Balancing Pain Management and Addictive Illness

Michigan State University
Case Management Conference
October 28, 2014

Mark A. Weiner, MD
Section Head of Addiction Medicine SJMH-AA
Pain Recovery Solutions
Disclosures:

• The content of this presentation is non-commercial and does not represent any conflict of interest.

• This talk includes discussion of the ‘off label’ use of several medications. I will inform you when this happens.
Special Thanks

- Herb Malinoff, MD
- Carl Christensen, MD, PhD
- Howard Kornfeld, MD
- Edward Covington, MD
- Doug Gourlay, MD
- Howard Heit, MD
- Donald Kurth, MD
- Edwin Salsitz, MD
- Ross Halpern, PhD
- Seddon Savage, MD
- Mel Pohl, MD
- Patrick Gibbons, DO

- SJMH Departments of Neurosurgery, Orthopedics, PM&R
- University of Michigan, Departments of Neurosurgery, Orthopedics, PM&R
- Tri-County Pain Management, Prizm Pain Management, Michigan Pain Institute, Michigan Pain Specialists, Cleveland Clinic
Objectives

- What Is the Problem?
  - Present 4 distinct but interrelated issues:
    - Addiction
    - Chronic Pain
    - Opiate Overuse
    - Benzodiazepine Overuse

- How Do You Know It’s There?
  - Identification Strategy

- What Do You Do About It?
  - Exit Strategy
Format For This Talk

• Intro

• The Four Sections
  • Addiction 101
  • Pain 101
  • Problems with Opiates and Sedatives
  • Assessment

• Exit strategies
Why Is This A “Hot Topic”?
Drug deaths now outnumber traffic fatalities in U.S., data show

Fueling the surge are prescription pain and anxiety drugs that are potent, highly addictive and especially dangerous when combined with one another or with other drugs or alcohol.

Sept 17, 2011
U.S. panel to take on rising prescription drug, heroin abuse
Tue, Apr 22 2014

(Reuters) - A panel of the U.S. House of Representatives has scheduled a hearing for April 29 on a rising tide of prescription drug and heroin abuse in the United States.

The House Energy and Commerce Committee "will review the growing concerns regarding heroin and prescription opioid abuse and related deaths," the panel said in a statement on Tuesday.

Data from the National Institute on Drug Abuse finds that heroin use has been increasing since 2007, with nearly double the number of Americans using heroin in 2012 than in 2006.

(Reporting by Ros Krasny; Editing by Peter Cooney)
• 38329 drug overdose deaths in the United States in 2010
• 22,134 or 57.7% involved pharmaceuticals
• Of the pharmaceutical-related overdose deaths, 16451 or 74.3% were unintentional, 3780 or 17.1% were suicides and 1868 or 8.4% were of undetermined intent
• Opioids present in 16,651 or 75.2% Rx OD deaths 2010
• Benzodiazepines present in 6497 or 29.4% Rx OD deaths 2010

• 7374 students (H.S. seniors) from 3 independent cohorts (2007, 2008, and 2009)

• 12.9% reported nonmedical use of prescription opioids
Doctors Training in Addiction

- National survey of residency training directors found that 56.3% had addiction in required curriculum which ranged from 3-12 hours
- CASA Columbia reviewed board certification exams in 6 medical specialties that interact most often and regularly with patients who may have SUD issues and found that it ranged from 0-2% of the exams.
Internal medicine residents’ training in substance use disorders; a survey of the quality of instruction and resident self-perceived preparedness to diagnose and treat addiction.

- Twenty-five percent of residents felt unprepared to diagnose and 62% felt unprepared to treat addiction.
- 13% felt very prepared to diagnose addiction.
- Seventy-two percent of residents rated the quality of addictions training as poor or fair.
- No resident answered all 6 knowledge questions correctly.
• 94% of primary care physicians failed to diagnose substance abuse when presented with early symptoms of alcohol abuse in an adult patient.
• 29.5% of patients (in treatment for addiction) said their physicians knew about their addiction and prescribed psychoactive drugs such as sedatives or Valium.

www.centerforhealthandjustice.org/BOSUDsandPrimaryCare.pdf
Public Policy Statement on Measures to Counteract Prescription Drug Diversion, Misuse and Addiction - ASAM BOD, 01/25/12.

• “Studies have shown that physicians have not received adequate education about the potential psychiatric and addiction consequences of the decision to prescribe scheduled medication”

• “Most practicing physicians have had little if any formal training in addiction.”

• “Confusion still exists whereby some clinicians mistake physical dependence (tolerance and withdrawal) for addiction”
Policy statement, ASAM 2012 ...

... “there is emerging data to suggest that when primary care physicians are targeted for focused education regarding pain, pain medication prescribing, and assessing patients for risk prior to the initiation of opioid analgesic therapy, trends in opioid overdose deaths can be reversed.”

Why Is This A “Hot Topic”?

- Accidental overdose deaths from prescriptions medications have exceeded deaths from motor vehicle accidents since 2008 and continue to rise.
- Addiction is poorly understood by primary care providers.
- This patient population is comprised of both addicts and non-addicts.
- The “standard of care” actually potentiates the problem.
- Better understanding of pharmacotherapy can reduce the risks and improve quality of life.
Why Is This A “Hot Topic”? 

- The chronic use of opiates leads to tolerance -> increase in dose -> CNS toxicity
- The chronic use of benzodiazepines leads to tolerance -> increase in dose -> CNS toxicity
- The use of these medications together increases the toxicity/lethality
- Most health care providers do not have a exit strategy
Opioid Prescriptions for Chronic Pain and Overdose
A Cohort Study
Kate M. Dunn, PhD; Kathleen W. Saunders, JD; Carolyn M. Rutter, PhD; Caleb J. Banta-Green, MSW, MPH, PhD; Joseph O. Merrill, MD, MPH; Mark D. Sullivan, MD, PhD; Constance M. Weisner, DrPH, MSW; Michael J. Silverberg, PhD, MPH; Cynthia I. Campbell, PhD; Bruce M. Psaty, MD, PhD; and Michael Von Korff, ScD

Primary Funding Source: National Institute of Drug Abuse.
Dunn, et al. 2010

- 9940 patients; 1997-2005
- Results

<table>
<thead>
<tr>
<th>Morphine Dose</th>
<th>Hazard Ratio of Serious Overdose</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0.19</td>
</tr>
<tr>
<td>1 - &lt;20 mg /day</td>
<td>1.00</td>
</tr>
<tr>
<td>20 - &lt;50 mg/day</td>
<td>1.19</td>
</tr>
<tr>
<td>50 - &lt;100 mg/day</td>
<td>3.11</td>
</tr>
<tr>
<td>100 + mg/day</td>
<td>11.18</td>
</tr>
</tbody>
</table>
Addiction 101
What is an Addict?

- Someone who says they are an addict
- Someone who asks for pills all the time
- Someone with weak will power
- Someone who is not smart enough to stop
- The last patient you ever want to deal with
What is Addiction

General Idea:
Continued use of a substance or engagement in an activity despite obvious harm.
What is Addiction

- A primary, chronic disease of brain reward, motivation, memory and related circuitry

- Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations.

- This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.

American Society of Addiction Medicine, Public Policy Statement: Definition of Addiction
What is Addiction

- Like other chronic diseases, addiction often involves cycles of relapse and remission.

- Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.
Mark A. Weiner, MD

VTA
Ventral Tegmental Area (midbrain)

"Pleasure Circuit"

Amphetamine
Cocaine
Opiates
Cannabinoids
Phencyclidine
Ketamine

GABA
ENK
VP

OFT

FCX

GLU

HIPP

AMYG

CRF

OPIOID

GABA

DYN

5HT

DA

BNST

OPIOID

GABA

ABN

HYPOTHAL

HYPOTHAL

ICSS

Opiates
Ethanol
Barbiturates
Benzodiazepines
Nicotine
Cannabinoids

Amphetamines
Cocaine
Opiates
Cannabinoids
Phencyclidine
Ketamine

Opiates

5HT

NE
LC

PAG

END

To dorsal horn

Raphé

RETIC
“Pleasure Circuit”

- Cortex (logic)
- Amygdala (emotions)
- Hipocampus (memory)
- Ventral Pallidum (motivation)
- Nucleus Accumbens (striatum)
- VTA (Ventral Tegmental Area, midbrain)

DOPAMINE flow from VTA to Nucleus Accumbens.
“Pleasure Circuit”

Addict

VTA

Nucleus Accumbens (striatum)

Pleasure Circuit

Amygdala (emotions)

Hippocampus (memory)

Ventral Pallidum (motivation)

Cortex (logic)

Amphetamine
Cocaine
Opiates
Cannabinoids
Phencyclidine
Ketamine

Opiates
Ethanol
Barbiturates
Benzodiazepines
Nicotine
Cannabinoids

DOPAMINE!!!

Ventral Tegmental Area (midbrain)
“Pleasure Circuit”

VTA (Ventral Tegmental Area, midbrain)

- Amphetamine
- Cocaine
- Opiates
- Cannabinoids
- Phencyclidine
- Ketamine

DOPAMINE

- Opiates
- Ethanol
- Barbiturates
- Benzodiazepines
- Nicotine
- Cannabinoids

Ventral Pallidum (motivation)

Hippocampus (memory)

Amygdala (emotions)

Nucleus Accumbens (striatum)

STRESS

glutamate

CUES

CRF/Norepi

Cortex (logic)

(Addict)
“Pleasure Circuit” (Addict)

Nucleus Accumbens (striatum)

Ventral Tegmental Area (midbrain)

Amygdala (emotions)

Hippocampus (memory)

Ventral Pallidum (motivation)

Cortex (logic)

Pleasure Circuit

Amphetamine
Cocaine
Opiates
Cannabinoids
Phencyclidine
Ketamine

Opiates
Ethanol
Barbiturates
Benzodiazepines
Nicotine
Cannabinoids

DOPAMINE!!!

VTA

Ventral Tegmental Area (midbrain)
Drug ADDICTION: Gardner 2006

Physiology of Addiction
Drug WITHDRAWAL: Gardner 2006

Physiology of Addiction
How To Assess Addiction

• Ask about current addiction
  • Nicotine addiction (aka “Smoking”)
  • Alcohol use (Heavy Drinking)
  • Illicit Drugs
  • Prescription Drug aberrancy

• Ask about past history of addictive behavior and consequences
  • DUI, MIP’s, incarceration, job loss, marital and family problems, treatment centers

• Family History of Addiction
Formalized Assessment Tools

- CAGE – (originally for alcohol only)
- DSM-IV Checklist
- AUDIT – short, 10 items, 5min
- MAST – oldest, 22 items, alcohol only
- DAST – MAST for drugs
The ASAM PPC – Disease Axis

**Dimension 1:** Acute Intoxication and/or Withdrawal Potential

**Dimension 2:** Biomedical Conditions / Complications

**Dimension 3:** Emotional, Behavioral or Cognitive Conditions / Complications

**Dimension 4:** Readiness to Change

**Dimension 5:** Relapse, Continued Use or Continued Problem Potential

**Dimension 6:** Recovery/Living Environment
The ASAM PPC – Treatment Axis

Describes treatment as a continuum marked by five basic levels of care:

Level 0.5 - Early Intervention
Level I - Outpatient Treatment
Level II - Organized Outpatient
Level III - Residential Services
Level IV - Inpatient Treatment
What to do if you find addiction?

- Be supportive and non-judgemental
- Share what you know about addiction
- Refer to a specialist for assessment
- Refer to mutual self-help group (patient and family)
- Avoid mood altering substances (esp. benzodiazepines and opiates)
How do we address addiction?

Acute Problem

Vs.

Chronic Illness
Did treatment work?
Did addiction treatment work?
Is addiction treatment as effective as treatment for other health problems?
How does asthma compare?

- Medication compliance: 30%
- Relapse Rate: 60 to 80%
How does hypertension compare?

Medication And Diet

Compliance: 30%

Relapse Rate: 60-80%
How does diabetes compare?

Medication, diet and foot care

Compliance: <50%

Relapse: 30-50%
Alcoholism?

Compliance: 30-50%

Relapse: 50%
Opiates?

Compliance: 30-50%

Relapse: 40%
Tobacco?

Compliance: 30-50%

Relapse: 70%
Cocaine?

Compliance: 30-50%

Relapse: 45%
What happens when we treat addiction as a chronic illness???
PHP’S

• Care management services for 5 years
• Residential, outpatient, therapy, family involvement
• Intensive monitoring
• Relapses are handled with swift re-intervention
• Sober social support including 12 step participation
PHP Success Rates


- Of physicians who completed or extended their contracts
  - 81% had no relapse and abstained from drugs and alcohol for the full length of monitoring
  - 19% had at least one positive drug test result
    - Among those detected only 26% had a repeat positive test over the 5 year duration
Summary

("Take Home Points")

• Addiction is a brain disease
• There are treatments that work
• Treat your addicted patients with kindness and respect understanding they are ill (just like cancer or diabetes)
• Get help with your addicted patients – this is not easy.
Why Did I Just Talk About Addiction?

- So you can differentiate it from dependence
- To understand that the treatment of dependence is not the same as the treatment of addiction
- The treatment of addiction requires a great deal more than prescribing drugs (topic of another talk)
Section Break
TIME FOR Q&A
Pain 101
Simple Approach to Treating Non-Malignant Pain

- If it hurts.....
- If it hurts a lot....
- If it REALLY hurts....
- If it still REALLY hurts....
- If it REALLY hurts for a long time....
- If it’s getting worse no matter what I prescribe....

- Give ibuprofen
- Give hydrocodone
- Give something stronger
- Give more
- Keep giving more
- Discharge patient

"Hmmm. Something is just not right."
CHARACTERISTICS OF PAIN PATIENTS PRESENTING TO ED/URGENT CARE/OP CLINICS

- Report high level of psychological distress.
- Display high levels of psychopathology
- Report high levels of functional impairment
- Have history of work-related injuries or MVA’s
- Frequent use of health care system
- Complain of constant pain
- Have had prior surgery (ies) for pain
- Are using narcotic medication
CHARACTERISTICS OF ADDICTED PATIENTS PRESENTING TO ED/URGENT CARE/OP CLINICS

- Report high level of psychological distress.
- Display high levels of psychopathology
- Report high levels of functional impairment
- Have history of work-related injuries or MVA’s
- Frequent use of health care system
- Complain of constant pain
- Have had prior surgery (ies) for pain
- Are using narcotic medication
What is Pain?
Clinical definition:

“Whatever the patient states it is unless proven otherwise by poor adherence to the agreed upon medical regimen.”

“No kind of sensation is keener and more active than that of pain, its impressions are unmistakable.”

The Marquis de Sade
A Brief History of Pain
Descartes and Pain
TRAITTE DE L'ESPRIT
DE L'HOMME,
DE SES FACULTEZ ET FONCTIONS,
ET DE SON UNION AVEC LE CORPS.
Suiuant les Principes de RENE DESCARTES.
Par LOVIS DE LA FORGE, Docteur en Medecine demeurant a Saumur.
“If the fire A is close to the foot B, the small parts of this fire, which, as you know, move very quickly, have the force to move the part of the skin of the foot that they touch, and by this means pull the small thread C, which you can see is attached, simultaneously opening the entrance of the pore d, e, where this small thread ends...the entrance of the pore or small passage d, e, being thus opened, the animal spirits in the concavity F enter the thread and are carried by it to the muscles that are used to withdraw the foot from the fire.”
Gate Theory of Pain Modulation
Pain is the Most Highly Modulated Sensory Experience

- Central Modulation (e.g., stimulation of periaqueductal gray)
- Inhibitory or facilitatory processes in spinal cord (ascending) or brain (descending)
- Opioid analgesics enhance inhibition initially, may facilitate as late phenomena (hyperalgesia)
- Addictive illness facilitates via multiple mechanisms

PAIN INDUCED ACTIVATION OF THE THALAMUS AND ANTERIOR CINGULATE CORTEX

Neural Correlates of Inter-Individual Differences in the Subjective Experience of Pain
INJURIES OF NERVES

AND THEIR CONSEQUENCES.

BY

S. WEIR MITCHELL, M.D.,

Member of the National Academy of Sciences;
Fellow of the Philadelphia College of Physicians; Physician to the Philadelphia
Orthopedic Hospital and Infirmary for Diseases of the
Nervous System, etc.

"I hold every man a debtor to his profession; from which as men of course do seek to receive
countenance and profit, so ought they of duty in endeavor themselves, by way of amends, to be a help
and ornament thereunto."—Bacon.

PHILADELPHIA:
J. B. LIPPINCOTT & CO
1872.
“Under such torments, the temper changes, the most amiable grow irritable, the bravest soldier becomes a coward…….”

Dr. S. Weir Mitchell, 1872
Chronic Pain Syndrome

- Intractable pain of more than 6 months duration
- Marked alteration in behavior, restriction in daily activities
- Excessive use of medication and medical services
- No clear relationship to organic disorder - multiple nonproductive tests/treatments/surgeries

Office of Disabilities, Social Security Administration
Summary Of Current Chronic Pain Theory

Neuroplasticity influenced by:
• excito-toxicity
• central sensitization (allergy to pain?)
• genetic predisposition
• trauma/abuse
• addiction/psychiatric co-morbidities
• with resulting neurochemical and neurohormonal derangements
Chronic Pain Responds Differently than Acute Pain

- Some of the treatments that work well for acute pain, may worsen chronic pain

- Examples:
  - Short acting opiates
  - “muscle relaxers” / sedatives
  - Medical procedures
Goals of Treating Chronic Pain

• Increase function!!!
• Decrease pain
• Use medications that do not have unacceptable side effects
Take Home Point

Chronic Pain is Different than Acute Pain
Section Break

TIME FOR Q&A
Problems with Opioids And Pain

- Tolerance
- Dependence/Withdrawal
- Opiate-Induced Hyperalgesia (OIH)
Hyperalgesia

- A heightened pain state
- Minor painful stimuli produce an intense and miserable pain state (“heightened misery state”)
- Universal at chronic high doses of opioids
- Central facilitatory/excitatory mechanisms responsible
- CNS pain filtering mechanisms are essentially absent

J Mao, DD Price and DJ Maye
Thermal hyperalgesia in association with the development of morphine tolerance in rats: roles of excitatory amino acid receptors and protein kinase C
Journal of Neuroscience, Vol 14, 2301-2312
Mechanisms of Opioid Induced Hyperalgesia

- Dynorphine System Activation
  - Kappa receptor overstimulation

- Descending Facilitation
  - CCK upregulation in rostral ventromedial medulla (Mitchell et al, 1998)
Mark A. Weiner, MD

Diminished Pain Tolerance in Methadone-Maintained Patients

Centralized Pain Syndromes

- Pain “generator” is in the CNS
- Always made worse with opiates and sedatives
- Examples:
  - Complex Regional Pain Syndrome (formerly RSD)
  - Fibromyalgia
  - Migraine
  - Interstitial Cystitis
  - Burning Mouth Syndrome
Benzodiazepines

Maybe Not Mother’s Little Helper
Definitions

- Benzodiazepine: A benzodiazepine is a psychoactive drug whose core chemical structure is the fusion of a benzene ring and a diazepine ring. Benzodiazepines enhance the effect of the neurotransmitter gamma-aminobutyric acid (GABA), which results in sedative, hypnotic (sleep-inducing), anxiolytic (anti-anxiety), anticonvulsant, muscle relaxant and amnesic actions.
Examples of Benzodiazepines

- Alprazolam (Xanax®)
- Diazepam (Valium®)
- Lorazepam (Ativan®)
- Temazepam (Restoril®)
- Midazolam (Versed® - IV only)
- Clonazepam (Klonopin®)
- Oxazepam (Serax®)
- Chlordiazepoxide (Librium®)
Definitions

• Benzodiazepine-like Substances: The nonbenzodiazepines, also called benzodiazepine-like drugs, are a class of psychoactive drugs whose pharmacological actions are similar to those of the benzodiazepines, but are structurally distant or unrelated to the benzodiazepines on a chemical level. They have similar side effects, benefits and risks as the benzodiazepines.
Examples of Benzodiazepine-Like Drugs

- zolpidem (Ambien®)
- zaleplon (Sonata®)
- eszopiclone (Lunesta®)
- carisoprodol (Soma®, a prodrug of meprobamate/Miltown®)
- Cyclobenzaprine (Flexeril®)
- baclofen (Kemstro®)
- ....and many more
Pharmacology of Benzodiazepines

• Benzodiazepines work by increasing the efficiency of GABA (gamma-Aminobutyric acid).

• GABA decreases the excitability of certain neurons. This reduces the communication between neurons and therefore has a calming effect on many of the functions of the brain.

• Specifically these substances bind the post synaptic GABA receptor, and allow it to unnaturally, powerfully inhibit the post synaptic neuron.
Therapeutic Uses for Benzodiazepines

- Panic Disorder
- Generalized anxiety disorder
- Insomnia / Sleep disturbance
- Seizure / status epilepticus
- Alcohol withdrawal
- Spasticity
Instead, we found evidence that benzodiazepine use was significantly associated with activity level, medical visitation, domestic disability, and to a lesser degree, disability days. With respect to illness behavior, therefore, benzodiazepine use appears to offer an alternative explanation for the observed “downhill spiral” thought to be associated with opioid use.
A comparison of cognitive impairment due to benzodiazepines and to narcotics.
American Journal of Psychiatry. 137(7):828-30,

In an attempt to determine the source of cognitive impairment in 106 consecutively admitted patients at the Johns Hopkins Chronic Pain Treatment Center, EEG, the Wechsler Adult Intelligence Scale, Memory Quotient, and Bender Gestalt tests were administered. Patients receiving benzodiazepines alone demonstrated alterations in cognitive functioning and EEG evidence of a sedative effect. Patients receiving narcotics alone and a group of patients not receiving medication did not show signs of cognitive impairment. The effects of benzodiazepines on sleep and perception of chronic pain, in combination with the cortical changes that they produce, imply that these drugs should not be used in most patients with chronic pain.
GUIDELINES

Management of generalised anxiety disorder in adults: summary of NICE guidance

Tim Kendall,1,2,3 John Cape,4,2 Melissa Chan,1 Clare Taylor,1 on behalf of the Guideline Development Group

Do not offer a benzodiazepine to treat generalised anxiety disorder in primary or secondary care except as a short term measure during crises. (New recommendation.)

Cite this as: BMJ 2011;342:c7460
doi: 10.1136/bmj.c7460
BMJ 2012;345:e6231 doi: 10.1136/bmj.e6231 (Published 27 September 2012)

RESEARCH

Benzodiazepine use and risk of dementia: prospective population based study

Sophie Billioti de Gage PhD student, Bernard Bégaud professor, Fabienne Bazin researcher, Hélène Verdoux professor, Jean-François Dartigues professor, Karine Pérès researcher, Tobias Kurth director of research, Antoine Pariente associate professor
Discussion

In this large, prospective, population based study of elderly people who were free of dementia and did not use benzodiazepines until at least the third year of follow-up, new use of benzodiazepines was associated with a significant, approximately 50% increase in the risk of dementia. This result remained stable after adjustment for potential confounding factors, including cognitive decline before starting benzodiazepine and clinically significant symptoms of depression. It also remained robust when we pooled five cohorts of new benzodiazepine users throughout the 15 year follow-up period and in a complementary nested case-control study.
Prevalence of Selected Benzodiazepines

<table>
<thead>
<tr>
<th>Drug</th>
<th>Rx’s in 1998 (millions)</th>
<th>Rx’s in 2007 (millions)</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>24.75</td>
<td>42.38</td>
<td>+71%</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>9.52</td>
<td>20.42</td>
<td>+115%</td>
</tr>
<tr>
<td>Temazepam</td>
<td>6.24</td>
<td>8.10</td>
<td>+30%</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>17.15</td>
<td>21.32</td>
<td>+24%</td>
</tr>
<tr>
<td>Diazepam</td>
<td>11.09</td>
<td>14.19</td>
<td>+28%</td>
</tr>
</tbody>
</table>

Benzodiazepine Side Effects

- Generalized cognitive impairment
- Visiomotor discoordination (falls, MVA’s)
- Anterograde amnesia
- Social phobia
- Depression
- Sleep disturbance
- Paradoxical disinhibition
- Emotional blunting
- “Zombified”
How To Recognize Benzodiazepine Overuse Syndrome (aka Sedativism)

- Flat Affect
- Cognitive Impairment
- Visual-Spatial Discoordination
- Memory Loss
- Sleep Disturbance
- Depression
Reasons to Consider Cessation of Benzodiazepine Treatment

- Emergence of undesirable side effects or benzodiazepine overuse syndrome
- Emergence of misuse or addiction
- History or onset of alcoholism or addiction
- Starting a new treatment where benzodiazepines are contraindicated (e.g. opioid treatment for pain, )
- Tolerance / Dependence
- Elderly patient (falls, MVA’s)
Benzodiazepine Withdrawal Syndrome

- Visiospatial discoordination
- Visual changes ("visual blurring")
- Tremor
- Emotional lability
- Cramping of fingers, toes
- Muscle spasms
- Nausea, anorexia
- Absence of motivation
Time for Q&A

Section Break
Practical Matters: Assessment and Rational Approach
Universal Precautions: Patient Triage

- **Group I: Who is your patient?**
  - No addiction, full function, no psychiatric comorbidities

- **Group II: Who is our patient?**
  - Remote addictive history without relapse, well treated psychiatric disorder, fully employed and functioning

- **Group III: Who is my patient?**
  - Active addiction (even tobacco), active psychiatric disorder, disability (e.g. not employed)

Addiction vs. Pseudoaddiction

- Pseudoaddiction looks like addiction in its aberrant behaviors - but is really under-treated pain
- “The key with pseudoaddiction is that with proper pain management, retrospectively, the patient’s behavior normalizes. However, with the disease of addiction,... behavior deteriorates with pain management.”

- Heit, 2005
“Red Flag” Behaviors

• “Red Flags” are not conclusive but can help alert you to possible misuse (not necessary addiction)

• Examples
  • Asking for a particular opiate by name
  • Frequent requests for early refills (NB: may also be inadequate treatment)
  • End of day/week “surprise” visits
  • Multiple prescribers
  • Frequent “lost, stolen or my-cat-spilled” opiates
Some Patients are Seeking Drugs

• “If you have a feeling your patient is manipulating you, it is more than a feeling.”

Mark A. Weiner, MD
April 26, 2014
BEAR COUNTRY...

Do Not Feed The Bears!
Remember, a trash or handout bear is a dead bear!

Food odors attract bears. Avoid unwelcome visitors by keeping a clean home site or camp site.

Keep all food and garbage secure. Garbage is food too!

Never leave food outdoors for wildlife or pets.

Do not store food in tents – put in bear proof food boxes or hang from a tree.

Improperly stored food may result in property damage. Intentional feeding will result in fines (36 CFR 261.50e).

Never approach or disturb bears – if there is no food available they will go away. Enjoy all wildlife from a distance. Do not run from a bear, just move calmly away. Remember, dogs antagonize bears, so leash your pet.

Bear in Mind...Bears Live Here

North American Bear Society/USDA Forest Service Challenge Coin Show Project.

North American Bear Society
SOUTHERN ARIZONA CHAPTER
TUCSON, ARIZONA
Rational Prescribing of Opiates

- Never prescribe on the first visit
- Opiate Agreement
- Urine Drug Screens
- MAPS
- DOCUMENT, DOCUMENT DOCUMENT!
Explanation of “Never prescribe on the first visit”

• *Never* prescribe on the first visit

• If you feel you must prescribe opiates to a patient you just met....
Explanation of “Never prescribe on the first visit” Revised

- Use common sense
- Just give enough until next visit (e.g., 2-3 days)
What You Should Do On The First Visit

- Collect data, lab results, medical records
- Urine toxicology on all patients
- MAPS Report
- Contact previous provider(s)
Opiate Agreement

• It is not a contract, it is a signed letter of understanding
• Risk and benefits including issues of withdrawal, addiction, tolerance
• Patient will be seen regularly without excessive missed appointments
• You are the only provider for pain meds
• One pharmacy
• Must inform you of all ER and urgent care pain meds
• No illegal use of controlled substances: marijuana, heroin, cocaine, etc
Opiate Agreement

- No prescription for pain meds will be called in urgently, especially after hours.
- Pill counts
- Safe use concepts (use care when driving, operating machinery, safeguarding from children, etc.)
- Clarifies the universal use of urine drug screens
Urine Drug Screen

• Introduce this as a policy for all patients on opiates or sedatives chronically
• UDS
  • Check for substances that SHOULD NOT be there
  • Checks to confirm substances that SHOULD be there
• Should be performed randomly and regularly (e.g. every 2 - 12 weeks)
• Have basic knowledge of your UDS!
• When in doubt, contact the clinical toxicologist at your lab.
# Urine Drug Screen

## Table 3. Detection time of drugs of misuse in urine

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cutoff level (ng/mL)</th>
<th>Detection time in urine*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine (multidrug misusers, dose unknown)</td>
<td>1000</td>
<td>Up to 5 days</td>
</tr>
<tr>
<td>THCOOH after smoking 1 marijuana cigarette</td>
<td>50</td>
<td>2 to 4 days†</td>
</tr>
<tr>
<td>Benzoylecgonine after 20 mg IV cocaine</td>
<td>300</td>
<td>Up to 1.5 days</td>
</tr>
<tr>
<td>Benzoylecgonine after street doses of cocaine†</td>
<td>300</td>
<td>2 to 3 days; up to 1 week at higher doses</td>
</tr>
<tr>
<td>Morphine from low-dose heroin (3-12 mg)†</td>
<td>300</td>
<td>1 to 1.5 days</td>
</tr>
</tbody>
</table>

THCOOH=9-carboxy-Δ⁹ tetrahydrocannabinol; IV=intravenous
*May not accurately reflect detection after extraordinarily high doses in chronic users; †Administered via different routes; †‡Up to 1 month with frequent use
## Urine Drug Screen

### Source of opioid analgesics

<table>
<thead>
<tr>
<th>Natural (from opium)</th>
<th>Semisynthetic (derived from opium)</th>
<th>Synthetic (man-made)</th>
</tr>
</thead>
<tbody>
<tr>
<td>codeine</td>
<td>hydrocodone</td>
<td>meperidine</td>
</tr>
<tr>
<td>morphine</td>
<td>oxycodone</td>
<td>fentanyl series</td>
</tr>
<tr>
<td>thebaine</td>
<td>hydromorphone</td>
<td>propoxyphene</td>
</tr>
<tr>
<td></td>
<td>oxymorphone</td>
<td>methadone</td>
</tr>
<tr>
<td></td>
<td>buprenorphine</td>
<td></td>
</tr>
</tbody>
</table>
UDS Case 1

• A 54 year old executive of a manufacturing company who is taking 60 to 75 hydrocodone 7.5mg/750mg per day for neck pain.

• He reports drinking 3-5 mixed drinks per night. He denies using any other prescription medications or street drugs excepts and occasional Ambien®.
### TOXICOLOGY

**02/16/09**

#### UDS Case 1

**CLINICAL URINE DRUG ABUSE SCREEN**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMPHETAMINE</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>BARBITURATES</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>BENZODIAZEPINE</td>
<td><strong>POS</strong></td>
</tr>
<tr>
<td>BENZODIAZEPINES GC/MS CONFIRM</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>COCAINE</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>ETHANOL</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>OPIATES</td>
<td><strong>POS</strong></td>
</tr>
<tr>
<td>TOTAL MORPHINE by GC/MS</td>
<td>&lt;100</td>
</tr>
<tr>
<td>TOTAL CODEINE by GC/MS</td>
<td>&lt;100</td>
</tr>
<tr>
<td>TOTAL HYDROCODONE by GC/MS</td>
<td>&lt;100</td>
</tr>
<tr>
<td>TOTAL HYDROMORPHONE by GC/MS</td>
<td>13329 ng/mL</td>
</tr>
<tr>
<td>TOTAL OXOCODONE by GC/MS</td>
<td>&lt;100</td>
</tr>
<tr>
<td>PHENCYCLIDINE</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>THC (CANNABIS)</td>
<td>NEGATIVE</td>
</tr>
</tbody>
</table>

**02/16/09 2238**

**BENZODIAZEPINES GC/MS CONFIRM**

The benzodiazepine screen failed to confirm by GC/MS. This could be due to a benzodiazepine not detected by the GC/MS assay, low drug levels or an interfering substance in the screen. The NSAID oxaprozin (Daypro) gives a false positive screen result.

**CREATININE URINE RANDOM ADULTERANTS**

<table>
<thead>
<tr>
<th>Result</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEGATIVE</td>
<td>20-300 mg/dL</td>
</tr>
</tbody>
</table>

**COMMENT:**

ADULTERANTS TESTED FOR INCLUDE CHROMATES AND NITRITES.
Urine Drug Screen

Figure 1. Metabolism of opioids*

- codeine → morphine → 6-MAM → heroin
- hydrocodone → hydromorphone

*Not comprehensive pathways, but may explain the presence of apparently unprescribed drugs

†6-MAM = 6-monoacetylmorphine, an intermediate metabolite

Gourlay D, Heit H. and Caplan Y Urine Drug Testing in Clinical Practice: Dispelling The Myths & Designing Strategies, 2006 (3)
Section Break
TIME FOR Q&A
Exit Strategies:
A return to safety
The Answer!

- Medication Transition
  - Opiates
    - using a partial opioid agonist (i.e., buprenorphine)
  - Benzodiazepones
    - Using GABA receptor modifying agents
Disclaimer

- There are often circumstances where patients are so dependent that it is necessary to refer to a specialist in treating medication toxicity and or addiction.

- In certain cases, hospitalization is necessary (yes, it is covered as long as it is not addiction treatment).
“If you can’t land, don’t take off.”

When you initiate a trial of opioid therapy, have an ‘exit strategy’.

Twelve Reasons for Considering Buprenorphine as a Frontline Analgesic in the Management of Pain

Mellar P. Davis, MD, FCCP, FAAHPM

Buprenorphine

• Available in several forms:
  • Buprenex injection
  • Generic SL buprenorphine
  • Transdermal Patch (Butrans®)
  • Suboxone Film*: naloxone added
  • Generic SL Buprenorphine/naloxone

• Dosing for chronic pain is often different than for chemical dependency

• *not FDA approved for pain
Buprenorphine

- Acts as a mu agonist:
  - Partial agonist; ceiling effect for analgesia and respiratory depression
  - Slower dissociation = milder withdrawal
  - High affinity: will displace some other μ agonists and precipitate withdrawal
  - Antagonist at the kappa receptor
Clinically Observed Affinity

Morphine
Oxycodone/hydrocodone
Buprenorphine
Hydromorphone
Methadone
Fentanyl(s)
Work-up For Chronic Pain Patients

- Take a complete medical history
- Review psychiatric history
- Review substance abuse history (including alcohol and tobacco use)
- Get a complete list of all medications (current and historical) MAPS (and repeat regularly)
- Urine Drug Screen
- Basic Labs (CBC, Chem profile, Thyroid fxn, etc)
- Carefully educate the patient as to risks, benefits and expectations.
Work-up For Chronic Pain Patients

- Consider all of the following:
  - Pain Psychology Consult
  - Psychiatry consult
  - Nutritional consult
  - Medicine / Cardiology consult
Indications For Change

- Worsening pain despite increasing doses of opiates (i.e., emergence of hyperalgesia)
- Emergence of intolerable side effects (esp. mood disorder and cognitive impairment)
- Lack of improvement in activity or social interaction
- Safety concerns (falls, MVA, unintentional overdose)
## Guidelines For Appropriate Use

<table>
<thead>
<tr>
<th>Drug</th>
<th>Maximum Appropriate</th>
<th>Possible Hyperalgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocodone</td>
<td>30 - 40 mg/day</td>
<td>&gt; 40 mg/day</td>
</tr>
<tr>
<td>Morphine</td>
<td>15 - 60 mg/day</td>
<td>&gt; 100 mg/day</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>30 - 40 mg/day</td>
<td>&gt; 90 mg/day</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>12 - 50 mcg/hr</td>
<td>&gt; 50 mcg/hr</td>
</tr>
<tr>
<td>Methadone</td>
<td>10 - 40 mg/day</td>
<td>&gt; 40 mg/day</td>
</tr>
</tbody>
</table>
Buprenorphine Induction Stratification

- Office-based
  - Lower doses of opioids
  - Low risk / little comorbidity
  - 3-4 hour observed visit

- Hospital Based
  - Toxic doses of opioids (i.e., medication toxicity)
  - High comorbidity
  - Hospital stay 3-5 days
Success Rates

- Patients report reduced pain and improvement in quality of life in $69^2 - 84^1\%$

- Family members frequently say “Thank you for giving me my [wife/husband/parent/child] back

- Patient usually “comes to” by the second month

- This is the beginning of a long process

Appropriate Consultation Before Discontinuing Benzodiazepines

• Consider all of the following:
  • Psychiatry consult
  • Neurology consult
  • Medicine / Cardiology consult

• When appropriate and possible, notify all prescribing physicians of intent to change medication

* For high dose benzodiazepine use or significant medical comorbidity consider hospitalization.
I Am About To Mention Medication Uses For Indications That Are Not FDA Approved

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbital</td>
<td>Epilepsy, status epilepticus, insomnia, preanesthesia, sedation</td>
</tr>
<tr>
<td>Gabapentin (Neurontin®)</td>
<td>Epilepsy, post-herpetic neuralgia</td>
</tr>
<tr>
<td>Oxcarbazepine (Trileptal®)</td>
<td>Epilepsy</td>
</tr>
<tr>
<td>Pregabalin (Lyrica®)</td>
<td>Management of neuropathic pain associated with diabetic peripheral neuropathy, postherpetic neuralgia, adjunctive for epilepsy, fibromyalgia</td>
</tr>
<tr>
<td>Trazadone</td>
<td>Depression</td>
</tr>
<tr>
<td>Quetiapine (Seroquel®)</td>
<td>Depression, bipolar disorder, schizophrenia</td>
</tr>
<tr>
<td>Mirtazapine (Remeron®)</td>
<td>Major depression</td>
</tr>
</tbody>
</table>
Pharmacologic Assisted Benzodiazepine Discontinuation

- **First Line:** Phenobarbital
  - Acts as a weak agonist at GABA receptor
  - Long half-life, minimal withdrawal
  - Generally well tolerated and effective

- **Dosing:**
  - 30 to 60 mg from one to four times per day, depending on benzo dose and response
  - At night, stop benzos and start phenobarbital
Pharmacologic Assisted Benzodiazepine Discontinuation

- **Course of Treatment:**
  1. Stabilize symptoms
  2. Begin slow taper, reducing dose monthly. (Expect emergence of mild benzo withdrawal each time.)
  3. Length of time varies with patient, benzo dose and length of treatment. Usually 6-9 months, range 1 – 24 months.
# Benzodiazepine Withdrawal vs. Phenobarbital Side Effects

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Benzodiazepine Withdrawal</th>
<th>Phenobarbital Side Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Fatigue</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Blurred Vision</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Loss of Balance</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Somnolence</td>
<td>rare</td>
<td>✓</td>
</tr>
</tbody>
</table>
Usual Outpatient Plan for Benzodiazepine Dependence Treatment

- Stop benzo and start phenobarbital at night.
- Instruct patient to take phenobarbital 2 hours prior to bedtime.
- Schedule a follow-up appointment in 1-2 weeks.
- Check phenobarb level as indicated (Target: 10-20 mcg/ml)
- Check MAPS, UDS + ETG, other rx and EtOH use
- “Consider” taper at each monthly visit
Usual Outpatient Plan for Benzodiazepine Dependence Treatment

- Expect mild withdrawal 5-7 days after each taper
- Assess for depression and anxiety disorder regularly and consider referral to “friendly” psychiatrist
- Expect (and encourage) phone calls
Take Home Points

• Not every patient who overuses medication is an addict

• Medication toxicity is frequently the result of over prescribing

• Medication-assisted withdrawal requires some expertise and patience but can dramatically improve quality of life and safety

• Do not forget to treat your patient with compassion and understanding
Thank You!

- How to reach me:
  - Pain Recovery Solutions
    734 434-6600
  - Email
    markola@me.com
  - Web
    www.painrecoverysolutions.com
References


www.centerforhealthandjustice.org/BOSUDsandPrimaryCare.pdf


American Society of Addiction Medicine, Public Policy Statement: Definition of Addiction


J Mao, DD Price, and DJ Mayer Thermal hyperalgesia in association with the development of morphine tolerance in rats: roles of excitatory amino acid receptors and protein kinase The Journal of Neuroscience, 1 April 1994, 14(4): 2301-2312;
References


N Hendler, C Cimini, T Ma, D Long A comparison of cognitive impairment due to benzodiazepines and to narcotics *Am J Psychiatry*, 1980

