Opioids for Pain Management in the Emergency Department

Concerns and Challenges

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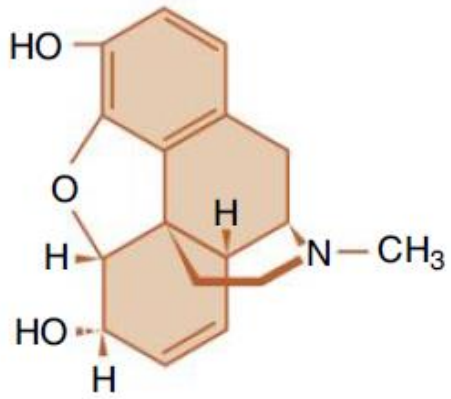
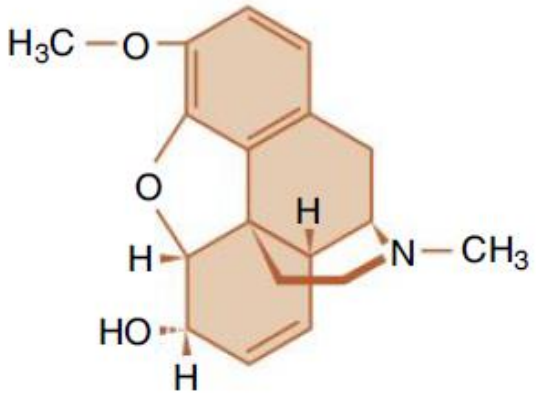
INTRODUCTION

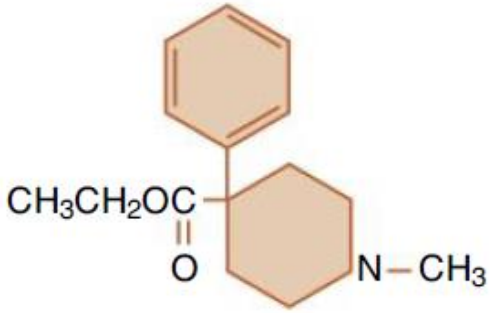
- Opioids remain the mainstay of ED treatment for severe pain.
- Most of opioids are morphine-like alkaloids.
- Many commonly used semi-synthetic opioids are created by simple modification of the morphine molecule.
- Codeine, for example, is the 3-methyl derivative of morphine.



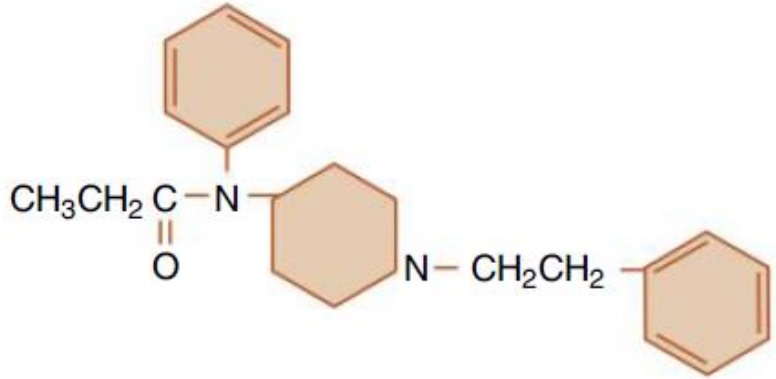
Morphine



Codeine



Meperidine



Fentanyl

MECHANISM

- Interacting with opioid receptors.
- Binding of opioid agonists with the receptors → Hyperpolarization of the cell → reduction of neuronal excitability
- Three classical opioid receptors have been identified:
  - **Mu (μ)**
  - **kappa**
  - **Delta**

Table 9.2 A Summary of Selected Features of Opioid Receptors

Feature	Mu (μ)	Delta (δ)	Kappa (κ)
Tissue bioassay[a]	Guinea pig ileum	Mouse vas deferens	Rabbit vas deferens
Endogenous ligand	β-Endorphin	Leu-enkephalin	Dynorphin
	Endomorphin	Met-enkephalin	
Agonist prototype	Morphine	Deltorphin	Buprenorphine
	Fentanyl		Pentazocine
Antagonist prototype	Naloxone	Naloxone	Naloxone
Supraspinal analgesia	Yes	Yes	Yes
Spinal analgesia	Yes	Yes	Yes
Ventilatory depression	Yes	No	No
Gastrointestinal effects	Yes	No	Yes
Sedation	Yes	No	Yes

- Opioids exert their therapeutic effects at multiple sites.
- Inhibit the release of substance P from primary sensory neurons in the dorsal horn of the spinal cord
- Brainstem: modulate nociceptive transmission in the dorsal horn of the spinal cord through descending inhibitory pathways
- Forebrain: change the affective response to pain

CLINICAL PHARMACOLOGY

PHARMACOKINETICS

- Pharmacokinetic differences are the primary basis for the rational selection and administration of opioids.

- METABOLISM

- In general, opioids are metabolized by the hepatic microsomal system.

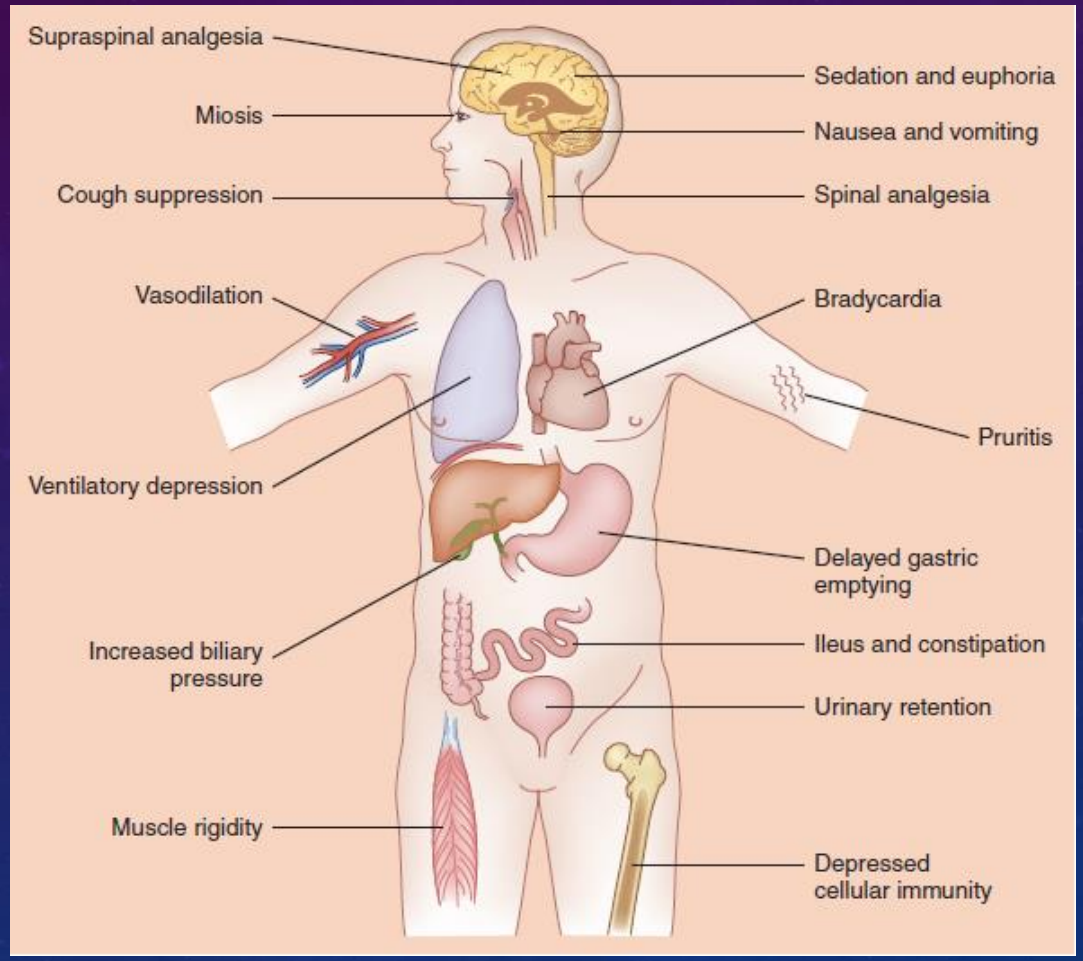
- For some drugs hepatic conjugation and subsequent excretion by the kidney are important.

PHARMACODYNAMICS

- In most respects, the mu agonist opioids can be considered pharmacodynamic equals with important pharmacokinetic differences.

- Pharmacodynamic differences do exist with nonopioid receptor mechanisms such as histamine release.

MAJOR PHARMACODYNAMIC EFFECTS OF OPIOIDS



- Depending on the clinical circumstances and clinical goals of treatment, some of these widespread effects can be viewed as **therapeutic** or **adverse**.

THERAPEUTIC EFFECTS

- Relief of pain
- Drowsiness
- Suppression of cough reflex

- Mu agonists are most effective in treating “second pain” sensations carried by slowly conducting, unmyelinated C fibers; they are less effective in treating “first pain” sensations (carried by small, myelinated A-delta fibers) and neuropathic pain.

- Other sensory modalities are not affected (e.g., touch, temperature, …).

- Opioids do not produce amnesia.

- **Opioids do not have ceiling effect for their analgesic properties.**

- The adverse effects limit their doses.

ADVERSE EFFECTS

- Respiratory depression
- Cardiovascular depression
- Muscle rigidity
- Nausea and vomiting
- Pupillary constriction
- Gastrointestinal effects
- Urologic effects
- Depression of cellular immunity

- **Respiratory depression**

- Primarily:
  - Respiratory rate decreases.
  - Tidal volume slightly increases.

- As the opioid concentration is increased, the respiratory rate and tidal volume progressively decrease, eventually culminating in an irregular ventilatory rhythm and then complete **apnea**.

- **Risk factors for ventilatory depression:**
  - Large opioid dose
  - Advanced age
  - Concomitant use of other central nervous system depressants
  - Renal insufficiency (for morphine)
  - Natural sleep

OPIOID MEDICATIONS

- Various opioid medications are available:
  - Morphine
  - Codeine
  - Hydromorphone
  - Fentanyl
  - Oxymorphone
  - Hydrocodone
  - Oxycodone
  - Methadone
  - Meperidine (Pethidine)

Morphine

- Intravenous (IV) morphine is the standard treatment.
- Morphine 0.1 mg/kg as an initial bolus has been found to be safe but may not be adequate in some patients.
- Dose range of IV morphine: 0.05-0.2 mg/kg
- **The 0.2 mg/kg dose should not be used as the initial bolus dose.**
- Peak effect: 15-20 min

- METABOLISM:
  - Morphine 3-Glucuronide: Main metabolite, Pharmacologically inactive
  - Morphine 6-Glucuronide: 10% of metabolism, Pharmacologically active

- Metabolites are excreted via the kidney
- M6G accumulation

Meperidine (Pethidine)

- Meperidine sometimes causes excitation of the CNS, characterized by tremors, muscle twitches and seizures.
- These adverse effects are largely due to accumulation of a metabolite, **normeperidine**.

- Meperidine has well-known **local anesthetic properties**.

- Bolus dose of 50-100 mg IV → variable degrees of pain relief

- Potency: 0.1 of Morphine
- 100 mg Petidine ≈ 10 mg Morphine

- **Most EDs have eliminated the use of meperidine.**

CONCERNS AND CHALLENGES

- DEPENDENCE
- TOLERANCE
- ADDICTION
- PSEUDOADDICTION

DEPENDENCE

- Physical dependence is defined as a state of adaptation that is manifested by a drug class-specific withdrawal syndrome that can be elicited by
  - Abrupt cessation
  - Rapid dose reduction
  - Decreasing blood level of the drug
  - Administration of an antagonist

TOLERANCE

- Tolerance describes the phenomenon that
  - the magnitude of a given drug effect decreases with repeated administration of the same dose, or
  - increasing doses are needed to produce the same effect.

TOLERANCE ≠ DEPENDENCE

- They are inherent property of opioids.

ADDICTION

- Addiction is a behavioral syndrome characterized by
  - Evidence of psychological dependence (craving)
  - Uncontrolled/ compulsive drug use despite harmful side effects
  - Other drug-related aberrant behavior (e.g., altering prescriptions, manipulating healthcare providers, drug hoarding or sales, unsanctioned dose escalation).

- The prevalence of opioid addiction is up to 34% in patients with chronic nonmalignant pain and about 8% in patients with cancer pain

PSEUDOADDICTION

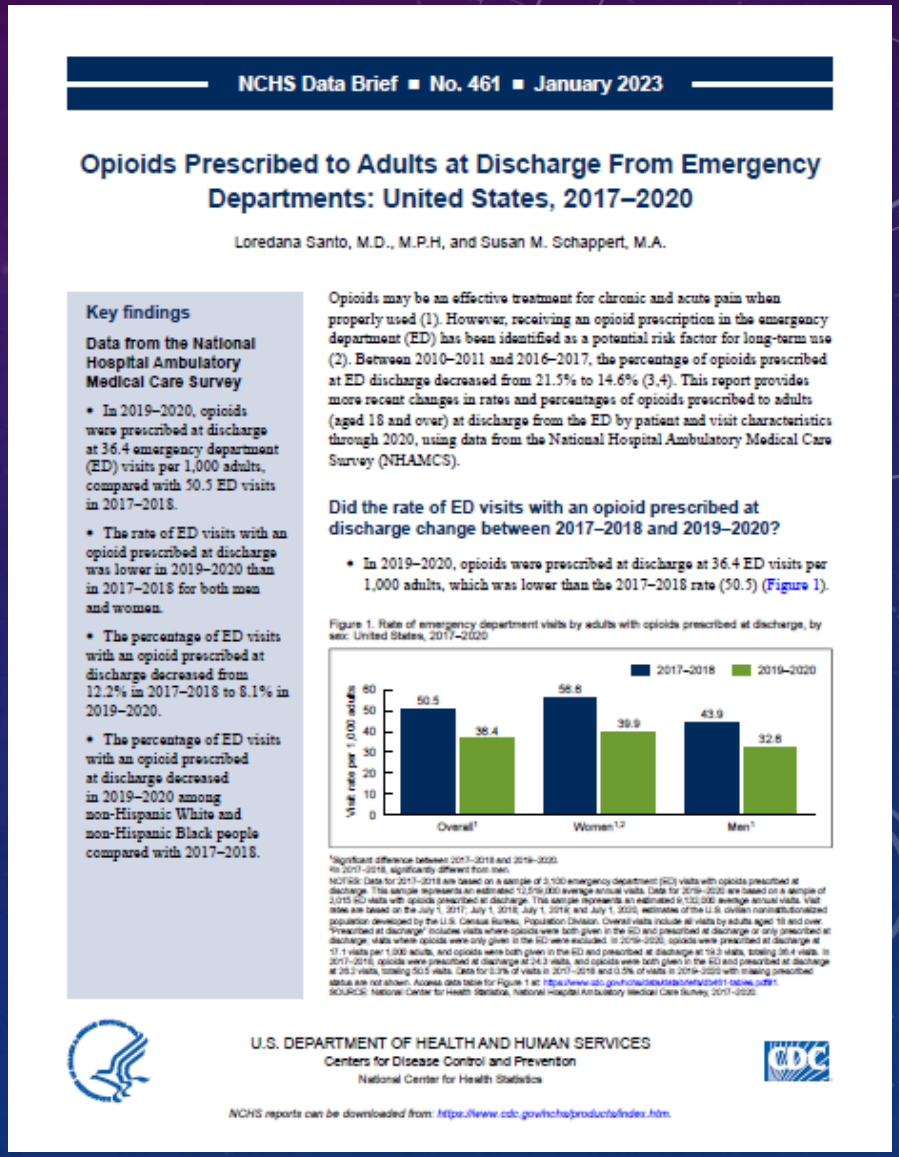
- The real, but unusual, need of a patient for opioid medications is erroneously interpreted by physicians and nurses ad addiction.

- Inadequate analgesia
- Labelled patient

- The Problem of Balancing Undertreatment of Pain and the Risk of Addiction

- Frequent monitoring of vital signs, as well as pain (the 5th vital sign)
- Education of physicians, nurses, and patients
- Use of non-opioid medications as adjuvant analgesics

- A study by US National Center for Health Statistics (NCHS)
- Receiving an opioid prescription in the emergency department (ED) has been identified as a potential risk factor for long-term use.



NCHS Data Brief ■ No. 461 ■ January 2023

Opioids Prescribed to Adults at Discharge From Emergency Departments: United States, 2017–2020

Loredana Santo, M.D., M.P.H, and Susan M. Schappert, M.A.

Key findings

Data from the National Hospital Ambulatory Medical Care Survey

- In 2019–2020, opioids were prescribed at discharge at 36.4 emergency department (ED) visits per 1,000 adults, compared with 50.5 ED visits in 2017–2018.
- The rate of ED visits with an opioid prescribed at discharge was lower in 2019–2020 than in 2017–2018 for both men and women.
- The percentage of ED visits with an opioid prescribed at discharge decreased from 12.2% in 2017–2018 to 8.1% in 2019–2020.
- The percentage of ED visits with an opioid prescribed at discharge decreased in 2019–2020 among non-Hispanic White and non-Hispanic Black people compared with 2017–2018.

Opioids may be an effective treatment for chronic and acute pain when properly used (1). However, receiving an opioid prescription in the emergency department (ED) has been identified as a potential risk factor for long-term use (2). Between 2010–2011 and 2016–2017, the percentage of opioids prescribed at ED discharge decreased from 21.5% to 14.6% (3,4). This report provides more recent changes in rates and percentages of opioids prescribed to adults (aged 18 and over) at discharge from the ED by patient and visit characteristics through 2020, using data from the National Hospital Ambulatory Medical Care Survey (NHAMCS).

Did the rate of ED visits with an opioid prescribed at discharge change between 2017–2018 and 2019–2020?

- In 2019–2020, opioids were prescribed at discharge at 36.4 ED visits per 1,000 adults, which was lower than the 2017–2018 rate (50.5) (Figure 1).

Figure 1. Rate of emergency department visits by adults with opioids prescribed at discharge, by sex: United States, 2017–2020

*Significant difference between 2017–2018 and 2019–2020.
†In 2017–2018, significantly different from men.

NOTES: Data for 2017–2018 are based on a sample of 3,100 emergency department (ED) visits with opioids prescribed at discharge. This sample represents an estimated 12,579,000 average annual visits. Data for 2019–2020 are based on a sample of 2,015 ED visits with opioids prescribed at discharge. This sample represents an estimated 9,132,000 average annual visits. Visit rates are based on the July 1, 2017; July 1, 2018; July 1, 2019; and July 1, 2020, estimates of the U.S. civilian noninstitutionalized population developed by the U.S. Census Bureau, Population Division. Overall visits include all visits by adults aged 18 and over. "Prescribed at discharge" includes visits where opioids were both given in the ED and prescribed at discharge or only prescribed at discharge; visits where opioids were only given in the ED were excluded. In 2019–2020, opioids were prescribed at discharge at 17.1 visits per 1,000 adults, and opioids were both given in the ED and prescribed at discharge at 19.3 visits, totaling 36.4 visits. In 2017–2018, opioids were prescribed at discharge at 24.3 visits, and opioids were both given in the ED and prescribed at discharge at 26.2 visits, totaling 50.5 visits. Data for 0.3% of visits in 2017–2018 and 0.5% of visits in 2019–2020 with missing prescribed status are not shown. Access data table for Figure 1 at: https://www.cdc.gov/nchs/data/databriefs/db461-tables.pdf#1.

SOURCE: National Center for Health Statistics, National Hospital Ambulatory Medical Care Survey, 2017–2020.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Center for Health Statistics

NCHS reports can be downloaded from: https://www.cdc.gov/nchs/products/index.htm.

Santo L, Schappert SM. Opioids prescribed to adults at discharge from emergency departments: United States, 2017–2020.
NCHS Data Brief, no 461. Hyattsville, MD: National Center for Health Statistics. 2022.
DOI: https://dx.doi.org/10.15620/ cdc:122879.


Thank you
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