Treatment of Opioid Addiction

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Why does the human brain become addicted?

Why can we only become addicted to some substances?
What is addiction?
Addiction

- A brain disease
- Compulsive seeking and self-administration of a drug, despite obvious harm to self or others
- Characterized by intense craving and loss of control
What is addiction?

• **Physical Dependence**
  - Withdrawal if discontinued
  - Used as needed to control pain
  - Tolerance
  - Slowly increasing need over time
  - Further increased need in response to increased pain
  - Generally taken as directed

• **Addiction**
  - Withdrawal if discontinued
  - Used for the purpose of becoming euphoric
  - Compulsive, escalating use
  - Continued use despite negative consequences
  - Legal, medical, psychological, and social impact
Why do we find some things pleasurable, and not others?
The Reward Pathway

• A particular pathway in the brain is activated by all of the activities that we find pleasurable
  • Food, water and sex; “appetites”
  • Interpersonal relationships, spirituality, exercise, art, music, beauty

• The common reward pathway in the brain for all pleasurable activities involves the neurotransmitter **Dopamine**
“The Lizard Brain”
The drugs that we can become addicted to are those that hijack the natural pleasure circuitry of the brain.
All addictive drugs act via dopaminergic pathways
How have scientists sorted out how the addicted brain works?
It turns out that rats are remarkably similar to humans.....
Experimental system for studying addiction in rats

The (few) drugs that are self-administered by a rat are exactly the same as those that humans will self-administer.

Wise RA, Biological Psychiatry 2002
Rat model of addiction

- Rat is given a microinjection of an addictive drug into the reward pathway, and can repeat the experience by pushing a lever.
- Initial random lever-pushing quickly becomes compulsive.
- When rat receives drug (cocaine) every time it pushes the lever, it will starve to death or die of thirst rather than leave the lever to go into another part of the cage to eat or drink.

Routtenberg, 1965
Measuring intensity of addictive potential

• When rat is only rewarded in a progressive ratio (every 2nd, 4th, 8th push, etc), eventually it reaches a point where it will walk away from the lever (breakpoint)
• Correlates with addiction potential of drugs in humans
• For some drugs, the breakpoint is in the 10,000 range
What about opioid addiction?
Picture of opioid addiction: heroin
Picture of opioid addiction: pain pills
Unintentional overdose deaths involving opioid analgesics now exceed the sum of deaths involving heroin or cocaine.

Source: National Vital Statistics system, multiple cause of death dataset, Len Paulozzi, CDC 2010
Unintentional overdose deaths involving opioid analgesics parallel per capita sales of opioid analgesics in morphine equivalents by year, U.S., 1997-2007

As of 2007, Hydrocodone is the most prescribed Drug in the US, with 117 million prescriptions in 2007

Source: National Vital Statistics System, multiple cause of death dataset, and DEA ARCOS
* 2007 opioid sales figure is preliminary.
Drug Overdose Death Rates, New Mexico and United States, 1990-2011

Leading Causes of Unintentional Injury Death, New Mexico, 2001-2011

Source: New Mexico Vital Records and Health Statistics.
What role do dentists play?

• Although most Oral-Maxillofacial Surgeons state that ibuprofen is most effective analgesic after 3rd molar extraction, 85% also prescribe an opioid
• Average 20 tablets hydrocodone/APAP
• Some prescribe much more
• Estimate: 61 million opioid tablets prescribed to people whose average age is 20
• ER study: 81% of patients presenting to ER with dental pain received opioid prescription

Denisco, JADA 2011
Moore, Gen Dent 2006
Hocker, NC Med J 2012
What can dentists do about opioid overprescribing?

- Prescribe opioids less often, in lower quantities
- Instruct patients to call if inadequate analgesia
- Warn patients of risk of opioid addiction
- Instruct patients to secure opioid tablets, and discard unused opioids
- Consider screening for problems with abuse/addiction

Denisco, JADA 2011
Most effective treatment is Medication Assisted Treatment
Why do we need new ways of treating opiate addiction?

- “Detox” has no impact on long-term outcomes
- Only 200,000 patients on methadone for addiction treatment
- Treatment access is limited

SAMHSA Nat Survey Drug Use and Health 2006
Treatment of Opiate Addiction is Effective

- Decreases death rate \(^1\)
- Decreases HIV infection \(^2-3\)
  - Opioid agonist treatment of injection drug users decreased HIV incidence by 54% \(^2\)
- Decreases crime \(^4\)

1. Kreek J, Subst Abuse Treatment 2002; Gueve PN, Addiction 2002
Opiate agonists:

Methadone & Buprenorphine
Methadone

- Causes a 2/3 reduction in heroin use; can also be used for pain pill addiction
- Crime decreased 84%, drug selling decreased 86%
- Hospitalization decreased 58%
- Highly cost-effective for society: savings $3-4 for every dollar spent on treatment

1 Gerstein DR et al, CALDATA General Report, CA Dept of Alcohol and Drug Programs, 1994
Methadone Clinic

• Effective for many patients
• Structure of treatment setting can be helpful
• Now paid for by NM Medicaid
Problems with methadone: structural factors

• Access; can only be prescribed in a federally-regulated methadone clinic when used for addiction

• Cost ($5-13 per day; some public support)

• Directly observed therapy

• Exposure to other drug users

1. Salsitz, Mt Sinai J of Medicine, 2000
Problems with methadone: drug factors

- Sedation, “high”
- Difficult detox
- High doses required to be effective
- Overdose potential
- “diversion”
- Stigma
What is buprenorphine (Suboxone)?

• Newer medication (2002) for Medication-Assisted Treatment for opiate addiction (heroin and pain pills)¹
• Detox or maintenance
• About as effective as methadone²,³
• Several advantages over methadone

1 TIP Series # 40, SAMHSA, 2004
2 Mattick RP, Cochrane Database Systemic Review 2004
3 Soeffing, JSAT, 2009
Buprenorphine vs Methadone

Like Methadone...
- Reduces IDU
- Retains pt in treatment
- Decreases craving
- Stops withdrawal
- Costs $ 5-13 per day

Unlike Methadone....
- Low potential for OD
- Prescribed in MD office
- No sedation
- Easy taper/detox
Suboxone 8 mg tablets

Also available as a fast-dissolving sublingual film

- Two new generic formulations of buprenorphine/ naloxone recently approved
- Cost will drop rapidly
Trial of buprenorphine

- 40 Heroin addicts
- Buprenorphine 8mg/day vs taper + placebo
- All received counseling, groups
- Followed for 1 year

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<thead>
<tr>
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<th>Buprenorphine</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>Retained at 1 yr</td>
<td>70%</td>
<td>0</td>
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<tr>
<td>% died</td>
<td>0</td>
<td>20%</td>
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</tbody>
</table>

Kakko et al, Lancet 2003
Overall Overdose Mortality

French population in 1999 = 60,000,000

No. of deaths

Years


0 100 200 300 400 500 600

564

120

Rapport OCRTIS, 1998
M. Auriacombe, Université Victor Ségalen Bordeaux 2, Bordeaux, France
How effective is buprenorphine for opiate addiction treatment?

<table>
<thead>
<tr>
<th>Author, Journal</th>
<th>Year</th>
<th>“n”</th>
<th>Setting</th>
<th>% still participating in treatment</th>
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</thead>
<tbody>
<tr>
<td>Fudala, NEJM</td>
<td>2003</td>
<td>461</td>
<td>Multicenter research trial</td>
<td>57% @ 6 months</td>
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<tr>
<td>Alford, JGIM</td>
<td>2006</td>
<td>85</td>
<td>Acad med Ctr/Community clinic; ½ patients homeless; nurse case mgr</td>
<td>81% @ 12 months</td>
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<tr>
<td>Mintzer, Ann Fam Med</td>
<td>2007</td>
<td>99</td>
<td>4 primary care practices</td>
<td>54% @ 6 months</td>
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<tr>
<td>Cunningham, Fam Med</td>
<td>2008</td>
<td>41</td>
<td>Urban community health center</td>
<td>71% @ 3 months</td>
</tr>
<tr>
<td>Soeffing, J Subst Abuse</td>
<td>2009</td>
<td>255</td>
<td>Urban academic health center</td>
<td>57% @ 12 months</td>
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</table>
Why is overdose potential low with buprenorphine?
What about diversion of buprenorphine?

- When patients abuse a drug, they usually crush it and inject it
- Buprenorphine is sold as Suboxone®, a pill that contains both buprenorphine and naloxone (Narcan®)
- When taken under the tongue, the naloxone is not absorbed and so is not active
- When injected, the naloxone is active and causes withdrawal (if the patient is opiate-dependent)
- Decreases, but does not prevent, misuse
What’s “diversion” all about?

• 2010 Harvard study of people seeking treatment concluded: "illicit buprenorphine rarely represents an attempt to attain euphoria. Rather, illicit use is associated with attempted self-treatment of symptoms of opioid dependence, pain, and depression."

• Interestingly, although absolute numbers of diverted tablets are increasing, diversion has remained relatively steady as a proportion of prescribed tablets

Schuman-Olivier, JSAT, 2010
Johanson, Drug Alcohol Dep, 2012
Survey of opioid addicts

- Treat opioid withdrawal symptoms: 76%
- Try to stop using other opioids: 66%
- Unable to afford treatment: 58%

Bazazi, J Addict Med 2011
Buprenorphine administrative issues

- 8 hours of training required
- Only physicians may prescribe
- Maximum 30 simultaneous patients in year one, 100 patients thereafter
- Medication costs about $450 per month, covered by Medicaid with PA
- Far too few physicians prescribe in NM
Buprenorphine is an effective treatment that can help your patients who are dependent on pain pills or other opiates.
Non-opioid treatment options for opioid addiction
Oral naltrexone

- Opioid blocker; does not decrease craving
- Minimally effective for treating opioid addiction
- Problem is non-adherence
- Effective in selected highly-monitored, highly motivated patients: 94% of health care professionals had long term sobriety

1. Minozzi, Cochrane Database Syst Rev 2006
2. Roth, J Subst Abuse Treatment 1997
Injectable Naltrxone

• FDA approved recently for opioid addiction treatment; “Vivitrol”, previously approved for treatment of alcohol addiction
• No head-to-head studies vs buprenorphine; NIDA trial pending
• Small amount of promising data on efficacy
• Cost: $1099 per injection

2. Lobmaier, Cochrane Syst Rev 2008
3. Comer, Arch Gen Psych 2007
Trial of injectable naltrexone vs Placebo for 24 weeks

Data from treatment completers

- Injectable naltrexone
- Placebo

Krupitsky, Lancet, 2011
Injectable naltrexone efficacy

• Studied in Russia, against placebo
• Sponsored by manufacturer
• Initiated during inpatient detox/rehab
• 24 wk trial with monthly Vivitrol vs placebo, and 2x per month counseling
• 54% did not complete trial
Injectable Naltrexone offers great promise, but more data are needed to understand risks & benefits as well as barriers in outpatient practice.
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... promotes care in underserved areas

The mission of Project ECHO® (Extension for Community Healthcare Outcomes) has been to develop the capacity to safely and effectively treat chronic, common, and complex diseases in rural and underserved areas, and to monitor outcomes of this treatment.

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