Myths and Facts about Opioids
Collaborators

Milken Institute School of Public Health
THE GEORGE WASHINGTON UNIVERSITY

GEORGETOWN UNIVERSITY
More resources available at the DC Center for Rational Prescribing
doh.dc.gov/dcrx
Presented by

- Adriane Fugh-Berman, MD
  - Associate Professor,
    Georgetown University Medical Center

- Anna Lembke, MD
  - Chief of Addiction Medicine,
    Stanford University Medical Center

- Christina Prather, MD
  - Assistant Professor of Medicine,
    George Washington University
    School of Medicine and Health Sciences
Course Faculty

- Jessica Bress, MPH
- Adriane Fugh-Berman, MD
- Travis Gayles, MD, PhD
- Anna Lembke, MD
- Kofi Onumah, PharmD, RPh
- Christina Prather, MD
- Shauna White, PharmD, RPh
- Susan Wood, PhD
Harrison Narcotics Act

- Passed in 1914
- Aimed at curbing cocaine and heroin abuse and addiction
- Required all importers, exporters, distributors, and manufacturers of opium to pay a tax

(Council on Foreign Relations 2016)
Important Information

The slides will progress at their own pace.

Do not attempt to speed up the video.

The Post Test will only unlock after viewing the entire video.

The video can be paused and resumed later.
Learning Objectives

Describe The public health impact of opioid abuse in the United States.

Outline The history of opioid prescribing and promotion.

Describe Neuroadaptation as it relates to opioids.

List common and severe adverse effects of opioids.
Harrison Narcotics Act

- Passed in 1914
- Aimed at curbing cocaine and heroin abuse and addiction
- Required all importers, exporters, distributors, and manufacturers of opium to pay a tax

(Council on Foreign Relations 2016)
Physician Payment Sunshine Act

- Federal program that collects gifts given to physicians and teaching hospitals from pharmaceutical and device companies.
- In 2015, Open Payments reported $7.52 billion in gifts to physicians and teaching hospitals.
- To see all gifts, visit openpaymentsdata.cms.gov or projects.propublica.org/docdollars/

(CMS 2016)
Addiction Rare in Patients Treated with Narcotics

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, Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

Jane Porter
Hershel Jick, M.D.
Boston Collaborative Drug Surveillance Program

Waltham, MA 02154
Boston University Medical Center

Chronic Use of Opioid Analgesics in Non-Malignant Pain: Report of 38 Cases

Russell K. Portenoy and Kathleen M. Foley

Pain 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)

Summary

Thirty-eight patients maintained on opioid analgesics for non-malignant pain were retrospectively evaluated to determine the indications, course, safety and efficacy of this therapy. Oxycodone was used by 12 patients, methadone by 7, and levorphanol by 5; others were treated with propoxyphene, meperidine, codeine, pentazocine, or some combination of these drugs. Nineteen patients were treated for four or more years at the time of evaluation, while 6 were maintained for more than 7 years. Two-thirds required less than 20 morphine equivalent mg/day and only 4 took more than 40 mg/day. Patients occasionally required escalation of dose and/or hospitalization for exacerbation of pain; doses usually returned to a stable baseline afterward. Twenty-four patients described partial but acceptable or fully adequate relief of pain, while 14 reported inadequate relief. No patient underwent a surgical procedure for pain management while receiving therapy. Few substantial gains in employment or social function could be attributed to the institution of opioid therapy. No toxicity was reported and management became a problem in only 2 patients, both with a history of prior drug abuse. A critical review of patient characteristics, including data from the 16 Personality Factor Questionnaire in 24 patients, the Minnesota Multiphasic Personality Inventory in 23, and detailed
Pain Specialist: Many Doctors Underprescribe For Chronic Pain

Inadequate pain treatment is a public health crisis
Drug war shouldn't claim new victims

Don't blame people for their pain, report says

Treating the Pain Epidemic
By JOHN TIERNEY NOVEMBER 5, 2009 3:23 PM
Copyright © 2007 Scott M. Fishman, MD
Published by Waterford Life Sciences, Washington, DC (202) 299-0600
Cover and book design: Gretchen Maxwell, GLM Design

This book is sponsored by a consortium of organizations with a common interest in promoting safe and effective pain management, including:

Abbott Laboratories
Alliance of State Pain Initiatives
Alpharma Pharmaceuticals LLC
American Academy of Pain Medicine
American Pain Foundation
American Society for Pain Management Nursing
Candlelighters Childhood Cancer Foundation
Center for Practical Bioethics
Cephalon, Inc.
Endo Pharmaceuticals
Federation of State Medical Boards Research and Education Foundation
International Association for Pain and Chemical Dependency
Mayday Fund
National Pain Foundation
Pain & Policy Studies Group, University of Wisconsin
Purdue Pharma L.P.
SAMHSA/CSAT (Substance Abuse and Mental Health Services Administration/Centers for Substance Abuse Treatment)

Care has been taken to confirm the accuracy of the information presented and to describe generally accepted practices. However, the author, editors, and publishers are not responsible for any errors or omissions or for any consequences from application of the information in this book and make no warranty, expressed or implied, with respect to the currency, completeness, or accuracy of the contents of the publication. Application of this information in any situation remains the professional responsibility of the practitioner. Case presentations in this book are adapted from actual cases and patient identifiers or facts that could link the patient to the case were omitted or substantially altered to protect the privacy of the patient.
### Pain Analog Scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No Pain</td>
</tr>
<tr>
<td>1</td>
<td>Mild, annoying pain</td>
</tr>
<tr>
<td>2</td>
<td>Nagging, uncomfortable, troublesome pain</td>
</tr>
<tr>
<td>3</td>
<td>Distressing, miserable pain</td>
</tr>
<tr>
<td>4</td>
<td>Intense, dreadful, horrible pain</td>
</tr>
<tr>
<td>5</td>
<td>Worst possible, unbearable, excruciating pain</td>
</tr>
</tbody>
</table>

![Scale with emoticons]

- **No Pain**: Smiling face
- **Mild, annoying pain**: Smiling face
- **Nagging, uncomfortable, troublesome pain**: Happy face with frown
- **Distressing, miserable pain**: Sad face
- **Intense, dreadful, horrible pain**: Face with tears
- **Worst possible, unbearable, excruciating pain**: Face with tears and contorted expression
Pain as the 5th Vital Sign

The Numeric Scoring of Pain: This Practice Rates a Zero Out of Ten

Steven M. Green, MD*; Baruch S. Krauss, MD, EdM
*Corresponding Author. E-mail: steve@stevegreenmd.com.

Measuring Pain as the 5th Vital Sign Does Not Improve Quality of Pain Management

Richard A. Mularski, MD, MSHS, 1,2 Foy White-Chu, MD, 3 Devorah Overbay, MS, RN, 4 Lois Miller, PhD, RN, 4 Steven M. Asch, MD, MPH, 1,2 Linda Ganzini, MD, MPH 5,6
1VA Greater Los Angeles Healthcare System, Department of Medicine, Los Angeles, CA, USA; 2The University of California, Los Angeles and RAND Health, Los Angeles, CA, USA; 3Department of Medicine, Oregon Health & Science University, Portland, OR, USA; 4School of Nursing, Oregon Health & Science University, Portland, OR, USA; 5Department of Psychiatry, Oregon Health & Science University, Portland, OR, USA; 6Portland Veterans Affairs Medical Center, Mental Health Division, Portland, OR, USA.

How Reliable is Pain as the Fifth Vital Sign?

Karl A. Lorenz, MD, MSHS, Cathy D. Sherbourne, PhD, Lisa R. Shugarman, PhD, Lisa V. Rubenstein, MD, MSPH, Li Wen, MD, Angela Cohen, MPH, Joy R. Goebel, RN, PhD, Emily Hagenmeier, MSW, Barbara Simon, MA, Andy Lanto, MA, and Steven M. Asch, MD, MPH
What GAO Found

Purdue conducted an extensive campaign to market and promote OxyContin using an expanded sales force to encourage physicians, including primary care specialists, to prescribe OxyContin not only for cancer pain but also as an initial opioid treatment for moderate-to-severe noncancer pain.
“Pseudoaddiction”


- This was a single case study of a 17 year old with leukemia.
  - “Inadequate treatment of the patient's pain led to behavioral changes similar to those seen with idiopathic opioid psychologic dependence.”
  - Pseudoaddiction was described as “the iatrogenic syndrome of abnormal behavior developing as a direct consequence of inadequate pain management.”
John Fauber’s Articles on Opioids

Emails point to 'troubling' relationship between drug firms, regulators

Charity's investment a prescription for profits for drug maker

Painkillers, tranquilizers an increasingly fatal mix

Painkiller boom fueled by networking
Opioid prescription rates vary across states

Number of painkiller prescriptions per 100 people

- 52 - 71
- 72 – 82.1
- 82.2 – 95
- 96 – 143

IMS, National Prescription Audit (NPA), 2012
Opioid Overdoses in the United States


Age adjusted rate of drug overdose deaths and drug overdose deaths involving opioids, United States, 2000-2014
# Scheduled Drugs

<table>
<thead>
<tr>
<th>Schedule I</th>
<th>Schedule II</th>
<th>Schedule III</th>
<th>Schedule IV</th>
<th>Schedule V</th>
</tr>
</thead>
<tbody>
<tr>
<td>High potential for abuse</td>
<td>High potential for abuse</td>
<td>Potential for abuse less than I and II</td>
<td>Potential for abuse less than III</td>
<td>Potential for abuse less than IV</td>
</tr>
<tr>
<td>No currently acceptable medical use</td>
<td>Currently acceptable medical use</td>
<td>Currently acceptable medical use</td>
<td>Currently acceptable medical use</td>
<td>Currently acceptable medical use</td>
</tr>
<tr>
<td>Use may lead to dependence</td>
<td>Use may lead to moderate or low dependence</td>
<td>Use may lead to limited dependence</td>
<td>Use may lead to limited dependence</td>
<td>Use may lead to limited dependence</td>
</tr>
<tr>
<td>LSD</td>
<td>Oxycodone</td>
<td>Buprenorphine</td>
<td>Benzodiazepines</td>
<td>Promethazine + codeine</td>
</tr>
<tr>
<td>Cannabis</td>
<td>Methadone</td>
<td>Ketamine</td>
<td>Tramadol</td>
<td>Some anticonvulsants</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>Amphetamines</td>
<td>Anabolic steroids</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
In Guilty Plea, OxyContin Maker to Pay $600 Million

By BARRY MEIER  MAY 10, 2007
The Opioid Epidemic We Failed to Foresee

By TIMOTHY W. MARTIN
November 2, 2011

Press Release

For Immediate Release: November 1, 2011
Contact: CDC Online Newsroom
(404) 639-3286

Prescription painkiller overdoses at epidemic levels
Kill more Americans than heroin and cocaine combined

Prince died from an overdose of a powerful painkiller described as 'heroin on steroids'

Injecting Opana: Indiana’s HIV Outbreak and America’s Opioid Epidemic
Naloxone Kit
Heroin Use and Overdose Deaths

Rate of past-year heroin abuse or dependence per 1,000 persons

Rate of heroin-related overdose deaths per 1,000 persons

MMWR 2015; 64(26);719-725.
In the 1960s, 80% of heroin addicts identified heroin as their first opioid.

Today, 80% of heroin addicts identify a prescription opioid as their first opioid.

CDC Guideline for Prescribing Opioids for Chronic Pain, 2016

Determined When to Initiate or Continue Opioids for Chronic Pain

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.

2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.

3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

Opioid Selection, Dosage, Duration, Follow-up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to 50 morphine milligram equivalents (MME) or more per day, and should avoid increasing dosage to 50 MME or more per day or carefully justify a decision to titrate dosage to 50 MME or more per day.

6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient, more than 7 days will rarely be needed.

7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Assessing Risk and Addressing Harms of Opioid Use

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/d), or concurrent benzodiazepine use are present.

9. Clinicians should review the patient’s history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, starting from every prescription to every 3 months.

10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.

12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

All recommendations are category A (applies to all patients outside of active cancer treatment, palliative care, and end-of-life care) except recommendation 10 (designated category B, with individual decision making required). Detailed ratings of the evidence supporting the recommendations are provided in the full guideline publication.
Adverse Effects of Opioids

- Constipation
- Depression
- Hyperalgesia
- Memory Problems
- Opioid Withdrawal
- Loss of Libido/Sexual Function
- Increased risk of myocardial infarction
Mixing Benzodiazepines Increase Risk of Overdose
Tolerance

When a patient begins to lose the beneficial effects of a drug.
Dependence

If a patient tries to discontinue a medication, the patient goes into withdrawal.
Myths about Opioids

- “Magic halo” effect
- Opioids work for chronic pain
- No dose is too high
- Pseudoaddiction
PROVEN TWICE-A-DAY (EVERY 12-HOUR) DOSING TO HELP YOUR PATIENTS STAY AHEAD OF PAIN®

Durable analgesic effect demonstrated in opioid-experienced patients with moderate to severe pain1

80% of patients maintained the analgesic effect of OPANAL® ER over a 3-month period2

<table>
<thead>
<tr>
<th>Average Pain Intensity Over Time for Opioid-Experienced Patients2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opiate,</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>0-2</td>
</tr>
<tr>
<td>2-3</td>
</tr>
<tr>
<td>3-4</td>
</tr>
<tr>
<td>4-5</td>
</tr>
<tr>
<td>5-6</td>
</tr>
<tr>
<td>6-7</td>
</tr>
<tr>
<td>7-8</td>
</tr>
</tbody>
</table>

80% of patients maintained the analgesic effect of OPANAL® ER over a 3-month period2

- Mean change from baseline to final visit in average pain intensity (VAS) was 8 mm for OPANAL® ER and 32 mm for placebo (P<0.001); median change was 2 mm for OPANAL® ER and 38 mm for placebo.
- Median daily dose of OPANAL® ER was 69 mg (20-250 mg).
- Mean stabilized dose of OPANAL® ER was 7.2 mg/day.
- The most common adverse drug reactions for OPANAL® ER (≥5%) in this clinical trial were nausea, constipation, headache, somnolence, vomiting, pruritus, and dizziness.

Important Safety Information^: Warnings: OPANAL® ER contains oxymorphone, which is a morphine-like opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid agonists.

Indication
- OPANAL® ER is indicated for the relief of moderate to severe pain in patients requiring continuous, around-the-clock opioid treatment for an extended period of time.
- OPANAL® ER is not intended for use as a prn analgesic.
- OPANAL® ER is not indicated for pain in the immediate post-operative period (0-24 hours following surgery) for patients not previously taking opioids due to the risk of prn analgesia and respiratory depression requiring reversal with opioid antagonists.
- OPANAL® ER is not indicated for pain in the post-operative period if the pain is mild or not expected to persist for an extended period of time.

Patients and their families should be instructed to flush any OPANAL® ER tablets that are no longer needed.

Rx Only

DBA Opioid Medicines

OPANAL is a registered trademark of Endo Pharmaceuticals.

Extended-release tablets 5 mg, 10 mg, 20 mg, 40 mg

* Please see Summary Brief, including baseline VAS, for end of treatment VAS score.

1. Opiates were not used as maintenance therapy in this study. Pain scores were measured at 24 hours after the start of the double-blind treatment period. Patients were allowed as much supplemental rescue medication as needed. OPANAL 3 mg tablets were given 4 times/day for the first 2 days of the double-blind treatment period. Patients were allowed as much supplemental rescue medication as needed. OPANAL 10 mg tablets were given 4 times/day for the first 2 days of the double-blind treatment period. Included in a maximum of 2 doses per day (totaling 30 mg OPANAL per day).

2. VAS = visual analog scale.

Patients reported a decrease, no change, or a ≤10 mm increase in VAS score from Day 1 until the end of the study.

Tramadol

❌ Myth:
Tramadol is a non-addictive, non-opioid alternative.

✅ Fact:
Tramadol is metabolized into an opioid and is addictive.
FDA Labeling

Abuse ≠ Deterrent

Non-addictive
These dose conversions are estimated and cannot account for all individual differences in genetics and pharmacokinetics.
## Rapid-Onset, Short- and Long-Acting Opioids

### Rapid-Onset
- Oral transmucosal fentanyl citrate
- Fentanyl buccal tablet
- Fentanyl buccal soluble film
- Sublingual fentanyl
- Intranasal fentanyl

### Short-Acting
- Codeine
- Buprenorphine
- Morphine
- Oxymorphine (Opana)
- Oxycodon (OxyIR, Percocet)
- Tapentadol (Nucynta)
- Hydrocodone (Vicodin)
- Hydromorphone (Dilaudid)

### Long-Acting
- Transdermal systems with fentanyl (Duragesic patches)
- Buprenorphine patch (Butrans)
- Extended release morphine (Kadian, MS Contin, Avinza)
- ER oxymorphone (Opana ER)
- ER Oxycodone (Oxycontin)
- Levorphanol (Levo-dromoran)
- Methadone
- ER hydromorphone (Exalgo)

*(Archer 2014)*
More resources available at the DC Center for Rational Prescribing
doh.dc.gov/dcrx
Other DCRx Modules

Medical Cannabis: An Introduction to the Biochemistry & Pharmacology

Medical Cannabis: Evidence on Efficacy

Medical Cannabis: Adverse Effects and Drug Interactions

Rational Prescribing in Older Adults

Drug Approval and Promotion in the United States

Generic Drugs: Myths and Facts

More resources available at the DC Center for Rational Prescribing
doht.dc.gov/dcrx