Pain and Safe Prescribing

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Addiction Medicine Review Course
CSAM, Newport Beach, CA

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## Disclosure of Relevant Financial Relationships

October 2010

<table>
<thead>
<tr>
<th>Name</th>
<th>Commercial Interests</th>
<th>Relevant Financial Relationships: What Was Received</th>
<th>Relevant Financial Relationships: For What Role</th>
<th>No Relevant Financial Relationships with Any Commercial Interests</th>
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<tbody>
<tr>
<td>Daniel P. Alford, MD</td>
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Pain

**Acute Pain**
- Symptom
- Resolves
- Beneficial

**Chronic Pain**
- Pathological
- >3-6 months
- Chronic disease

**Chronic Pain Syndrome**
- Restriction in daily activities
- Alteration in behavior & affect
- Excessive reliance on medications & medical services
- Multiple, non-productive tests, treatment & surgeries
Is his **chronic** pain real?

- There are no "pain meters" & vital signs are not reliable
- Pain is subjective to the patient & to the examiner
- It is difficult to distinguish **inappropriate** drug-seeking from **appropriate** pain relief-seeking
- There is no way on the **first visit(s)** to know for certain if the patient’s pain is real or not
Nervous System Plasticity

Normal terminations of primary afferents in the dorsal horn

Dorsal root gangli

Aβ
C

Superficial
Deep

Dorsal horn

Midline

After nerve injury, C-fibre terminals atrophy and A-fibre terminals sprout into the superficial dorsal horn

Superficial
Deep

Woolf CJ, Mannion RJ. Lancet 1999
Opiophobia...

The OxyContin Underground

How a prescription painkiller is turning into a pernicious street drug.
By Paul Tough

"I showed a lot of people," said Curt, a former user and dealer. "People told me now, yeah, you're the one who showed me how to snort this thing.

Televangelist Crosses Over - Coed Golf - The Legacy of Birmingham

The Politics of Pain

Law enforcement is clamping down on doctors who prescribe high doses of the most powerful and dangerous painkillers. Is this protecting patients — or hurting them? | BY DRAKE BENNETT
Exhibit 2: Past Year Initiation of Non-Medical Use of Prescription-type Psychopharmaceutics, Age 12 or Older: In Thousands, 1965 to 2005

New Users (x 1000)

Source: SAMHSA, OAS, NSDUH data, July 2007
Where Pain Relievers Were Obtained
Nonmedical Use among Past Year Users Aged 12 or Older 2006

Source Where Respondent Obtained

- More than One Doctor: 1.6%
- One Doctor: 19.1%
- Bought/Took from Friend/Relative: 14.8%
- Drug Dealer/Stranger: 3.9%
- Bought on Internet: 0.1%
- Other: 4.9%

Source Where Friend/Relative Obtained

- More than One Doctor: 3.3%
- Free from Friend/Relative: 7.3%
- Bought/Took from Friend/Relative: 4.9%
- Drug Dealer/Stranger: 1.6%
- Other: 1.6%

Source: SAMHSA, OAS, NSDUH data, July 2007
Over-Prescribing

- Medication mania
- Hypertrophied enabling
- Confrontation phobia

Parran T. Medical Clinics of North America 1997
No Excuse For Pain

Doctors have the means at hand to relieve the suffering of millions of Americans. Why aren’t they doing it?

By Alice Dembner

Twenty days of unremitting agony. That’s how Lester Tomlinson’s family describes the end of his life.

As the 85-year-old retired refinery worker lay dying in a California nursing home, his doctor never prescribed enough medicine to ease the pain of his incurable lung cancer, according to the family. Although Tomlinson signed a directive requesting pain medicine even if it hastened his death, he got no pain pills at all until his daughter begged for help.

So Ginger Tomlinson did something unusual: She sued the doctor and nursing home after her father’s death in 2001, charging elder abuse. She recently won an out-of-court settlement and is awaiting the outcome of disciplinary charges filed against the doctor by the Medical Board of California.

“He suffered excruciating pain,” Tomlinson said. “He was moaning and grimacing and praying to die because he couldn’t take the pain. Nobody should have to die like that.”

Tomlinson is in the vanguard of a drive to use the courts and medical licensing...
## Issues Preventing Opioid Prescribing

*n=111*

<table>
<thead>
<tr>
<th>Issue</th>
<th>Percentage</th>
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<tr>
<td>Potential for patients to become addicted</td>
<td>89%</td>
</tr>
<tr>
<td>Potential for patients to sell or divert</td>
<td>75%</td>
</tr>
<tr>
<td>Opioid side effects</td>
<td>53%</td>
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<tr>
<td>Regulatory/law enforcement monitoring</td>
<td>40%</td>
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<tr>
<td>Hassle and time required to track/refill</td>
<td>28%</td>
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*Upshur CC et al. J Gen Intern Med 2006*
Iatrogenic Addiction

• 140 pts seeking buprenorphine treatment

• Primary outcome was response to: “Who introduced you to opiates?”
  ▪ 29% introduced to opioids by a physician
    ▪ 100% initially used for pain
  ▪ 71% started with illicit opioids
    ▪ 11% initially used for pain

Tsui JI et al. JSAT 2010 in press
What is the Addiction Risk?

- Published rates of abuse and/or addiction in chronic pain populations are 3-19%

- **Known risk factors** for addiction to any substance are **good predictors** for problematic prescription opioid use
  - Past cocaine use, h/o alcohol or cannabis use\(^1\)
  - Lifetime history of substance use disorder\(^2\)
  - Family history of substance abuse, a history of legal problems and drug and alcohol abuse\(^3\)
  - Tobacco dependence\(^4\)
  - History of severe depression or anxiety\(^4\)

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\(^1\) Ives T et al. BMC Health Services Research 2006  
\(^2\) Reid MC et al JGIM 2002  
\(^3\) Michna E el al. JPSM 2004  
\(^4\) Akbik H et al. JPSM 2006
Making the Diagnosis…

Diagnosing **Opioid Dependence** in Patients on Chronic Opioids is Difficult

Requires **3 or more** criteria occurring over 12 months

1. Tolerance – **YES**
2. Withdrawal/Physical dependence – **YES**
3. Taken in larger amounts or over longer period - **MAYBE**
4. Unsuccessful efforts to cut down or control - **MAYBE**
5. Great deal of time spent to obtain substance - **MAYBE**
6. Important activities given up or reduced - **MAYBE**
7. Continued use despite harm - **MAYBE**

American Psychiatric Association DSM IV-TR 2000
Addiction is...

• A clinical syndrome presenting as...
  – Loss of Control
  – Compulsive use
  – Continued use despite harm
  – Craving

• Not equal to physical dependence

Savage SR et al. J Pain Symptom Manage 2003
Aberrant Medication Taking Behavior

A spectrum of patient behaviors that may reflect misuse:

- Health care use patterns (e.g., inconsistent appointment patterns)
- Signs/symptoms of drug misuse (e.g., intoxication)
- Lying and illicit drug use
- Problematic medication behavior (e.g., noncompliance)

Implications

- Concern comes from the “pattern” or the “severity”
- Differential diagnosis

Butler et al. Pain. 2007
Total Chronic Pain Population

Aberrant Medication Taking Behaviors (AMTBs)
A spectrum of patient behaviors that *may* reflect misuse

Prescription Drug Misuse

Opioid Addiction
Opioids and Mu Receptors

• Inhibit nociceceptor activation in periphery
• Inhibit C-fibers terminals in the spinal cord
• Inhibit ascending transmission of pain signal
• Turn on descending inhibitory systems in the PAG
• *Stimulate the reward pathway*
Opioid Efficacy in Chronic Pain

- Most literature surveys & uncontrolled case series
- RCTs are short duration <4 months with small sample sizes <300 pts
- Mostly pharmaceutical company sponsored
- Pain relief modest
- Limited or no functional improvement

Balantyne JC, Mao J. NEJM 2003
Kalso E et al. Pain 2004
Eisenberg E et al. JAMA. 2005
Furlan AD et al. CMAJ 2006
Opioid Responsiveness
Potential Variations

Key:
OM – Opioid Metabolizer
OT – Opioid Transporter
OR – Opioid Receptor
OS – Opioid Signaler
OTS – Opioid Target Site

Smith HS. Pain Physician 2008
Opioid Safety

- **Allergies** are rare
- **Side effects** are common
  - Nausea, **sedation**, constipation
  - Urinary retention, sweating
- **Organ toxicities** are rare
  - Hypothalamic-pituitary-gonadal axis - ↑prolactin, ↓ LH, FSH, testosterone, estrogen, progesterone
- **Overdose** especially when combined w/ other sedatives
How Much is Too Much?

- Compared with patients receiving 1-20 mg/d of morphine equivalents, patients receiving 50-99 mg/d had a 3.7-fold increase in overdose risk.
- Patients receiving 100 mg/d or more had an 8.9-fold increase in overdose risk with a 1.8% annual overdose rate.
- Morphine equivalent doses over 120 mg/d doubled the risk of alcohol- or drug-related health services utilization encounters (withdrawal, intoxication, overdoses).

Braden JB et al. Arch Intern Med 2010
When Are Opioids Indicated?

- Pain is moderate to severe
- Pain has significant impact on function
- Pain has significant impact on quality of life
- Non-opioid pharmacotherapy has failed
- Patient agreeable to have opioid use closely monitored
Opioid Choice

• Duration and onset of action
  – “Rate hypothesis” - fast on, fast off – most rewarding - addicting

• Patient’s prior experience
  – $Mu$ polymorphisms – differences in opioid responsiveness

• Route of administration, side effects & cost

• **Currently there are NO abuse resistant opioids or opioid formulations!!**
Methadone is Different

1. NMDA receptor antagonist
2. Less euphoria (po)
3. 5HT, NE uptake inhibition
4. No neurotoxic metabolites
5. Inexpensive
6. Long, variable, unpredictable half-life
7. QTc prolongation, risk of torsade de points
Preventing Opioid Misuse

- Scant evidence to guide practice
- Expert guidelines for responsible prescribing
  - Federation of State Medical Boards model policy
  - Clinical guidelines by Chou et al.
- Use consistent approach “universal precautions”, but set level of monitoring to match risk
- Use a risk/benefit framework: Judge the treatment not the patient

FSMB. J Pain Palliat Care Pharmacother. 2005
Gourlay DL, Heit HA. Pain Medicine 2005
Assessing Benefit
One useful tool...

PEG (Pain, Enjoyment, General activity) scale (0-10)

1. What number best describes your pain on average in the past week? (No pain - Pain as bad as you can imagine)

2. What number best describes how, during the past week, pain has interfered with your enjoyment of life? (Does not interfere - Completely interferes)

3. What number best describes how, during the past week, pain has interfered with your general activity? (Does not interfere – Completely interferes)

Assessing for Harm

“Universal Precautions”

- Use risk screening tools (e.g., Screener and Opioid Assessment for Patients w/ Pain, Opioid Risk Tool)
- Agreements/contracts
- Monitor for aberrant medication taking behavior
- Monitor for adherence and harm
  - Urine drug testing
  - Pill counts
- Use prescription monitoring program data

FSMB Guidelines 2004 www.fsmb.org
Gourlay DL, Heit HA. Pain Medicine 2005
Chou R et al. J Pain 2009
Monitoring: Urine Drug Tests

- Evidence of therapeutic adherence
- Evidence of non-use of illicit drugs
- Know limitations of test and your lab
- Know a toxicologist/clinical pathologist
- Complex patient-physician communication
- Efficacy not well established

Heit HA, Gourlay DL. J Pain Symptom Manage 2004
Standridge JB et al. Am Fam Physician 2010
Urine Toxicology Monitoring in Patients on Opioids for Chronic Pain

<table>
<thead>
<tr>
<th>BEHAVIOR ISSUES</th>
<th>YES</th>
<th>NO</th>
<th>TOTAL</th>
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<tbody>
<tr>
<td>URINE TOX POSITIVE</td>
<td>10 (8%)</td>
<td>26 (21%)</td>
<td>36 (29%)</td>
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<tr>
<td>NEGATIVE</td>
<td>17 (14%)</td>
<td>69 (57%)</td>
<td>86 (71%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>27 (22%)</td>
<td>95 (78%)</td>
<td>122</td>
</tr>
</tbody>
</table>

26/122 (21%) of patients had no aberrant behavioral issues BUT had abnormal drug test

Katz NP et al. Clinical J of Pain 2002
Documentation

• Patient Evaluation
• Treatment & Opioid Management Plan
• Informed Consent
• Treatment Agreement
• Monitoring (pain, function, adverse events, adherence to prescribed therapies)
• Assessment and plan
• Consultation

Federation of State Medical Boards Model Guidelines 2004 Available at www.fsmb.org
Continuation of Opioids

• You must convince yourself that there is benefit

• Benefit must outweigh observed harms

• If small benefit, consider increasing dose as a “test”.

• If no effect = no benefit, hence benefit cannot outweigh risks – so STOP opioids. (Ok to taper and reassess.)

• You do not have to prove addiction or diversion – only assess Risk-Benefit ratio
Increased Risk → Increase Level of Monitoring

- Opioid Renewal Clinic (Urban VA)
- Primary care based Nurse Practitioner and Clinical Pharmacist with “back up” by a multispecialty pain clinic supported PCPs who continued as opioid prescribers
- 335 pts. “high risk patients” referred over 2 years
  - 51% (171) had aberrant behaviors on referral
    - 45% improved adherence, behaviors resolved
    - 38% self discharged
    - 13% referred for addiction treatment
    - 4% tapered

Weidemer NL Pain Medicine 2007
Exit Strategy
Discussing Lack of Benefit

- Stress how much you believe / empathize with patient’s pain severity and impact
- Express frustration re: lack of good pill to fix it
- You are abandoning the treatment, NOT the patient
- Focus on patient’s strengths
- Encourage therapies for “coping with” pain
- Show commitment to continue caring about patient and pain, even without opioids
- Schedule close follow-ups during and after taper
It is not just about opioids…

- Non-steroidal anti-inflammatory drugs (NSAIDS)
- Acetaminophen
- Tricyclic anti-depressants
- SSRI (selective serotonin reuptake inhibitors)
- SNRI (serotonin–norepinephrine reuptake inhibitors)
- Anxiolytics
- Anti-convulsants
- Muscle relaxants
- Topical preparations—e.g., anesthetics
- Others (tramadol)
Mechanism-Specific Pain Management

Descending inhibition
(NE, 5HT)

Peripheral sensitization
(Na⁺ channels)

Central sensitization
(Ca²⁺ channels, NMDA receptor)

Brain

Spinal cord

PNS

TCA
Lidocaine
Lamotrigine

TCA
SSRI
SNRI
Tramadol

TCA
Gabapentin
Exploit Synergism
“Sensible Poly-pharmacy”

Morphine, Gabapentin, or Their Combination for Neuropathic Pain

Ian Gilron, M.D., Joan M. Bailey, R.N., M.Ed., Dongsheng Tu, Ph.D., Ronald R. Holden, Ph.D., Donald F. Weaver, M.D., Ph.D., and Robyn L. Houlden, M.D.
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It is not just about medications…

Use full spectrum of treatments

- Physical therapy – conditioning***
- Behavioral therapy – relaxation / counseling / expectations orientation**
- Massage Therapy*
- Spinal Manipulation*
- Acupuncture*
- TENS units
- Nerve blocks*
Pain Management in Patients with History of Addiction

- Both stimulant and opioid abusers have less pain tolerance than peers in remission or matched controls.
- Former opioid abusers have decreased pain tolerance to pain compared with non-addict siblings.
- Therefore, patients with a history of addiction may be more pain sensitive and require higher opioid doses.

Acute Pain Management in Patients on Opioid Maintenance Therapy

- Patients on opioid maintenance treatment (i.e. methadone or buprenorphine) have less pain tolerance than matched controls.

- Patients who are physically dependent on opioids (i.e. methadone or buprenorphine) must be maintained on daily equivalence before ANY analgesic effect is realized with opioids used for acute pain management.

PCSS…

- answers questions about opioids, including methadone, for treatment of chronic pain
- is free, for interested physicians and staff
- is supported by SAMHSA and administered by the ASAM
Ask a clinical question…

• get a response from an expert PCSS mentor
  – on line by email  PCSSproject@asam.org
  – by phone 877-630-8812

From  www.PCSSmentor.org...

• download clinical tools, helpful forms and concise guidance's (like FAQs) on specific questions