

TREATING PAIN IN ADDICTION MEDICINE



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Pain Treatment in Patients with an Addiction

These patients suffer thrice:

1. from the painful disease
2. from the addiction, which makes pain management difficult
3. from the health care provider's ignorance

Pain Treatment in Patients with an Addiction

Must consider:

1. High tolerance to medications
2. Low pain threshold
3. High risk for relapse
 1. Pain treatment
 2. Inadequate pain treatment
 3. Psychological status

Pain Treatment in Patients with an Addiction

1. Use adjunctive modalities and medications
 2. Avoid the patient's drug of choice
 3. Consider safer longer acting opioids
 4. Use medication with lower street value
- n Avoid self administration, if possible
 - n Case management

Pain Treatment in Patients with an Addiction

1. Explain potential for relapse
2. Explain the rationale for the medication
3. Educate the patient and the support system
4. Encourage family/support system involvement
5. Frequent follow-ups
6. Consultations and multidisciplinary approach

Pain Treatment in Patients with an Addiction

1. Address addiction
2. Use non-medication approaches, if effective
3. Use non-opioid analgesics, if effective
4. Provide effective opioid doses, if needed
5. Treat associated symptoms, if indicated
6. Pain Management Teams and Pain P&P
7. Address addiction

Non Pharmacologic Interventions

1. Behavioral Interventions- ie guided imagery, biofeedback
2. Meditation
3. Osteopathic Manipulation, Chiropractic, Body work, etc
4. Acupuncture with or without stimulation
5. Physical Therapy modalities
6. Regional anesthetic blocks- epidural

Treatment of Chronic Pain in Patients with an Addiction

1. Search for physical causes
2. Identify and address possible non-pain sustaining factors
3. Address and improve functional status
4. Treat associated symptoms, if indicated
5. Case management

Pain Control for Opioid Maintained Patients

1. Must satisfy baseline opioid requirements before treating pain
2. The usual maintenance dose (e.g., methadone) will not control the pain
3. The usual methadone dose needs to be supplemented with appropriate medication(s) for pain control
4. May need slightly higher amounts for slightly longer periods of time

Buprenorphine maintained patients

1. If non-opioids are ineffective, may need to increase the BUP or stop buprenorphine and add a pure Mu agonist for pain (OR-fentanyl)
2. May need to switch to pure Mu agonist for maintenance (baseline requirements)
3. Care needed if/when buprenorphine is restarted for maintenance

Chronic Pain Patients

Goals of treatment

1. Pain reduction
2. Functional improvement
3. Safe and Tolerable side effects
4. Prevention of addiction or relapse

Chronic Pain Patients

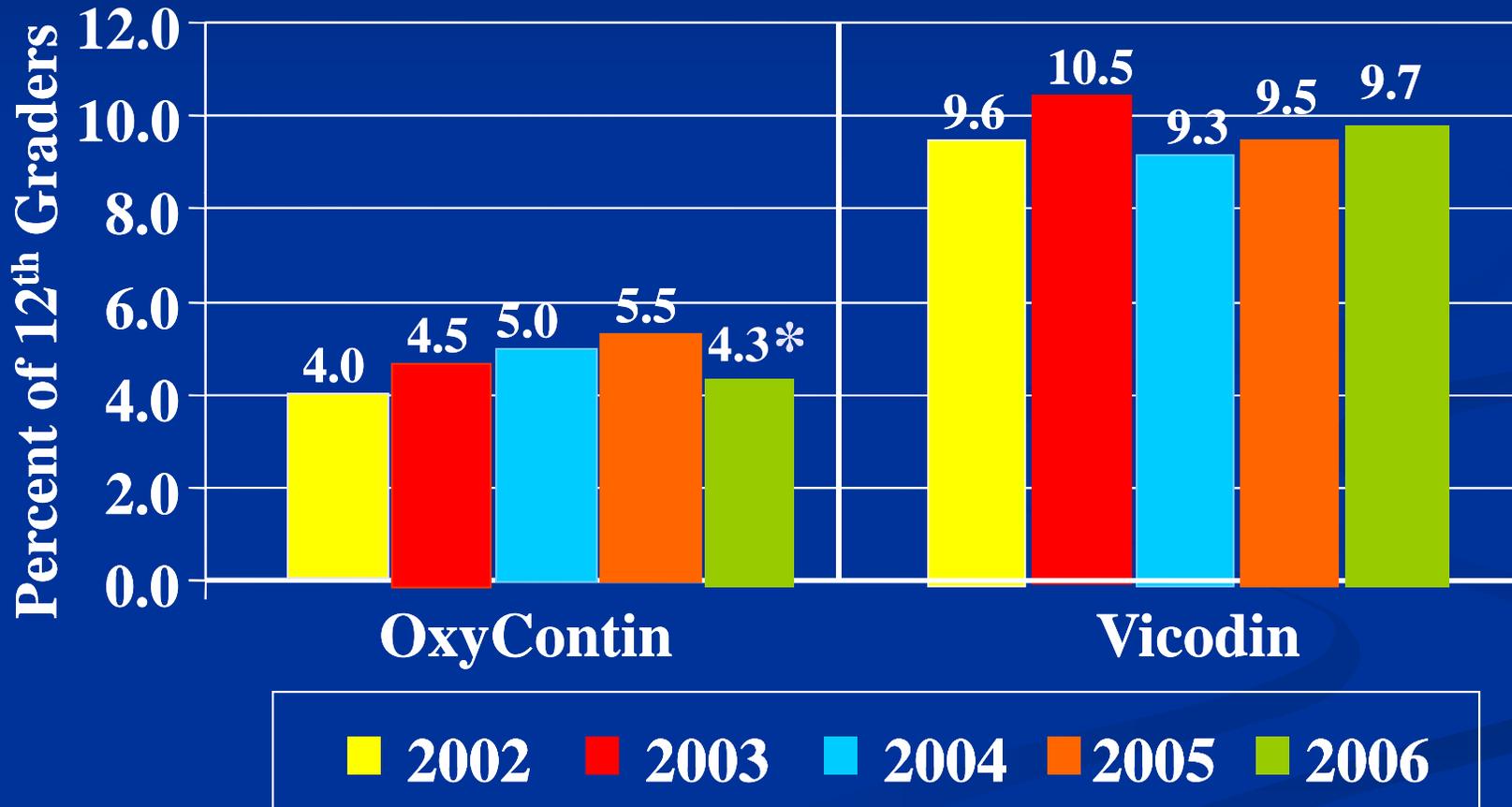
Treatment

1. Case series studies suggest that opioids are safe and effective for most patients
2. Long-term randomized controlled trials have not been performed
3. Trials of opioid treatment are indicated for patients who have moderate to severe pain, significant functional interference, and poor response to other treatments

Issues of Concern:

Past Year Nonmedical Use of OxyContin and Vicodin Remains High

Nearly 1 in 10 Seniors Have Abused Vicodin



* Significant decline between 2005 and 2006

Source: Monitoring the Future Study, 2006

Unintentional OD: 2nd Leading Cause of Accidental Death!

CDC: 2007

ATLANTA - Unintentional fatal drug overdoses in the United States nearly doubled from 1999 to 2004, overtaking falls to become the nation's second-leading cause of accidental death, behind automobile crashes, the government reported.

Fatal Med Errors Upper Graph Fig 2a

- n Type 1 (*Home with "EtOH/Street"*) has increased by **3196%**
 - n Steep and accelerating rate ($p < 0.001$)
- n Type 2 (*Home without EtOH/Street*) and Type 3 (*Non-Home with EtOH/Street*) increased 564% and 555%, respectively
- n Type 4 (*Non-Home without "EtOH/Street"*) only increased 5%

Lower Graph Fig 2b

- n Type 1 has three components:
 - n Fatal Medication Errors
 - n Occurring at home
 - n In conjunction with EtOH/Street drugs
- n The 3 components graphed separately show slight increase
- n Component combined (Type 1) shows steep increase by **3196%**

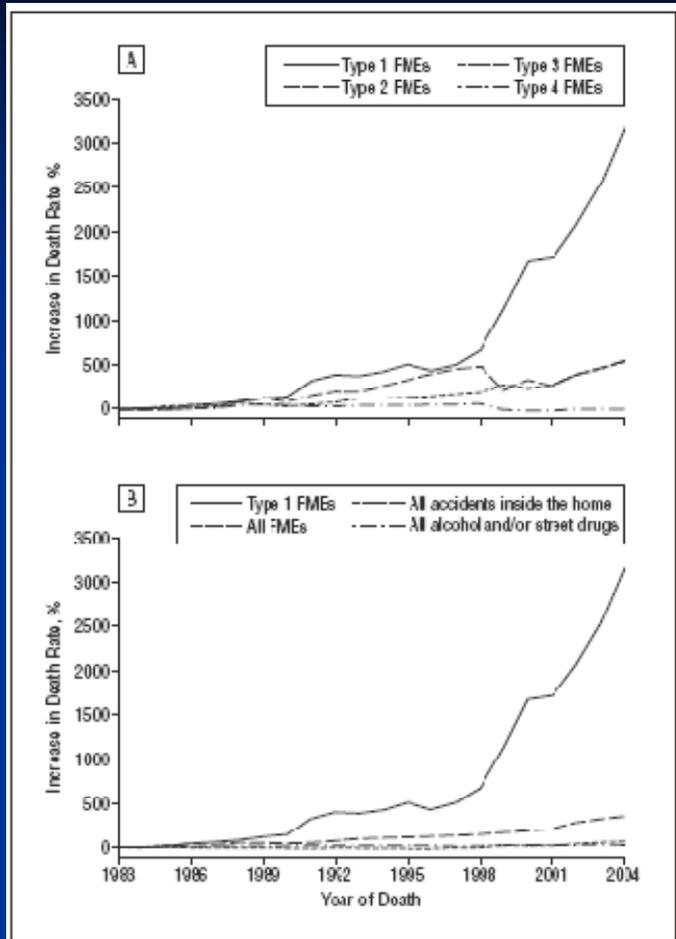
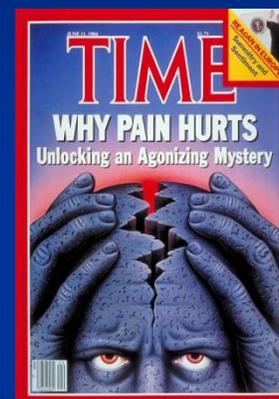
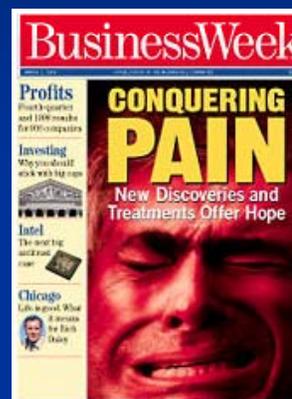


Figure 2. Trends in the US fatal medication error (FME) death rate by type of circumstance in which the FME occurs (A) and for various comparison groups (B) (January 1, 1983–December 31, 2004).

The Problem of Pain

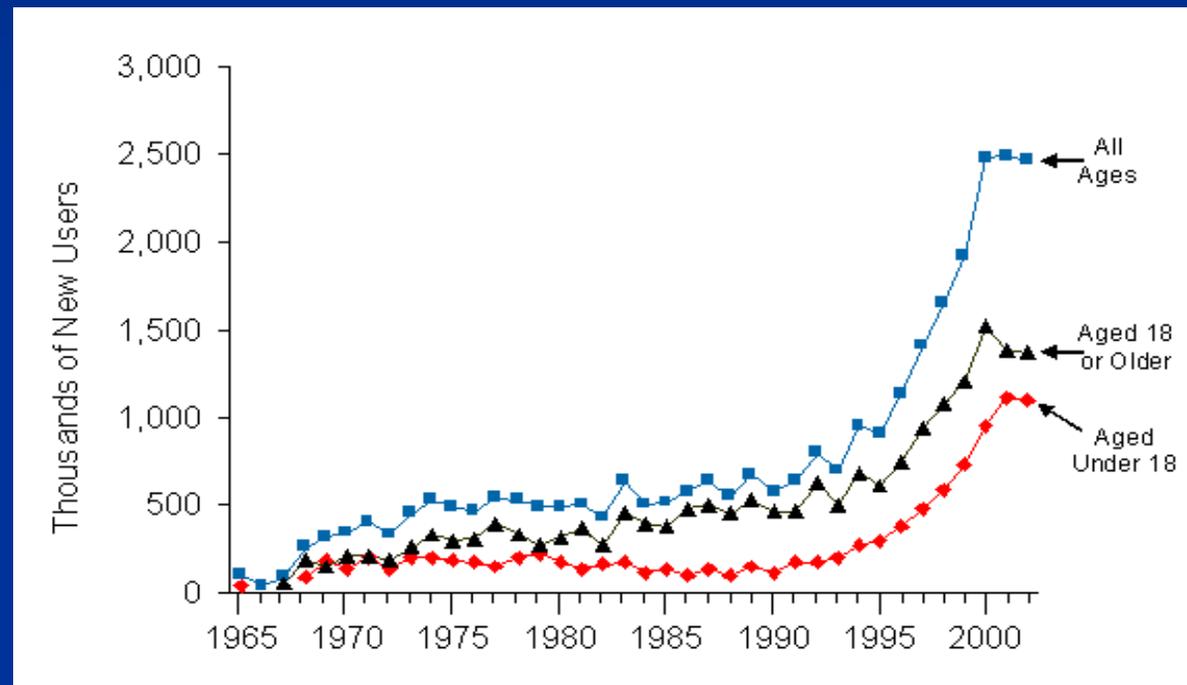
- Costs US economy estimated \$100 billion/year
 - Healthcare
 - Welfare & disability payments
 - Lost tax revenue
 - Lost productivity (work absence)
- 40 million physician visits annually
 - Most common reason for medical appointments
- Push toward opioid maintenance therapy in non malignant pain



National Institutes of Health. *New Directions in Pain Research*. Sept 1998. PA-98-102.

Addiction to Pain Medications

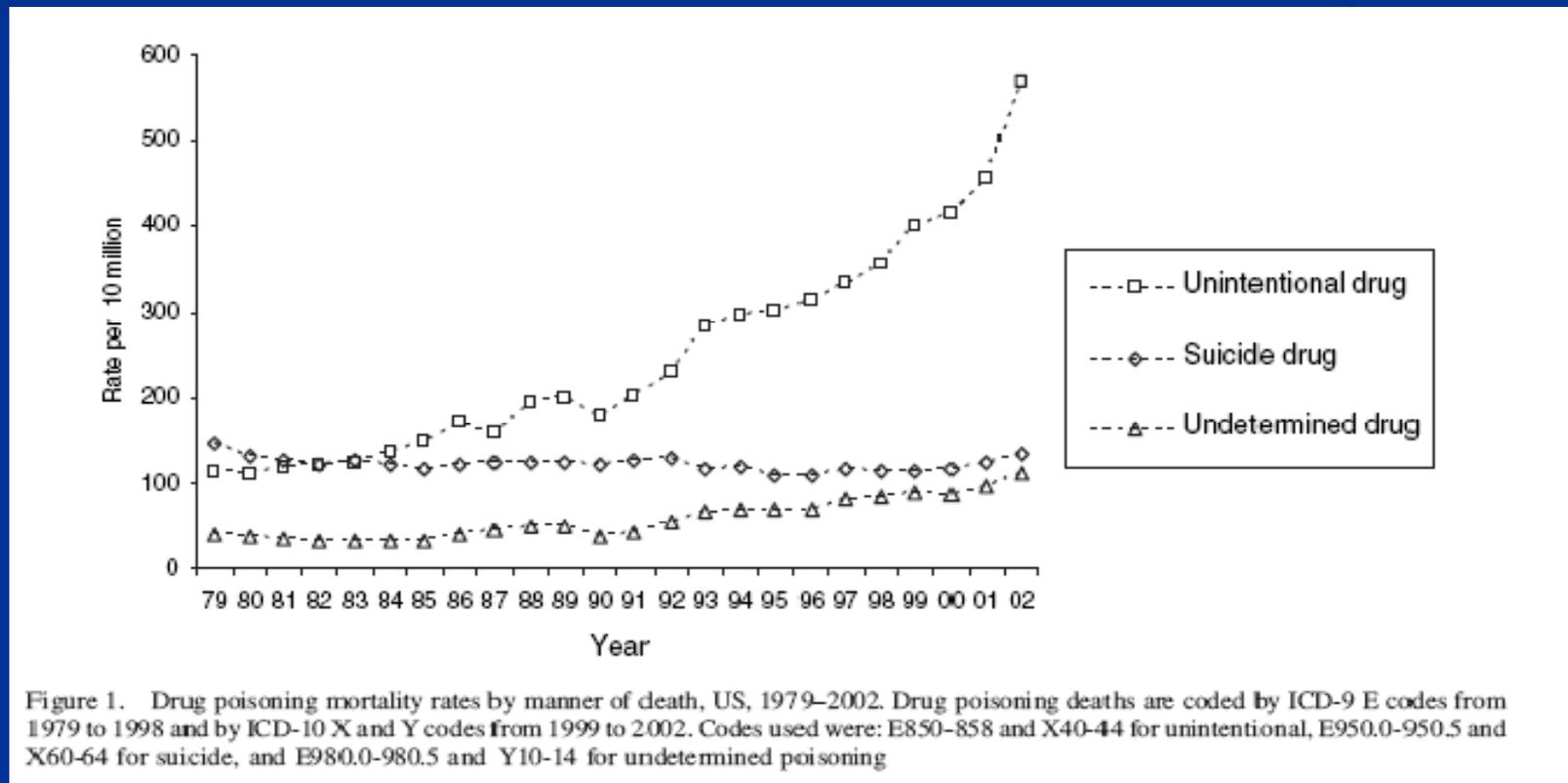
Annual Numbers of New Non Medical Users of Pain Relievers: 1965–2002



Source: 2002 National Survey on Drug Use and Health (NSDUH).
Results from the 2002 National Survey on Drug Use and Health:
National Findings. Department of Health and Human Services

“Between 1999 and 2002....opioid analgesic poisonings increased by 91.2%”

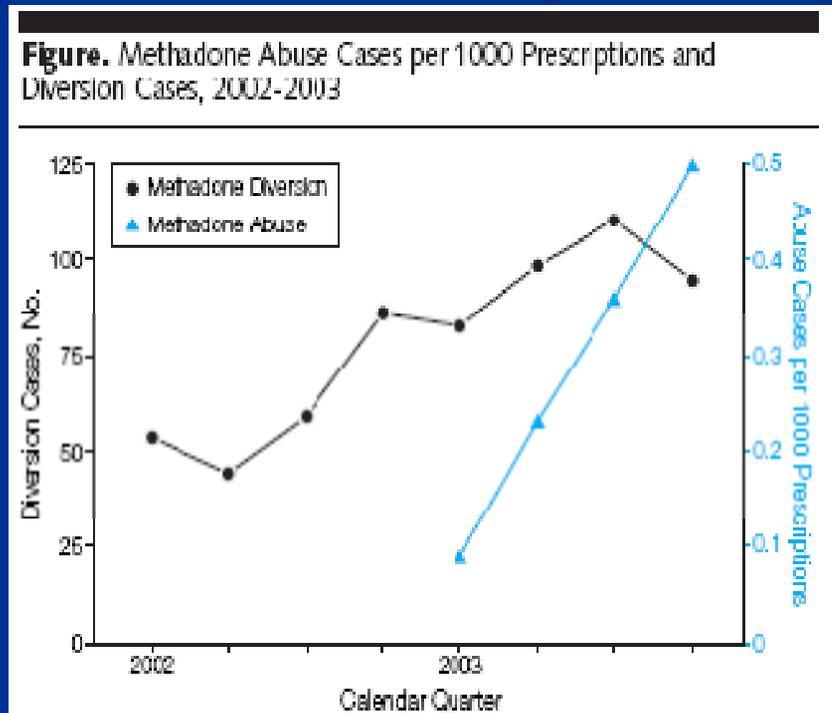
Paulozzi et al; Pharmacoepidemiology and Drug Safety 2006; 15: 618-627



FDA Methadone Warning

FDA ALERT [11/2006]: Death, Narcotic Overdose, and Serious Cardiac Arrhythmias

FDA has reviewed reports of death and life-threatening side effects such as slowed or stopped breathing, and dangerous changes in heart beat in patients receiving methadone. These serious side effects may occur because methadone may build up in the body to a toxic level if it is taken too often, if the amount taken is too high, or if it is taken with certain other medicines or supplements. Methadone has specific toxic effects on the heart (QT prolongation and Torsades de Pointes). Physicians prescribing methadone should be familiar with methadone's toxicities and unique pharmacologic properties. **Methadone's elimination half-life (8-59 hours) is longer than its duration of analgesic action (4-8 hours).** Methadone doses for pain should be carefully selected and slowly titrated to analgesic effect even in patients who are opioid-tolerant. Physicians should closely monitor patients when converting them from other opioids and changing the methadone dose, and thoroughly instruct patients how to take methadone. Healthcare professionals should tell patients to take no more methadone than has been prescribed without first talking to their physician.

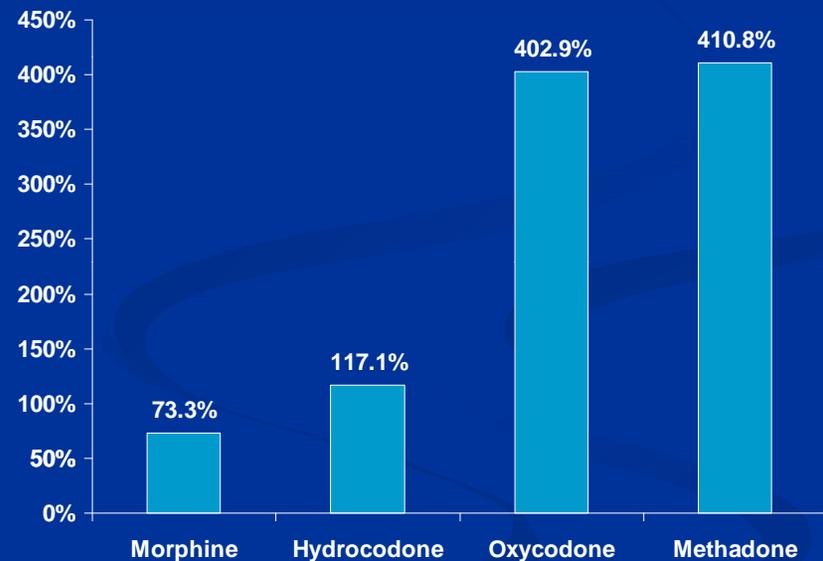


NASPER

National All Schedules Prescription Electronic Reporting Act

- Signed into law by President Bush August 2005
- Point of care reference to all controlled substances prescribed to a given patient
- Each state will implement it's own program
- Treatment tool vs. Law enforcement tool?

Sale of Opioids 1997-2002

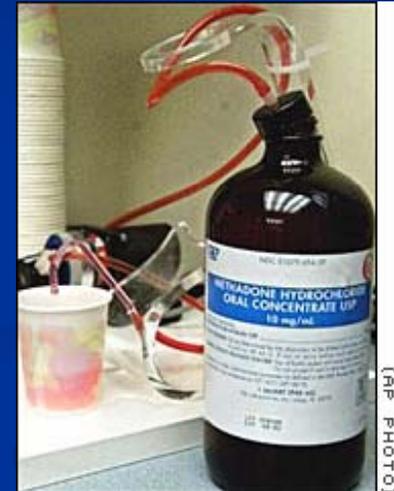


Source: 2002 National Survey on Drug Use and Health (NSDUH).
Results from the 2002 National Survey on Drug Use and Health: National Findings. Department of Health and Human Services

Narcotic Addict Treatment Act of 1974- Schedule II substances

Who can Rx Methadone?

- ADDICTION:
 - Must be federally approved methadone treatment facility.
 - Once daily dosing
- PAIN:
 - Any provider with a schedule II DEA can prescribe.
 - Divided dosing.



Drug Abuse Treatment Act (DATA) 2000 Schedule III substances

- **ADDICTION:**
 - Obtain DEA waiver; MD/DO
 - 30 patients only for addiction
 - 2007: 30/100 pt limit
 - Once daily dosing
- **PAIN:**
 - Any provider with a schedule III DEA can prescribe.
 - Divided dosing.



Suboxone Tablets 8mg. and 2mg

Exposure to Opioids Carries Risk

Fentanyl Abuse and Dependence: Further Evidence for Second Hand Exposure Hypothesis

Mark S. Gold, MD
Richard J. Melker, MD, PhD
Donn M. Dennis, MD
Timothy E. Morey, MD
Lakshmi K. Bajpai, PhD
Raymond Pomm, MD
Kimberly Frost-Pineda, MPH

ABSTRACT. We have proposed a novel hypothesis regarding the potential role of occupational or second-hand exposure in physician substance use, abuse, and addiction. While only 5.6% of licensed physicians in Florida are anesthesiologists, nearly 25% of physicians followed for substance abuse/dependence are anesthesiologists. When we sort by drug of choice, anesthesiologists

- Anesthesiologists Opioid Addiction >>>
 - drug abuse researchers, oncologists, others who handle opioids every day
- IV Fentanyl, Sufentanyl 80-800 times more potent than morphine
- LC/MC/MS Assay measures IV anesthetic/analgesics in the air
 - Detectable concentration of propofol and fentanyl in OR air
 - Highest concentration near patients mouth
- “2nd hand exposure” in the operating room hypothesized to change the brain
- Very few anesthesiologist in recovery successfully return to the OR

Journal of Addictive Diseases, Vol 25(1) 2006

Pain Definitions

- Tolerance
 - Decreased effect over time
- Physical Dependence
 - Withdrawal symptoms upon discontinuation
- Addiction
 - Impaired control, compulsive use, continued use in spite of negative consequences
- Pseudo Addiction
 - Behavior surrounding obtaining adequate pain meds
- Pseudo Tolerance
 - Worsening of underlying condition

Universal Precautions: In Pain Medicine

Gourlay, Heit, Pain Medicine Vol 6, No 2, 2005

1. Make a Diagnosis with Appropriate Differential

- Cause of pain identified
 - Documented workup...somewhere
- Therapy directed toward pain generator
 - Nosioceptive Pain
 - Neuropathic Pain
 - Inflammatory Pain

Universal Precautions: In Pain Medicine

Gourlay, Heit, Pain Medicine Vol 6, No 2, 2005

2. Psychological Assessment Including Risk of Addictive Disorder

- Personal and two generation CD history
 - 30-40% risk CD with 1st degree relative
 - Generation Skip
- Urine Drug Testing (UDT)
 - EKG Analogy
- Questionnaires;
 - Depression, Mood, Sleep
 - SOAAP

Universal Precautions: In Pain Medicine

Gourlay, Heit, Pain Medicine Vol 6, No 2, 2005

3. Informed Consent

- Risks versus benefits of opioids
- Alternate treatments
- Opioids result in:
 - Tolerance
 - Physical dependence
 - Withdrawal symptoms
 - Risk of addiction

Universal Precautions: In Pain Medicine

Gourlay et al, Pain Medicine Vol 6, No 2, 2005

4. Treatment Agreement

- Written or Verbal
 - Slack is gained and lost
 - Go with the first story
- One provider prescribing
- One pharmacy filling
- Pill Counts for early refills
 - It's easy to bring in an empty bottle!

32% Misuse their meds or violate guidelines for treatment

Ives et al BMC Health Services Research, April 4 2006, 6, 46

- 169 pts on opioids in an academic medical center
 - Opioid Misuse
 - Neg UDS for opioids
 - Positive UDS for illicit
 - Multiple prescribers
 - Diversion
 - Forgery
 - 62 Pts “misused”
 - 40% UDS + coc/amph
 - 24% UDS – for Rx
 - 9% + non Rx meds
 - 3% diverted/forged
- “Failure to guard against diversion and drug misuse represents a public health threat” DEA**

Universal Precautions: In Pain Medicine

Gourlay et al, Pain Medicine Vol 6, No 2, 2005

5. Pre- and Post- Intervention Assessment of Pain Level and Function

- Pain Questionnaire
 - Numerical scales, Visual analog
 - Medication effects, Side effects
- Roland Disability Scale
- Mood Survey
- Beck Depression Index, etc

Universal Precautions: In Pain Medicine

Gourlay et al, Pain Medicine Vol 6, No 2, 2005

6. **Appropriate Trial of Opioid Therapy**
With or without adjunctive medication
 - Emphasis on trial

Universal Precautions: In Pain Medicine

Gourlay, Heit, Pain Medicine Vol 6, No 2, 2005

7. Reassessment of Pain Score and Level of Function

- Response to therapy should show improvement in pain and function and mood

Universal Precautions: In Pain Medicine

Gourlay, Heit, Pain Medicine Vol 6, No 2, 2005

8. Regularly Assess the 4 “A’s” of Pain Medicine

- Analgesia
 - Ideally <5 on a 1-10 scale
- Activity
- Adverse Effects
- Aberrant Behavior
 - Don't ignore it!

Universal Precautions: In Pain Medicine

Gourlay, Heit, Pain Medicine Vol 6, No 2, 2005

9. Periodically Review Pain Diagnosis and Co-morbid Conditions, Including Addictive Disorders

- Pseudotolerance, Urine drug screens, Attitude toward Recovery

Universal Precautions: In Pain Medicine

Gourlay, Heit, Pain Medicine Vol 6, No 2, 2005

10. Documentation

- Legible

Chronic Pain Patients

Factors which make chronic pain patients more challenging

1. History of drug diversion
2. History of substance abuse disorders
3. Passive and Active suicidality
4. Personality disorders
5. Hepatic or renal disease

Aberrant Drug Related Behaviors - Less Predictive of an Addiction

1. Aggressively complaining of the need for more drug
2. Drug hoarding during periods of reduced pain
3. Requesting specific drugs
4. Openly acquiring similar drugs from other medical sources if primary provider is absent or under-treated
5. Unsanctioned dose escalation or other non-compliance on one or two occasions

Aberrant Drug Related Behaviors - Predictive of an Addiction

1. Selling prescription drugs
2. Prescription forgery
3. Stealing or "borrowing" drugs
4. Obtaining prescription drugs from non-medical sources
5. Concurrent abuse of alcohol or illicit drugs
6. Multiple dose escalations or other non-compliance with therapy

Aberrant Drug Related Behaviors - Predictive of an Addiction

1. Multiple episodes of prescription "loss"
2. Prescriptions from other clinicians/EDs without seeking primary prescriber
3. Deterioration in function that appears to be related to drug use
4. Resistance to change in therapy despite significant side effects from the drug

Differential Diagnoses of Aberrant Drug Related Behaviors

1. Addiction
2. Pseudoaddiction
3. Other psychiatric disorder
4. Encephalopathy
5. Family disturbance
6. Criminal intent
7. Exacerbation of pain syndrome
8. Side effect(s) of opioid

Differential Diagnosis of Functional Downturn

1. Syndrome of opioid abuse/dependence
2. Other substance use disorder
3. Other psychiatric disorder
4. Exacerbation of pain syndrome
5. Other medical problem
6. Side effect of opioid

Buprenorphine: Dosage Forms

- **Buprenex:** Buprenorphine IM formulation *
- **Suboxone 8/2 mg, 2/0.5mg** **
Buprenorphine/Naloxone sublingual tablet
- **Subutex 2mg, 8mg****
Buprenorphine sublingual tablet
- **Transdermal Buprenorphine** Not FDA approved in the US
- **Implant** Investigational

**Intramuscular form FDA approved for pain*

***Sublingual form FDA approved for addiction*

Buprenorphine: Considerations for Pain Management

Rolley E Johnson et al. *Journal of Pain and Symptom Management*, Vol 29, No 3,
March 2005, pp297-326

Buprenorphine: Considerations for Pain Management

Rolley E. Johnson, PharmD, Paul J. Fudala, PhD, and Richard Payne, MD
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Johns Hopkins University School of Medicine, Baltimore, Maryland; Department of Psychiatry
(P.J.F.) and Behavioral Health Service (P.J.F.), University of Pennsylvania School of Medicine,
VA Medical Center, Philadelphia, Pennsylvania; and Department of Neurology (R.P.), Memorial
Sloan-Kettering Cancer Center, New York, New York, USA*

Abstract

New effective analgesics are needed for the treatment of pain. Buprenorphine, a partial mu-opioid agonist which has been in clinical use for over 25 years, has been found to be amenable to new formulation technology based on its physicochemical and pharmacological profile. Buprenorphine is marketed as parenteral, sublingual, and transdermal formulations. Unlike full mu-opioid agonists, at higher doses, buprenorphine's physiological and subjective effects, including euphoria, reach a plateau. This ceiling may limit the abuse potential and may result in a wider safety margin. Buprenorphine has been used for the treatment of acute and chronic pain, as a supplement to anesthesia, and for behavioral and psychiatric disorders including treatment for opioid addiction. Prolonged use of buprenorphine can result in physical dependence. However, withdrawal symptoms appear to be mild to moderate in intensity compared with those of full mu agonists. Overdoses have primarily involved buprenorphine taken in combination with other central nervous system depressants. J Pain Symptom Manage 2005;29:297-326. © 2005 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.

Parental Morphine Equivalency

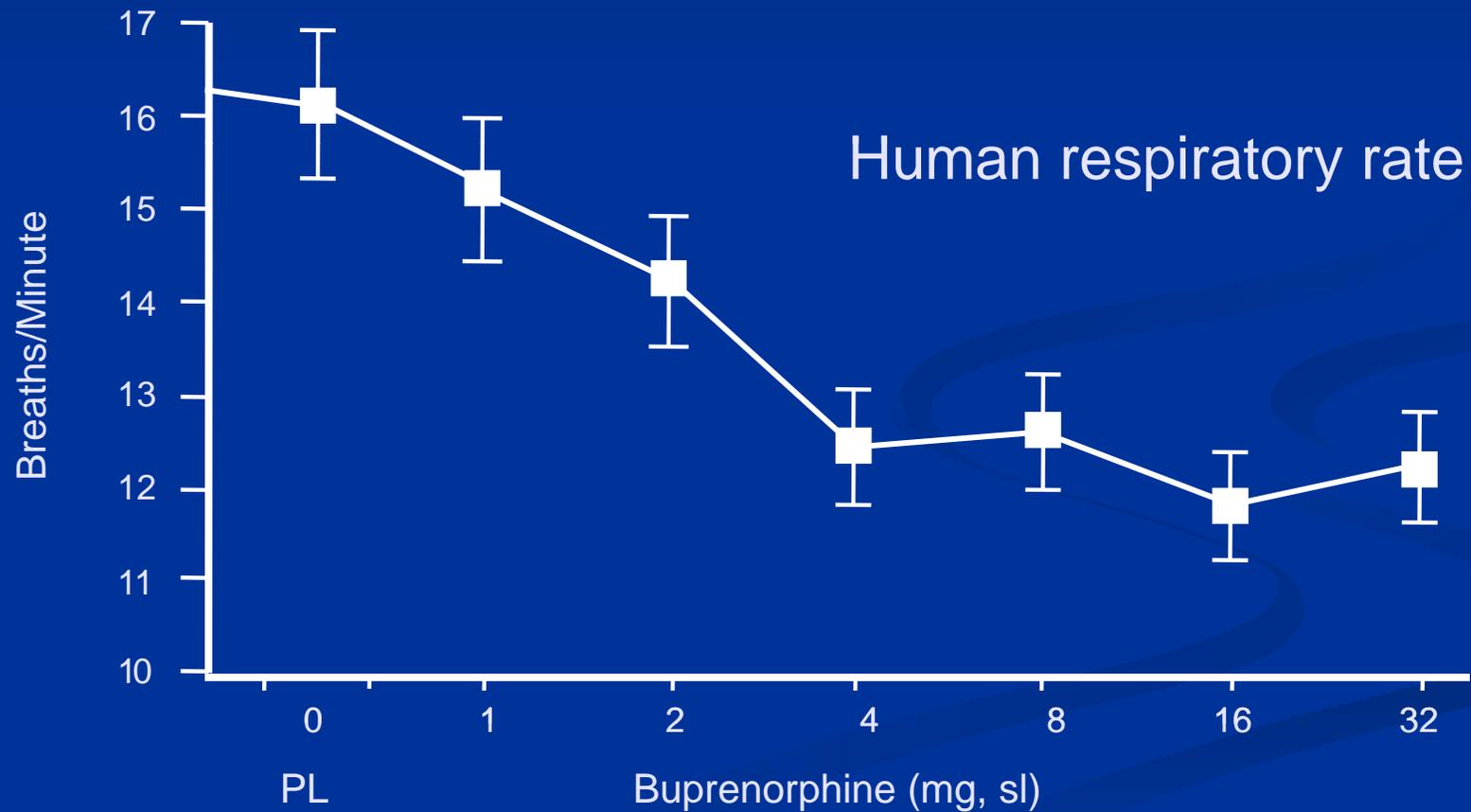
Morphine	10mg
Buprenorphine	0.3mg
Methadone	10mg
Oxycodone	10-15mg
Pentazocine	30mg
Codiene	120mg

Sublingual Buprenorphine Is Effective in the Treatment of Chronic Pain Syndrome

Herbert L. Malinoff,^{1*} Robert L. Barkin,² and Geoffrey Wilson¹

- Open label study 95 consecutive patients on long term opioid therapy (LTOA) failing treatment based on:
 - Increased pain
 - Decreased Functional Capacity
 - Emergence of opioid addiction (8%)
- Induced on buprenorphine 4-16mg (8mg mean dose)
- 86% Experienced moderate to substantial pain relief
 - Mood and function improved
- 8% Discontinued due to side effects or increased pain

Ceiling effect on respiratory



Adapted from Walsh et al., 1994

Buprenorphine-Benzodiazepine Relative Contraindication

- CNS depressants and sedatives (eg, benzodiazepines):
 - All opioids have additive sedative effects when used in combination with other sedatives
 - Increased potential for respiratory depression, heavy sedation, coma, and death (France, IV aprazolam and buprenorphine)
- Despite favorable safety, use caution with concomitant psychotropics (eg, benzodiazepines)

The effect of buprenorphine and benzodiazepines on respiration in the rat

Suzanne Nielsen^{a, b, *}, David A. Taylor^a

^a *Department of Pharmaceutical Biology and Pharmacology, Victorian College of Pharmacy, Monash University 381 Royal Parade, Parkville 3052, Vic., Australia*

^b *Turning Point Drug and Alcohol Centre, 54-62 Gertrude St, Fitzroy 3065, Vic., Australia*

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- Plateau effect on respiratory depression lost with pre-administered benzodiazepine
- Also looked at methadone which potentates respiratory depression
- Buprenorphine not worse than methadone

Drug and Alcohol Dependence 79 (2005) 95-101

Buprenorphine v. other Opioids

- Opioid agonists:
 - Blockade effect, buprenorphine limits the effects of additional opioid use
 - Precipitated withdrawal if buprenorphine taken too soon after a full *mu* agonist
- Opioid antagonists:
 - Buprenorphine incompletely reversed by naloxone

Some Resources

- www.painedu.com
 - PainEdu Manual
 - Opioid Risk Management Supplement
- www.pain.com
 - Links to many pain sites
- www.legalsideofpain.com
 - Current status of laws regarding opioid Rx
- www.partnersagainstpain
 - Purdue site with access to patient management forms