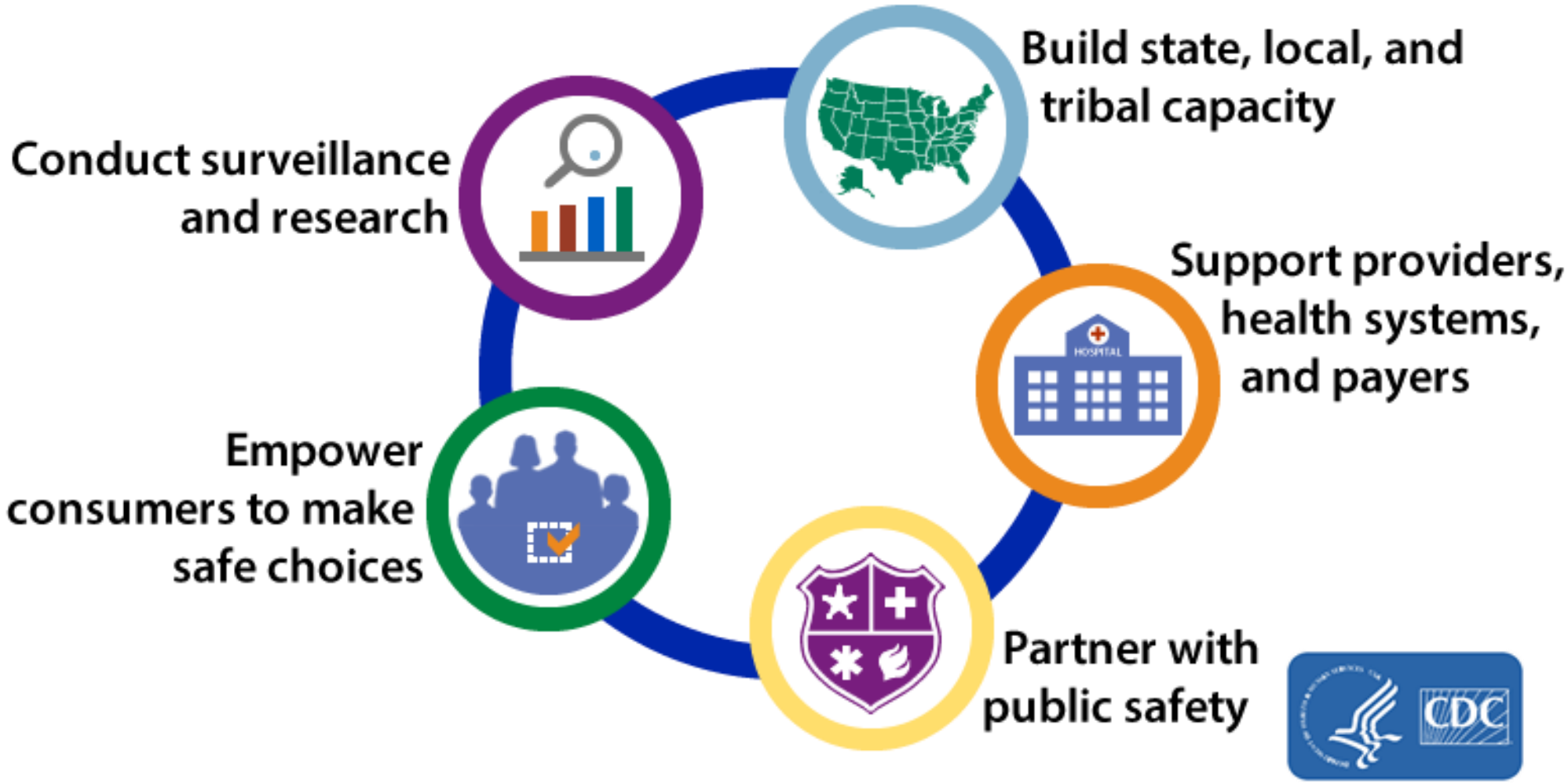
Risk of Opiate Overdose

- Greatly increased if medications are combined
  - Vast majority of fatal overdoses from opiates also had benzodiazepines and alcohol in their system
- Increased if taking a prescription medication that belongs to someone else
- History of substance abuse
- History of depression

Response to Opioid Crisis

- Monitoring prescriptions via Prescription Drug Monitoring Databases
- Teaching physicians alternative methods of treating acute and chronic pain in the community
- Educating community on risks of opioid medication treatment
- Developing interdisciplinary models for chronic pain programs

Preventing Opioid Overdoses and Related Harms



Response to Opioid Crisis

- **NOT** avoiding opiates at all costs
- **NOT** limiting access to appropriate use of opiates in cancer-related pain or end of life symptom management
- **NOT** punishing patients or physicians

Opiates in End of Life Care

- Not anticipating long term, chronic use
- Not anticipating that pain will resolve or stabilize
- Minimal concern for addiction

Opiates in End of Life Care

- Not anticipating long term, chronic use
- Not anticipating that pain will resolve or stabilize
- Minimal concern for addiction

What is addiction?


I love the smell of socially acceptable chemical dependence in the morning.
Unknown
wordables.

Tolerance

An adaptive state that develops from repeated drug administration, which results in increasing doses of medicine being needed to give the same result

Dependence

An adaptive state that develops from repeated drug administration, and which results in withdrawal upon cessation of drug use

Abuse

A pattern of repeated drug or alcohol use that often interferes with health, work, or social relationships

Addiction

A **chronic, relapsing disorder** characterized by compulsive drug seeking, continued use despite harmful consequences, and long-lasting changes in the brain

Addiction

A chronic, relapsing disorder characterized by **compulsive drug seeking**, continued use despite harmful consequences, and long-lasting changes in the brain

Addiction

A chronic, relapsing disorder characterized by compulsive drug seeking, continued use despite **harmful consequences**, and long-lasting changes in the brain

Addiction

A chronic, relapsing disorder characterized by compulsive drug seeking, continued use despite harmful consequences, and l**ong-lasting changes** in the brain

Opiates in End of Life Care

- Treatment of pain
- Use of opiates for ancillary effects
- Variety of effective delivery methods

Opiates in End of Life Care

- Few adverse effects, compared to alternatives
  - NSAIDs (ibuprofen, naproxen, aspirin)- limited use in heart disease, gastrointestinal disease and renal failure
  - Steroids (prednisone, dexamethasone)- limited use in gastrointestinal disease, many potential adverse effects
  - Acetaminophen (Tylenol)- limited use in liver disease
  - Adjunct medications (gabapentin, depakote)- many potential adverse effects

Opiate Formulations

- Oral
- Buccal (through cheek/tongue)
- Rectal
- Transdermal (patches)
- IV
- Intramuscular (ouch!)
- Subcutaneous (under the skin)
- Intrathecal (into the space around the spinal cord)
- Inhaled
- Topical and into wound bed

Opiate Formulations

- Long acting
  - Oxycontin
  - MS Contin
  - Fentanyl patches
  - Methadone
- Short acting
  - Oxycodone
  - Morphine
  - Hydromorphone
  - Fentanyl (oral/IV)

Opiate Formulations

- Long acting
  - Oxycontin
  - MS Contin
  - Fentanyl patches
  - Methadone
- Short acting
  - Oxycodone
  - Morphine
  - Hydromorphone
  - Fentanyl (oral/IV)
- Continuous (IV/subcutaneous)
  - Morphine
  - Hydromorphone
  - Fentanyl
  - Methadone

Long acting Opiates

- Constant pain
- Frequent use of short acting opiates
- Pain that is worse upon waking
- Pain that is unlikely to decrease suddenly

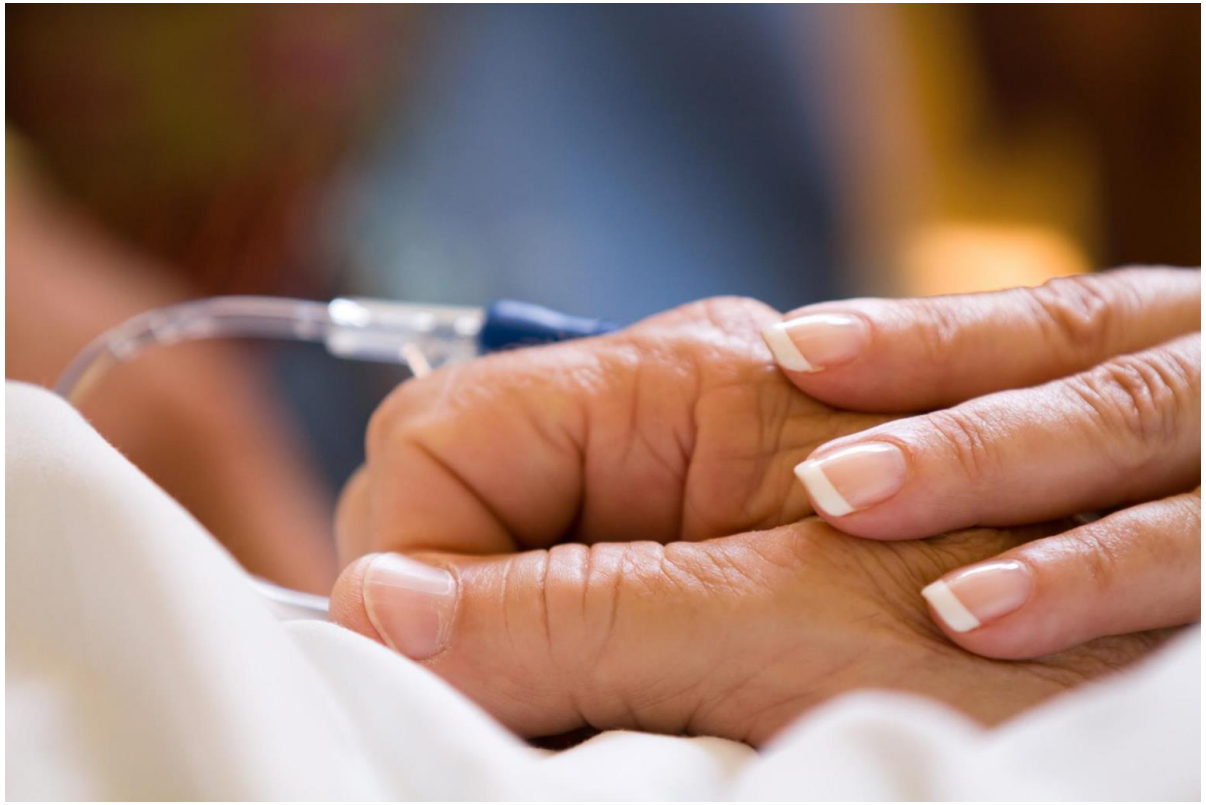
Short acting Opiates

- Breakthrough pain (with use of a long acting)
- Occasional pain
- Pain that is changing/decreasing (injuries, fractures)

Ancillary Effects of Opiates

- Decreased respiratory drive
- Constipation
- Urinary retention
- Confusion/euphoria

- Opiate toxicity



Decreased Respiratory Drive

- Effect varies from person to person
- Effect varies from drug to drug
- Tolerance can develop
- Dose dependent

Decreased Respiratory Drive Benefits

- Very effective in treating shortness of breath (not hypoxia)
- Any opiate works (especially short acting)
- More effective than lorazepam at treating air hunger
- Studies mixed at best showing that inhaling opiates better at treating shortness of breath than oral

Decreased Respiratory Drive Treatment

- Naloxone (Narcan) can be used to reverse this (CAUTION!)
- Holding medication also effective
- Pushing fluids, if possible/desired
- Education of patient, family, staff

Constipation

- 100% of patients on opiates develop this
- 100% of opiates cause this
- No tolerance develops
- Not dose dependent
- Slows transit (no “push”)

Constipation Benefits

- Can be useful in cases where disease causes fast transit
  - some cancers
  - short gut syndrome
  - **NOT** C. difficile

Constipation Treatment

- Does not respond to fiber, diet, increased water
- Does not respond to stool softeners (docusate/Colace)
- Must use an agent that gives some “push”
  - senna
  - bisacodyl
  - polyethylene glycol
  - Magnesium
- Can also use methylnaltrexone (Relistor)

Urinary Retention

- Effect varies from person to person
- Effect varies from drug to drug
- Tolerance can develop
- Dose dependent
- More common in older patients
- More likely when also using benzodiazepines, anti-psychotics, antidepressants or some hypertension medications

Urinary Retention Benefits

- Opiates classically used to treat bladder spasms (B&O suppositories)
  - Indwelling catheter use
  - Bleeding in the urinary tract
  - Cancer of the urinary tract

Urinary Retention Treatment

- Indwelling catheter
- Minimize other medications that may cause retention
- Ensure constipation is treated
- Decrease opiate dose
- Rotate to another opiate

Confusion/Euphoria

- Psychomotor depression (“downer”)
- Street value of opiates
- Abuse and diversion
- Chemical coping

Confusion/Euphoria

- Varies based on route
  - snorting
  - injecting quickly
- Tolerance develops
- Dose dependent
- Varies based on drug
  - Heroin, hydrocodone more euphoric
  - Fentanyl, hydromorphone euphoric when injected
  - Methadone, morphine, oxycodone less euphoric

Confusion/Euphoria Treatment

- Likely to abate over time (tolerance)
- Encourage fluids
- Rotate to another opiate
- Minimize other medications that may cause confusion

Opiate Toxicity

- Doses escalated quickly
- Started at too high dose
- Progressive renal failure
  - very common at end of life
  - may have to decrease dose to make up for kidneys not clearing

Opiate Toxicity Symptoms

- Escalating pain
- Hyperalgesia (pain all over)
- Confusion
- Twitching

Opiate Toxicity Treatment

- Decrease dose
- Switch to another opiate
- Fluids
- Lorazepam (for twitching)

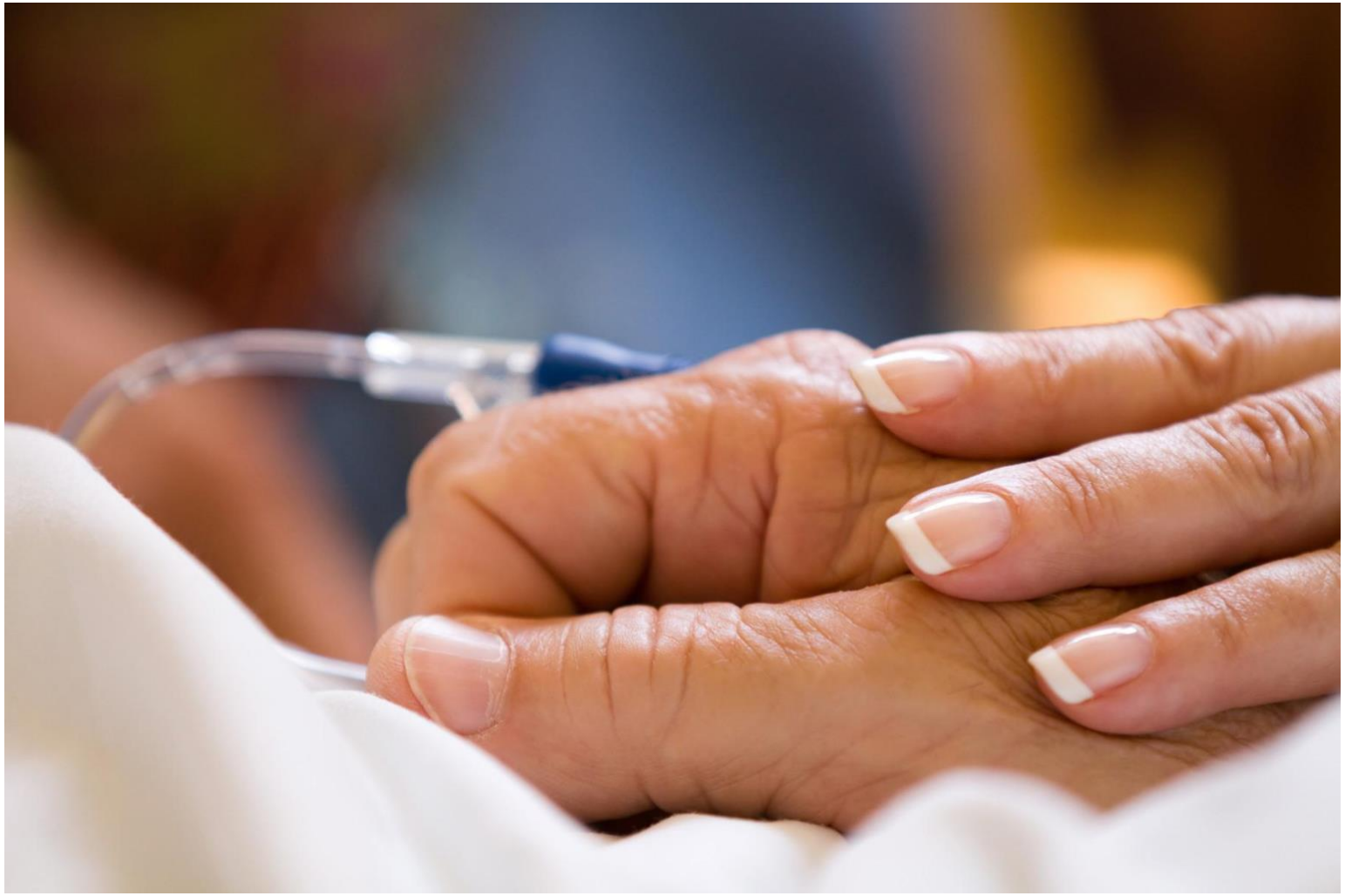
History

Current Context

Opiates at End of Life

Appropriate Use of Opiates

Ancillary Effects of Opiates



Questions?

References

- Norn S, Kruse PR, Kruse E.[History of opium poppy and morphine]. an Medicinhist Arbog. 2005;33:171-84.
- https://www.deamuseum.org/ccp/opium/history.html
- Jones MR, Viswanath O, Peck J. A Brief History of the Opioid Epidemic and Strategies for Pain Medicine. Pain Ther. 2018 Jun; 7(1): 13–21.
- WHO . Cancer pain relief. Geneva: WHO; 1986.
- https://www.who.int/substance_abuse/information-sheet/en/

References

- https://www.cdc.gov/opioids/strategy.html
- Verhamme KM, Sturkenboom MC. Drug-induced urinary retention: incidence, management and prevention. Drug Safety, 2008; 31 (5): 373-88.
- D Doyle. Oxford textbook of Palliative Medicine, Third Edition. Oxford University Press, 2005