

Buprenorphine in the Treatment of Opioid Dependence

**Ron Horn, MD
Medical Director**

“Addiction doesn’t come heralded by a brass band, it sneaks up on you, and sometimes with extraordinary speed.”

C. Everett Koop (former US Surgeon General), 2003

Heroin: The American Story

- 2.3 million Americans reported using heroin ≥ once (1998)
- 149,000 new users (1999)
- 980,000 persons using at least weekly (1998)
- 810,000–1 million chronic users of heroin
- Only 170,000–200,000 receiving treatment

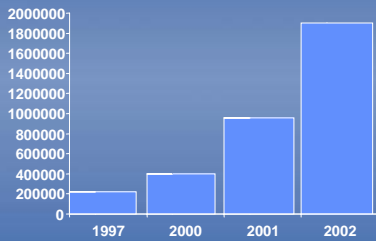
(National Household Survey on Drug Abuse, 1999; Office of National Drug Control Policy, 1997; SAMHSA, Office of Applied Studies, National Household Survey on Drug Abuse, 2000 and 2001)

Worrying Trends with Prescription Opioids

- Abuse of prescription painkillers has risen rapidly in the US:
 - OxyContin, Vicodin, Demerol
 - Dramatic press coverage fuelled demand
- Prescription opioids causing Emergency Department visits 1994–2001:
 - 41,687⇒90,232 (117% increase)
- Significant diversion and abuse of methadone

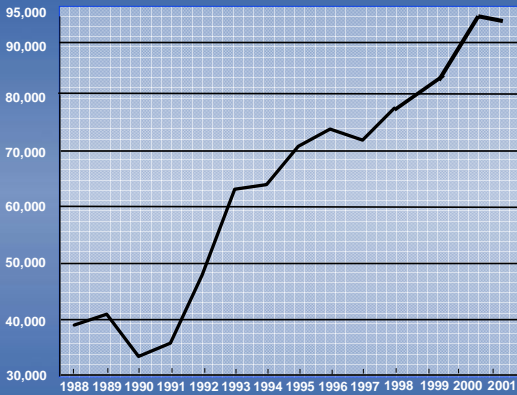
Abuse of Prescription Opioids: A Growing Problem

Non-medical OxyContin use – 2002



Prescription drug monitoring: American Society of Interventional Pain Physicians, 2002

Estimated Total Number of Heroin/Morphine-Related Hospital Emergency Department Visits by Year (DAWN, 2002)



What is the Cost to Society?

- \$20 billion per year total cost of heroin abuse (Harwood *et al.*, 1998)
- The economic cost of drug use and dependence estimated to be \$98 billion (Harwood *et al.*, 1998)
- The social impact of drug addiction:
 - Crime / legal costs
 - Absenteeism from work / unemployment
 - Welfare / medical costs

Choosing to Use?

- A non-dependent user controls his/her use.
- A dependent person is controlled **by** his/her addiction.
 - People suffering from addiction often seek treatment because they "want their life back."

Diagnosing Addiction?

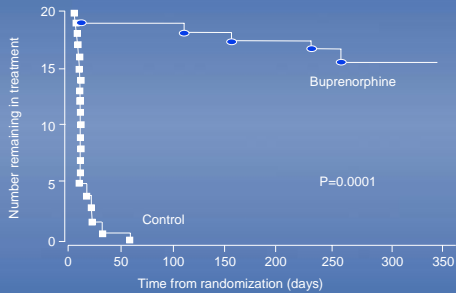
- More than 3 of the following during last 12 months:
 - Tolerance
 - Withdrawal syndrome
 - Use of the drug to avoid/reverse withdrawal symptoms
 - Compulsion to use drug, especially when trying to stop
 - Narrowed repertoire of behaviors associated with drug use
 - Drug-related behaviors more important than other previously more important activities/behaviors
 - Early relapse after withdrawal

DSM IV 2005

Are Opioid-Dependent Individuals Bad or Sick?

- Opioid dependence has several features in common with diabetes and hypertension
 - Chronic, relapsing nature
 - Genetic vulnerability
 - Physiologic brain changes
 - Responds to chronic disease management strategies, not short-term symptomatic relief, nor abstinence-based therapy.

Buprenorphine in Medical Withdrawal and Maintenance



Kaplan-Meier curve of cumulative retention in treatment (Kakko et al, 2003)

Once dependent, why isn't it easy to stop?

- Withdrawal from opioids is associated with an extremely unpleasant syndrome:
 - Physical pain (muscle aches, cramps)
 - Nausea and vomiting
 - Diarrhea
 - Dysphoria
 - Depression
 - Irritability and anxiety
 - Dysregulation of brain reward systems
 - Lacrimation
 - Rhinitis
 - Piloerection
- Pharmacologic intervention proven to help relieve symptoms of withdrawal

Cost-Effectiveness of Maintenance Treatment

- Treatment saves society money in costs of dependence, eg,
 - Emergency admissions from overdose
 - Crime
 - Unemployment, absenteeism
 - Recidivism, multiple rounds of failed detox
- ↑ treatment access = ↑ savings for society
- Potential for substantial net cost savings in:
 - Patients involved in extensive criminal activity
 - Patients who undergo multiple detoxifications each year

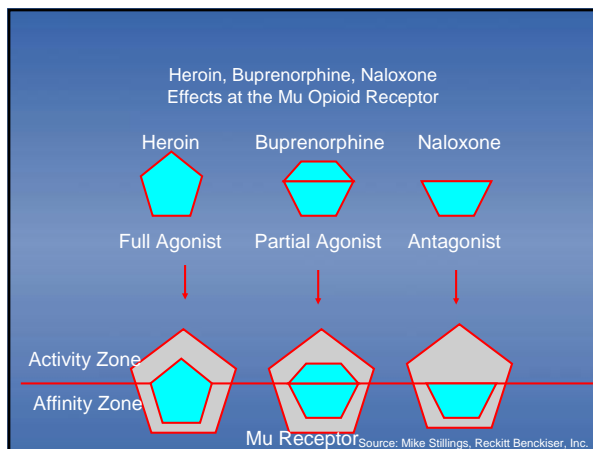
What is DATA (Drug Addiction Treatment Act) 2000?

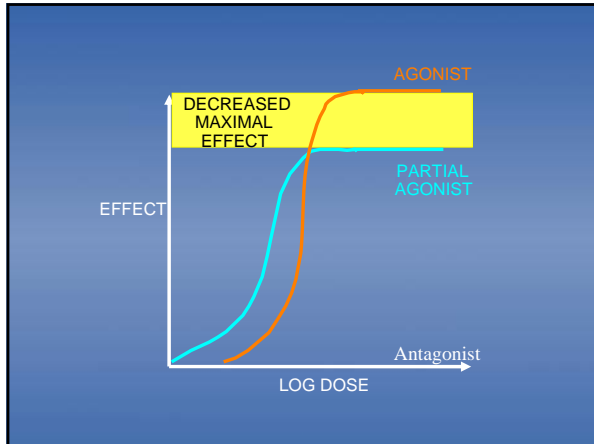
Provisions

An Amendment to the Controlled Substances Act that allows certified physicians to prescribe and dispense Schedule III, IV, and V medications that have been approved by the Food and Drug Administration for use in addiction treatment (i.e., **maintenance** or **medical withdrawal** (detoxification)).

Buprenorphine

- A synthetic opioid
- High affinity for the μ receptor
 - Binds more tightly to opiate receptors than other opiates or opiate antagonists.
- Slow dissociation from the receptor
 - Milder withdrawal
- Partial agonist at the mu opioid receptor
 - Low intrinsic activity only partially activating opioid receptors.
 - Exhibits a 'ceiling effect' on respiratory depression.





Buprenorphine Preparations

- Subutex® (buprenorphine monotherapy) & Suboxone® (buprenorphine and naloxone) registered as Schedule III medications.
- Sublingual tablet registered for treatment of opioid dependence
 - 2mg/0.5mg (2 mg)
 - 8 mg/2mg (8 mg)
- Typical doses: 4 to 24 mg per day
- Buprenex (IM buprenorphine) FDA approved for analgesia.

Duration of Effects

- Rapid onset of action: 20 – 60 minutes (after sublingual administration)
- Peak effects: 1 – 4 hours
- Duration of action is dose related
 - low dose : 4 – 12 hrs
 - med dose : ~ 24 hrs
 - high dose : 2 – 3 days
- Elimination half-life ~24 to 36 hours

Pharmacological & Clinical Properties

Pharmacological property

- Substitutes for opioids
- Opiate-like effects
- Blocks' effects of opiates
- Long duration of action
- Side effects

Clinical implication

- Prevents withdrawal
- Can be used for maintenance / withdrawal
- Reduces cravings
- Increases treatment retention
- Reduces illicit opioid use
- Allows for daily dosing
- Similar to other opioids, but less sedating and safer in overdose

Clinical Guides for Maintenance Treatment of Suboxone

- Dose to patient response/clinical effect
- Majority of patients respond to 4-24 mg daily
 - Maximum recommended dose is 32 mg daily
- No maximum or minimum duration
- Provides opportunity for health care providers to address all aspects of needed care (e.g. psychosocial, medical, etc.)
- Variability between patients (e.g., absorption, metabolism, elimination) requires individualized dosing

Induction

- Accurate history
- Objective signs of withdrawal/COWS (Clinical Opioid Withdrawal Scale)
- Day 1:
 - Initial dose 4 mg
 - Second dose of 4 mg after assessing initial response
 - 4 mg take home dose has been given prn
- Day 2:
 - First day's dose plus 2–4 mg as indicated by patient's response
- Day 3:
 - Target 16 mg according to patient's response

Always Dose to Desired Clinical Effect

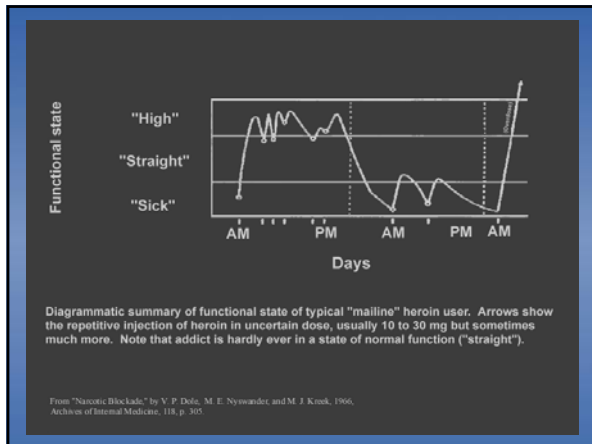
- Variability in patient metabolism of buprenorphine requires individualized dosing
- Majority respond to 4–24 mg daily
- Maximum recommended dose 32 mg
 - Use of illicit opioids and treatment retention improves with increasing dose (Ling, *Addiction* 1998)
- No maximum or minimum duration of treatment

Finishing Treatment With Buprenorphine

- Buprenorphine binds tightly to the receptor
 - High affinity to the receptor prolongs effect
 - Slow dissociation from the receptor prolongs effect
 - Gives rise to a “smooth” physiological withdrawal
- Patients do better with comprehensive psychosocial, vocational, medical, psychiatric and behavioral therapy

(McLellan et al, 1993 and 1994)

What does it feel like to be opioid dependent?



- ### Five Key Factors to Successful Treatment with Buprenorphine
- Willingness to change.
 - Strong support system.
 - Caring, patient, knowledgeable physician.
 - Appropriate and effective counseling.
 - Maintenance treatment with Suboxone.

Lummi Suboxone Clinic

Daily dose in clinic
 Clinic six days a week
 Half days
 Two whole days , Mon Tues
 Physician's Assistant on Mon. Tues
 MOA with Tribal Clinic, Pharmacy, Lab
 No take home
 Daily CD and MH Groups
 Saturday Clinic with double dosing,
 max 40 mg Suboxone
 Facilities, Operational, Business Plans are works in Progress

Summary

- Opioid dependence is a chronic, relapsing, progressive and sometimes fatal medical condition.
- Profound neurobiologic changes accompany the transition from opioid use to abuse.
- Pharmacologic treatments are safe and effective in decreasing illicit opioid use, medical and social complications.

Web Resources

<http://buprenorphine.samhsa.gov/>

<http://ceattc.org>

(continuing education for counselors)

<http://suboxone.com>

<http://opioiddependence.com>

<http://turningtohelp.org>

Thank you!
