The 3 “Rx’s” of Prescribing Controlled Substances: Rules, Regulations, and Risks

June 17, 2016
The Hattiesburg Clinic Support Service Center
Hattiesburg, Mississippi

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## SMA Meeting on Prescribing Controlled Substances
June 17, 2016 ◊ Hattiesburg Clinic Support Services Building ◊ Hattiesburg, MS

### Schedule at a Glance

#### FRIDAY, JUNE 17

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
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<tbody>
<tr>
<td>8:00-8:30</td>
<td><strong>Breakfast</strong>&lt;br&gt;Sponsored by SMA Services, Inc.</td>
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<tr>
<td>8:30-8:35am</td>
<td><strong>Welcome</strong>&lt;br&gt;Dr. Ben Carmichael</td>
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<tr>
<td>8:35-8:45</td>
<td><strong>Overview and Objectives</strong>&lt;br&gt;Dr. Scott Hambleton, Chair</td>
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<tr>
<td>8:45-9:45</td>
<td><strong>Collegiate Addiction: The Importance of Recovery Programs</strong>&lt;br&gt;Gregory J. Snodgrass, MSW and Blake Schneider, MA</td>
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<tr>
<td>9:45-10:45</td>
<td><strong>Amphetamines: History, Use and Misuse, and Societal Influence</strong>&lt;br&gt;Dr. Mark Williams</td>
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<tr>
<td>10:45-11:45</td>
<td><strong>Opioid Prescribing Pearls: How to Avoid Obvious Pitfalls &amp; Use Appropriately</strong>&lt;br&gt;Dr. John Mutziger</td>
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<tr>
<td>11:45-1:00</td>
<td><strong>Lunch Break</strong>&lt;br&gt;On Your Own</td>
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<tr>
<td>1:00-2:00</td>
<td><strong>Addictive Disorders: Management Principles and MPHP Approach</strong>&lt;br&gt;Dr. Scott Hambleton</td>
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<tr>
<td>2:00-3:00</td>
<td><strong>Sedative-Hypnotics: Their Use and Misuse</strong>&lt;br&gt;Dr. John Mutziger</td>
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<td>3:00</td>
<td><strong>Adjourn</strong></td>
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### ONLINE CME REQUEST FORM AND EVALUATION

CME credit is handled through an on-line process. Your certificate will be emailed to you within 2 weeks of receipt of the completed online form. A clickable link was also included in a post-meeting email.

https://www.surveymonkey.com/r/2016_PCS_SMS
NEEDS STATEMENT
According to the CDC, the United States is in the midst of a prescription painkiller overdose epidemic with ten of the highest prescribing states for painkillers in the South. The amount of prescription painkillers prescribed and sold in the U.S. has nearly quadrupled since 1999, yet there has not been an overall change in the amount of pain that Americans report. People who take prescription painkillers can become addicted with just one prescription. Overdose deaths increased from 4,000 annually to 16,600 during the same period. In fact, such overdoses are now the second leading cause of accidental death in the U.S., and more than 2.4 million people were considered to be opioid abusers in 2010. Approximately one in five college students abuse or misuse prescription stimulants such as Adderall* and Ritalin*, often as a way to manage daily demands. A survey by the Partnership for Drug-Free Kids found that 28% of young adults who have been legally prescribed prescription stimulants share their medicine. More than half of these students are also pressured by their friends to share or sell their stimulants.

LEARNING OBJECTIVES
After participating in this activity, learners should be better prepared to:

1. Discuss the epidemiology of addiction.
2. Interpret the brain disease model of addiction.
3. Describe the Physician Health Program (PHP) management of addictive disorders as a potential template for the management of patients with addictive disorders in the general population.
4. Discuss the clinical uses of benzodiazepines.
5. Compare the pharmacology and physiology of sedative hypnotics.
6. Discuss toxicity and side effects.
7. Describe trends in abuse and misuse of sedative-hypnotics.
8. Employ the new mandates just released about prescribing opioids.
9. Discuss the risks of prescribing opioids.
10. Recognize how to minimize the risk of prescribing opioids.
11. Discuss the importance of Collegiate Recovery Programs.
12. Describe the intertwined relationship between prescription drugs and college students.
13. Recognize societal pressures and perspectives when considering the use of amphetamines.
14. Discuss the possible role of pharmaceutical and manufacturing strategies in advancing the use of their products.
15. Consider future uses of amphetamines and similar compounds.

TARGET AUDIENCE
This activity is designed for all physicians and healthcare professionals prescribing controlled substances.
CONFERENCE SYLLABUS/FACULTY SLIDES
Notice was sent via email to all registrants that the faculty slides were available on a private website prior to the conference for electronic download. A printed copy of the slide presentations will not be provided onsite.

To access the files, go to:
http://sma.org/education-sma/events/prescribing-controlled-substances-conference/presentations/

CONTACT INFORMATION
Southern Medical Association is the accredited sponsor of this CME activity. For questions about this activity or to become a member of the SMA, use the following contact information:
Tel: 800-423-4992, ext. 620; Fax to 205-945-1830; Email: customerservice@sma.org; Mail: SMA, 35 W. Lakeshore Drive, Suite 201, Birmingham, Alabama 35209: website: sma.org.

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Southern Medical Association designates this Live activity for a maximum of 5 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in this activity.

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The American Academy of Nurse Practitioners Certification Program (AANPCP) accepts AMA PRA Category 1 Credit™ from organizations accredited by the ACCME. Individuals are responsible for checking with the AANPCP for further guidelines.

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to [5] MOC points in the American Board of Internal Medicine’s (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider’s responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

DISCLAIMER
The primary purpose of this CME conference is education. Information presented, and techniques discussed are intended to inform physicians and other providers of medical knowledge, clinical procedures, and experiences of physicians willing to share such information with colleagues. It is recognized that a diversity of professional opinions exists in the contemporary practice of medicine, which influence the selection of methods and procedures. The views and approaches of faculty are offered solely for educational purposes. The Southern Medical Association disclaims any and all liability for injury or other damages to any individual attending this CME conference and for all claims, which may result from the use of the information presented at this conference.
CME REQUEST FORM and CONFERENCE EVALUATION

Upon the completion of this conference, please go to the following link and complete the CME request form and conference evaluations. Your CME certificate will be processed and sent via e-mail approximately 2 weeks after the conference based on the lectures you attend.

https://www.surveymonkey.com/r/2016_PCS_SMS

ACKNOWLEDGEMENT

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DISTINGUISHED FACULTY

Scott Hambleton, MD, FASAM, Chair
Dr. Hambleton became the Medical Director of the Mississippi Professionals Health Program in 2010. He is a 1994 graduate of the University of Tennessee School of Medicine. Dr. Hambleton completed the Accelerated Family Practice Residency at the University of Tennessee in 1996. He completed the University of Florida Addiction Medicine Fellowship at Pine Grove Behavioral Health in Hattiesburg, Mississippi in 2007. Dr. Hambleton is the immediate past president of the Mississippi Society of Addiction Medicine. He is board certified by the American Board of Family Medicine and the American Board of Addiction Medicine. Dr. Hambleton is a Fellow in the American Society of Addiction Medicine. He has served as Medical Director of The Oxford Centre in Oxford, Mississippi for treatment of adult males with chemical dependency; Medical Director at Pine Grove Women’s Center for treatment of females with chemical dependence and/or eating disorders; and Medical Director of Pine Grove’s Gentle Path Program for treatment of sexual addiction.

Mark S. Williams, MD, JD, MBA, CPE
Dr. Williams is the Chief Physician Executive for Tenet’s Brookwood Baptist System in Birmingham, Alabama. He is the immediate past president of the Southern Medical Association. From 2008 to 2014 he served as the Chief Medical Officer of the North Mississippi Health System in Tupelo, Mississippi – the largest rural health care systems in the United States and the recipient of the 2012 National Malcolm Baldrige Award for Organizational Performance. A graduate of the University of South Alabama School of Medicine, Dr. Williams completed his post-graduate training as the chief resident in the department of anesthesiology at the University of Alabama in Birmingham. He is formerly a member of the governor’s Medicaid redesign committee and Healthcare Workforce committee in Mississippi, past board chairman of the Alabama Quality Assurance Foundation, and served as chief of staff of Carraway Methodist Medical Center from 2005 to 2007. From 2006 to 2008 he was the Chief Medical Officer for the St. Vincent’s system in Birmingham, Alabama and chairman of Ascension Health’s Physician Informatics Committee and Chair of Ascension’s Task Force on Disclosure of Unanticipated Outcomes. He is a 2001 graduate of the Alabama School of Law and a member of the Alabama State Bar. He completed the MBA program at Samford University in 1995 and is a former medical director for Alabama Power Company. He enjoys white water rafting in the wilds of Idaho and Montana. He and his wife Sandi have four children and one grandchild.
John Mutziger, DO
Dr. Mutziger grew up in Natchez, Mississippi. Dr. Mutziger attended Tulane University and then the University of Health Sciences in Kansas City, Missouri. He returned to Philadelphia, Mississippi to practice on a National Health Services Scholarship. Meridian is his home and has been since he moved there in 1990. Dr. Mutziger has been an Addictionologist since 1995 and received his certification by the American Board of Addiction Medicine. He was a previous CME director for the Mississippi Osteopathic Medical Association (MOMA) for 7 years. Dr. Mutziger is a past president of MOMA and the Mississippi Society of Addiction Medicine. Dr. Mutziger has now retired from Family Practice and is practicing Addiction Medicine Full time for the Alliance Health Center in Meridian, MS. He just received his FASAM this year for the American Society of Addiction Medicine.

Blake Schneider, MA
Mr. Schneider is the Program Coordinator of the Collegiate Recovery Community at Mississippi State University. He received his master’s in Communication Studies from the University of Alabama, with an emphasis in organizational communication. As a Graduate Teaching Assistant of public speaking he learned how to foster a collaborative environment among college students, and the qualities required to be an effective public speaker. He has experience working in recovery settings including recovery residences, inpatient programs, and the CRC at the University of Alabama. His goals include providing a true college experience to students of the CRC and recruiting new members from all walks of life.

DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIPS

SMA Faculty Disclosure Policy and Conflict of Interest Resolution: In accordance with the ACCME’s Standards for Commercial Support, it is SMA’s policy that all individuals involved with planning and implementation of the content of an SMA CME/CE activity are required to disclose to the audience 1) any relevant financial relationships with a commercial interest producing, marketing, re-selling, or distributing health care goods or services consumed by or used on patients and 2) unlabeled/unapproved uses of drugs or devices discussed in their presentation. Perceived conflicts of interest (COI) will be resolved prior to the activity.

Scott Hambleton, MD, Program Chair and Faculty
• No relevant financial relationships to disclose.

Kendra Blackmon, SMA Staff
• No relevant financial relationships to disclose.

Ben Carmichael, MD, Program Moderator
• No relevant financial relationships to disclose.

John Mutziger, MD, Faculty
• No relevant financial relationships to disclose.

Blake Schneider, MA, Faculty
• No relevant financial relationships to disclose.

Mark S. Williams, MD, MBA, JD, CPE, Faculty
• No relevant financial relationships to disclose.

Steven Strode, MD, MBA
• No relevant financial relationships to disclose.

Philip Hartman, MD
• No relevant financial relationships to disclose.

Thomas Fowlkes, MD
• No relevant financial relationships to disclose.

Michael Gosney, MD, JD, MBA
• No relevant financial relationships to disclose.
References and Resources


FDA Blueprint for Prescriber Education for ER and LR Analgesics.

J. Hicks, Fast Times: The Life, Death and Rebirth of Amphetamines, Chemical Heritage Magazine, Spring 2012

L. Kamienski, The Drugs That Built a Super Soldier, The Atlantic, April 8, 2016


National Institute on Drug Abuse (NIDA) - Benzodiazepine Abuse


Principles of Addiction Medicine - Fourth Edition

Principles of Addiction Medicine - ASAM Publication - Fifth Edition


Substance Abuse - A Comprehensive Textbook - Fourth Edition


Utah Clinical Guidelines on Prescribing Opioids-Utah Dept. of Health.

A. Zaitchick. The Speed of Hypocrisy: How America Got Hooked on Legal Meth. www.motherboard.vice.com
Lecture Summary: The lecture planned will provide listeners with a greater awareness and understanding of prescription drug use among college students and the impact it has on Collegiate Recovery Communities. Addiction is a deadly disease and many addicts develop a habit beginning with a prescription to controlled substances. A takeaway will be the importance of Collegiate Recovery Professionals and Healthcare Professionals collaborating to provide the utmost care to students in recovery.

Objectives: Upon completion of this lecture, attendees should be better prepared to:
- Discuss the importance of Collegiate Recovery Programs
- Describe the intertwined relationship between prescription drugs and college students

NOTES:
Saving, Sustaining, and Enhancing Student’s Lives: the Exigency and Benefits of Collegiate Recovery

Blake Schneider, MA

“It is somewhat ironic that there are thousands of substance abuse prevention and treatment programs but only a handful of programs supporting recovery communities.”

(Cleveland et al., 2007)

Exigency

• Collegiate Alcohol Use Each Year:
  • 1,800+ college students die
  • 97,000 victims of sexual assault
  • 400,000 students engage in unsafe sex
  • 100,000 too intoxicated to remember if they gave consent
  • 599,000 unintentional injuries
  • 696,000 assaults
  • 2,700,000 students drove under the influence (22% increase in 7 years)
  • 23% of college students suffer academically

• In One Day:
  • 3-5 students die
  • 190-250 victims of sexual assault
  • 3,000 injuries

(Corrant et al., 2012; Frean et al., 2001)

Health Promotion and Wellness Collegiate Recovery Community
Exigency

• Substance abuse and addictions take a toll on students and universities
• Studies report that more than 40% of student attrition involves substance abuse (Sullivan & Ruder, 2002). Loss of education, profession, life, self...
• However, only 4% of students with alcohol/drug related problems will seek help (Clements, 1999).
• Substance abuse affects overall student retention rates at colleges and universities, wastes resources, fails university mission, fails students.

• With a supportive environment, such as a CRC, a minimum of 50% of students who seek help for their substance abuse issues could be retained and supported in their recovery (Harris et al., 2005).
• Importantly, more students would seek that help, not just 4%.
• CRC provides a safe, supportive, positive system for students in recovery and those seeking recovery.

• At TTU, the Center for the Study of Addiction and Recovery (their CRC) supports 80 of the estimated 213 addicted students seeking help on campus. CRC members come from all over campus. Grades and graduation rates are significantly higher than general population of students.
• By ensuring their continued enrollment in the university, the Collegiate Recovery Community allows TTU to keep $430,500 annually in direct tuition revenue that would be lost due to relapse and subsequent dropout. (Harris, et al., 2005)
Exigency

- Creating a safe place
  - There are recovering students at MS State right now that receive year round support
  - Reputation of CRC brings students to MS State

- A 2nd Chance program
  - For those who were not successful first go around at higher education.
  - For those who thought college was never an option.
  - This is also bring students to MS State.

What is Collegiate Recovery

- National movement
- Emerging and innovative field
- Addresses the unique challenges recovery students face in a collegiate environment

(Laudet et al., 2013)

What is a Collegiate Recovery Community (CRC) or Program (CRP)?

- Institutionally sanctioned community or program that promotes academic achievement, social engagement, and long-term recovery
- Abstinence based model that may incorporate recovery from eating disorders and addictive behaviors
- Mutual aid support
- Continuum of care
Areas of Support

- Academic
- Career
- Social
- Financial
- Recovery

Component Options

- Administrative Support
- Staff
- Students (Application process)
- Physical Space
- Board (Advisory or Working)

CRC is NOT

- Addiction Treatment
- 12-Step Replacement
- Group Therapy
Departmental Hosts

- Other, 29%
- Student Dev, 13%
- Student Life, 8%
- Student Health, 21%

Lauden, A., Harris, K., Mabry, K., Moberg, P. & Kimball, T. (2014)

Space

- Single Room, 31%
- Building, 8%
- Other, 34%

Benefits: Programming & Engagement

- Safe Place on campus
- Study space and study hours
- Connections on Campus
- Academic Scholarships
- Sober social events
- Service opportunities
- Retreats
- Conferences
- Recovery Night
- Seminar
Benefits: National Trends

National Retention and Graduation Rates of CRC students:
- 91.8% CRC Retention
- 80.8% Institution-wide
- 89% CRC Graduation
- 60.5% Institution-wide

Annual Budget: $80,870 to $495,000
- 80% Have NO Budget
- Est. cost to program per student: $1,635 (0-$5,000)
- Program capacity: mean 16 months
- Number of students currently served: 27 (0-500)

Abstinence duration:
- Mean: 16 months
- Longest: 16.7 years


Benefits: Cultural Shift

- Reduce stigma of addiction
- Part of a broader cultural shift
- Strengthens local recovery community

THE Benefit: Student Perspectives

- “I would never have gone to college if I hadn’t found out about this program…”
- “The center made it really possible to meet people that were in recovery quickly and establish a good network with them.”
- “I think I would have relapsed, dropped out, or like gone into severe depression…”
- “It played a crucial role in my first year of sobriety.”

(Bell et al., 2009)
Not A One Size Fits All, But It Will Fit Your Size

“We are too big...”
“We are a very small campus...”
“We have a struggling recovery community...”
“That won’t work for us...”
“Our students would rebel at 12 step...”
“Our students only believe in 12 step...”

I promise......
• Collegiate Recovery Programs Work

References


Lecture Summary: Amphetamines continue to find important therapeutic roles in the management of certain conditions. Their spectrum of use over the last several decades has been significantly shaped by societal perspectives and pharmaceutical marketing strategies. The evolution of other potential drugs of abuse demonstrate similar trajectories. This presentation illustrates this history and helps the practitioner to recognize and appropriately manage expectations of appropriate therapeutic use and efficacy in this class of drugs.

Objectives: Upon completion of this lecture, attendees should be better prepared to:
  - Better recognize societal pressures and perspectives when considering the use of amphetamines.
  - Discuss the possible role of pharmaceutical and manufacturing strategies in advancing the use of their products.
  - Consider future uses of amphetamines and similar compounds.

NOTES: 

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Amphetamines
A Brief Review

Southern Medical Association’s. The 3 “Rs” of Prescribing Controlled Substances: Rules, Regulations, and Risks
Hattiesburg, Mississippi
Mark S. Williams, MD, MBA, JD

Topics
• Basic chemistry
• Evolution of ‘Drug Control’
• Current drug classification
• History of amphetamine and its uses
• Current indications
• Amphetamine withdrawal
• Amphetamines and Cognitive Enhancement

Amphetamine - Chemistry

Potent CNS Stimulant

Smooth Muscle Relaxant

Many others

Raises Systolic and Diastolic Pressures
Amphetamines - Mechanism of Action

• Effects stem largely from influences on neurotransmitters
• Predominantly work via increasing levels of dopamine and norepinephrine
• Explains many of their therapeutic benefits

The Commission recommended decriminalization of simple possession, finding:

"...the criminal law is too harsh a tool to apply to personal possession even in the effort to discourage use. It implies an overwhelming indictment of the behavior which we believe is not appropriate. The actual and potential harm of use of the drug is not great enough to justify intrusion by the criminal law into private behavior, a step which our society takes only 'with the greatest reluctance'"
**Schedule I Drugs**

- Drug or other substances have a high potential for abuse
- Drug or other substances have no currently accepted medical use in treatment in the U.S.
- Lack of accepted safety for

  - Heroin
  - Psilocybin
  - LSD

**Schedule II Drugs**

- Drug or other substances have a high potential for abuse
- Drug or other substances have currently accepted medical use in treatment in the U.S.
- Abuse of the drug or other substances may lead to severe psychological or physical dependence

  - Cocaine
  - Amphetamine
  - Oxycodone
  - Fentanyl

**Alternatives to Scheduling**

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<tr>
<th>Category</th>
<th>Parameter</th>
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<td>Physical Harm</td>
<td>Acute</td>
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<td>Parenteral</td>
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<td>Dependence</td>
<td>Intensity of pleasure</td>
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<td>Psychological dependence</td>
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<td>Physical dependence</td>
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<td>Social Harms</td>
<td>Intoxication</td>
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<td></td>
<td>Other social harms</td>
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<tr>
<td></td>
<td>Healthcare costs</td>
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</tbody>
</table>

*Drug Classification: making a hash of it?, UK Science and Technology Select Committee, 2006*
Drug harms in the UK: a multi-criteria decision analysis

David J Nutt, Lancet 2010

Government Policy in Conflict with Scientific Evidence?

Harm Caused by Drugs

- Alcohol
- Heroin
- Crack Cocaine
- Methamphetamine
- Amphetamines
- Ecstasy
- Cannabis
- Inhalants
- Sedatives
- Opiates
- Hallucinogens
- Ecstasy
- LSD
- Buprenorphine
- Mushrooms

Physical Harm

32,000@$15,118= $483,776,000

% of Population % of Imprisoned

WWJD? Reform Alabama's horrible criminal sentencing laws

As former Chief Justice of Alabama, I am proud to have devoted my career to the cause of justice and law. But as charming and gifted as our Lord Jesus is, I know He did not come to sit today in our jails, death row, and courts and hand over a law that is cruel, unjust and irrational. If we love our children and our nation, we cannot be indifferent to the many injustices of our system. And if we love our family and our nation, we cannot be silent on this one. Jesus did not come to sit in our criminal justice system.

Our prisons should be of the penitent because we correct wrongs not as we do not make them. In our jails, we say that we understand that there are cheaper and more effective ways to punish our most culpable offenders than to locking them up in prison. Militarily every system we have ever created is based on an environment that entices sanctioned violence.

Amphetamines - Brief History

- Adrenaline, 1901 at Johns Hopkins
- Amphetamine synthesized by George Alles, 1928, approached Smith, Kline and French (SKF)
- SKF introduced Benzedrine inhaler, 1932
- SKF introduced Benzedrine sulfate tabs in 1936 - offered free to any physician, no clinical trials

‘Initially, a drug looking for a disease’
On June 3, 1929, a doctor injected 50 mg of amphetamine into Alles’ body . . .

7 minutes later, his nose was dry and clear, at 17 minutes he had palpitations but also a feeling of ‘well being’ . . . he grew chatty at a dinner later that evening and found himself to be unusually witty . . . during the night, his mind “seemed to run from one subject to another”

A 1932 patent declared him the inventor of amphetamine sulfate and amphetamine hydrochloride - substances lacking any obvious medical application at that time

Amphetamines - Role in the Military

- Heavy pharmaceutical and physician promotion during 30s and 40s
- Germans, then British and then Americans embraced use of amphetamines
- Britain purchased 72 million Benzedrine tablets from SKF, America purchased 250 million
For the ‘Patient with Mild Depression’
JAMA, 1937

Symptoms included:
apathy,
discouragement,
difficulty in thinking,
subjective feelings of weakness.
‘hypochondria’
Not the only example, . . .

1960s - Diet Doctors and Weight Loss Clinics

Subsidiaries of off-brand diet pill manufacturers

Cost Selling Price

$0 $3,000 $6,000 $9,000 $12,000

100,000 off-brand tablets

Schedule II All Amphetamine Products

Bureau of Narcotics and Dangerous Drugs (forerunner to DEA)

1970 Comprehensive Drug Abuse Prevention and Control Act (precursor of modern schedules)

Schedule II All Amphetamine Products

The $22 Billion Gold Rush

Six million Americans gobbled Redux and Pondimin to lose weight. A few thousand got very sick. For this Wyeth has paid a colossal sum. How much went to undeserving claimants and their lawyers?

(Yorkshir 61) Lawyer Gailly on Seven Counts in Fen Phen Trial

Fen Phen Injury Lawsuit Center

Have you or a loved one used Fen Phen? You may be entitled to substantial financial compensation!

$22 Billion Gold Rush
Amphetamines - Current Indications

- Narcolepsy
- Attention Deficit Hyperactivity Disorder (ADHD)
- Other ‘off-label’ uses
  - Use as anorectics
  - Atypical depression and dysthymic disorder

ADHD

- Described in 1901
- One of most common childhood disorders (psychiatric behavioral)
- Three types
  - Hyperactive-Impulsive (HI)
  - Predominantly Inattentive (IN)
  - Combined (CB) - most common

New York Times
March 31, 2013

National Survey of Children’s Health, Department of Health and Human Services, 2013
“It is highly implausible that there has been a 50% increase in ADHD in the last decade . . . trend is being driven by Big Pharma, pressure from overwhelmed teachers . . . and now by parents and students who are seeking 'performance enhancement' . . . perhaps it is time for elite high schools and colleges to 'drug test' for Adderall and Ritalin so that students who are not taking performance enhancing medications aren't left by the wayside”

*Ethics of Mental Enhancement*
J Thomas, Modern Healthcare, July 2013

Some believe that children who are more high spirited or high-strung are being mistakenly diagnosed with ADHD (see www.adhdfraud.org)

Congressional testimony has included statements describing the excessive use of psychostimulants for ADHD (Breggin 2000)

'Most experts are in agreement that ADHD is a psychiatric condition that responds well to psychostimulant medication . . . environmental studies help to explain the increasing number of children affected by ADHD'

America’s First Amphetamine Epidemic 1929-1971, N Rasmussen, RedOrbit, June 2008

‘When a drug is treated not only as a legal medicine but as a virtually harmless one, it is difficult to make a convincing case that the same drug is terribly harmless if used non-medically’
‘Epidemics’ of Amphetamine Abuse

- Introduction of ‘medical use’ to a large segment of population
- Widespread dissemination of the amphetamine ‘experience’
- Development of a core of amphetamine users
- Initial oversupply of amphetamine
- Development of clandestine labs and distribution channels

Amphetamines - Issues of Abuse and Dependency

‘Potential for amphetamine abuse has curtailed many legitimate uses and contributed to success of illegal drug trade’


‘Abuse’
‘Dependency’
‘Addiction’

Why are we here discussing these issues?

What about the medical profession . . . us?
Amphetamines - Toxicity and Deaths

- Hypertensive cerebral hemorrhage
- Cardiovascular collapse secondary to ventricular fibrillation (usually <30 years of age)
- Hyperpyrexia
- Miscellaneous - septicemia from bacterial endocarditis, etc

Amphetamines - Tolerance

- Tolerance = reduction in effects with same dose of drug
- Side effects of amphetamines typically diminish over 6 - 8 weeks of use
- Effects subject to tolerance include the hyperthermic, appetite suppressant, mood elevating and cardiovascular effects
- Beneficial effects on behavior may persist for years

Amphetamines - Chronic Use and Abuse

- Many individuals take amphetamines for long periods of time without any obvious effects or need to increase dose
- Certain individuals begin using larger doses to intensify the pharmacological euphoria
- Repeated and higher doses are needed to achieve the intense euphoric sensations
- Numerous factors are believed to influence specific cases of dependence
Amphetamines - Withdrawal

- Effects of withdrawal often do not occur before several days
- Include dysphoria, fatigue, depression, vivid dreams, agitation and sleep disturbances
- May crave excessive amounts of food and develop affective disorders
- Withdrawal from high doses may evoke more intense symptoms including drug craving and depression

Amphetamines - Treatment of Dependence

- No one treatment effective for withdrawal or dependence
- During withdrawal, symptoms are managed with appropriate measures
- Treatment similar to that for cocaine dependence
- Therapies include tricyclic antidepressants and behavioral therapies (Matrix Model)

Methamphetamine

- Desoxyephedrine (Desoxyn)
- Used in treatment of ADHD
- Widely known for clandestine manufacture
- ‘Matchbook + iodine + ephedrine = ‘Meth’
- More potent CNS activity, less potent cardiovascular effects (adds to abuse potential)
Methamphetamine - Abuse

• America’s first epidemic - Haight-Ashbury, 70s
• ‘Speed freak’ versus the ‘love drug’
• Studies suggest that 4.3% of population has used methamphetamine at least once
• 50% of users smoke the drug
• Can devastate small communities

• Significant restrictions on chemical ingredients in U.S.
• Most ‘meth’ is of poor quality and is produced in Mexico
• ‘Meth’ users have depleted stores of dopamine and significant loss of transporters
• Areas of brain associated with emotions and memory may reveal severe changes
• Imaging studies in certain regions of brain suggest that recovery may be very prolonged or unlikely

Methamphetamine - Consequences of Abuse

• Malnutrition, severe dental problems
• Anorexia, anemia, hypertension, cardiac irregularities
• Ischemic bowel disease, nasal septal defects, COPD, impotence
• Psychosis, paranoia, memory loss
• Use may contribute to spread of HIV, other
Amphetamines - Claims as to Improvements in Cognitive and Performance Enhancement

- W H Auden
  - Improved academic performance, recall
  - Increased creativity
  - Writing
  - Mathematics
  - Painting
  - Musicians
  - Increased endurance

Jean-Paul Sartre  
Graham Greene

"Safe and effective cognitive enhancers will benefit both the individual and society"

From Commentary in the Journal Nature  
H. Greely, Dec 2008

Ethics of Mental Enhancement'  
Modern Healthcare, July 2013

'Do I have a right to know if someone I am competing against in the workforce is mentally enhanced in any way?'

'I can definitely see a time in the near future when, just like in professional sports, doctors, lawyers, accountants and hospital CEOs are going to demand to know if their colleagues have an "edge."
I have not argued that direct brain enhancements are good, let alone that they should be added to the water supply. I have argued that they are not necessarily bad. Their appropriate use will depend on their safety and effectiveness, along with how we choose to use them and what steps we take to mitigate the challenges to fairness they may pose or the invasions on individual autonomy they may provoke . . .

I am confident, though, that a knee-jerk rejection of all direct brain enhancements will be at least a missed opportunity and at worst an opening for a damaging underground and uncontrolled world of enhancements . . .

Henry T. Greely, JD
Professor of Law and Genetics, Stanford University
Director, Stanford Center for Law and Biosciences

From Enhancing Brains: What Are We Afraid Of?

"Amphetamine is like a Christmas package with a time bomb inside" (1969)
The Cognition-Enhancing Effects of Psychostimulants Involve Direct Action in the Prefrontal Cortex
• Procognitive actions associated only with low doses
• Involve preferential elevation of catecholamines in PFC
• Moderately elevated doses appear to improve certain cognitive processes at the expense of others
• Differential modulation of these processes appears to be associated with differential involvement of noradrenergic alpha-2 versus alpha-1 receptors

Amphetamine’s persistence - both as a recreational and a medical treatment - suggests a nearly irresolvable dilemma
• It blurs the line between treatment and enhancement
• Prompts the question “how important is a subjective feeling of well being?”
• When does a lack of such feeling become a medical problem?
• How should it be treated?
• How should society regard those who “abuse” such a drug?

Thanks
Questions?
Mark S. Williams, MD, MBA, JD
Lecture Summary: This is a new lecture incorporating the new guidelines just put out by the government on prescribing opioids. They will be incorporated into review of responsibilities, obligations, and management of prescribing controlled substances.

Objectives: Upon completion of this lecture, attendees should be better prepared to:

- Employ the new mandates just released about prescribing opioids.
- Evaluate the risks of prescribing opioids.
- Recognize how to minimize the risk of prescribing opioids.

NOTES:
Prescribing Opioids & Obvious Pitfalls
Thereof (Taking Into Consideration CDC
Guideline for Prescribing Opioids for
Chronic Pain – 2016)

JUNE 17, 2016 JOHN C. MUTZIGER DO, FASAM

Course Objectives

- Education of prescribers about responsibilities, obligations, and
  management of prescribing controlled substances.
- Education of prescribers about the New Guidelines from the CDC
  about prescribing opioids for chronic pain.
- Provide a framework for approaching this controversial area.
- To minimize the risk of prescribing addictive substances for chronic
  conditions.

Scope of the Problem

Americans consumed 80% of the global supply of prescription opioids
from 1997 to 2007.
Average sales per person increased 432%.
Opioid analgesics are the most misused class after marijuana.
20% of patients presenting with noncancer pain receive an opioid Rx.
For their pain.
In 2012 there were 259 million opioid prescriptions.
Scope of the Problem

- Overall cost of the opioid prescription problem is probably in the 500 to 600 Billion dollar range.
- Opioid related ER visits increased 111% from 2004 to 2008.
- 14.6% of adults in the US have widespread or localized pain greater than 3 months.
- Deaths involving opioid analgesics quadrupled from 1999 to 2008.
- This year deaths from overdoses from drugs is greater than highway accident deaths.
- From 1999 to 2014, there were 165,000 overdoses involving pain prescriptions.

Scope of the Problem

- In 2013, DSM IV noted that there were 1.9 million abusers or dependent people.
- In 2011 there were greater than 420,000 ER visits involving opioids.
- Therefore the CDC has reviewed the evidence regarding this problem, and has released a Guideline for Prescribing Opioids for Non-cancer pain.

Primary Clinical Questions

1. What is the effectiveness of long-term opioid therapy or non-opioid therapy for long term outcomes?
2. What are the risks of opioids vs. no opioids?
3. What are the effective opioid dosing strategies?
4. What is the accuracy of instruments for predicting risk for opioid overdoses?
5. What are the effects of prescribing opioid therapy versus not prescribing opioid therapy for acute pain or long term use?
Key Question 1 – What is the effectiveness of long-term opioids?
- There is no evidence on the effectiveness of long-term opioid treatments.
- There were no studies that evaluated outcomes related to pain, function, or quality of life.
- The body of evidence is insufficient.

Key Question 2 – What are the risks of prescribing opioids?
- In the general population there are between 3-26% of the patients having the DSM IV criteria for addiction.
- In pain clinics this ranges from 2-14%.
- Recent opioid use is associated with increased risk for any overdose events.
- Higher doses are associated with higher risk.
- There is an increased fracture risk for concurrent opioid use.
- There is also evidence the opioid dosages greater than 20 MME/day are associated with increased odds of road trauma among drivers.

Key Question 3 – What is the evidence for dosing strategies?
- The initiation of the use of ER/LA opioids is associated with greater risk for nonfatal overdose vs. initiation with a short-acting opioid.
- There is no evidence for comparisons related to dosing strategies.
Key Question 4 – What is the accuracy of assessment tools?

- 4 studies have shown that the accuracy of assessment instruments for predicting opioid abuse or misuse are inaccurate.
- There are no studies evaluating the effectiveness of risk mitigation strategies.
- These include risk assessments, opioid management plans, patient education, use of PDMP data, use of monitoring instruments, more frequent monitoring intervals, pill counts, or use of abuse-deterrent formulations for improving outcomes related to overdose, addiction, abuse or misuse.

Key Question 5 – What are the effects of opioid therapy for acute pain on long term use?

- Use of opioids within 7 days of surgery for opioid-naïve patients who had undergone low risk surgery was associated with increased risk for use of opioids for one year following.
- Early use of opioids for back pain within 2 weeks of the injury leads to an increased risk of receiving 5 or more prescriptions within 2 years.

The New Recommendations

- 1. Determining when to initiate or continue opioids for chronic pain.
- 2. Opioid selection, dosage, duration, follow-up, and discontinuation.
- 3. Assessing the risk and addressing the harms of opioid use.
Determining When to Initiate or Continue Opioids for Chronic Pain

1. Non-pharmacologic therapy and non-opioid pharmacologic therapy are preferred for chronic pain.
2. You should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient.
3. If opioids are used, they should be combined with non-pharmacological therapy and non-opioid pharmacologic therapy as appropriate.
4. Before starting opioid therapy for chronic pain, you must establish treatment goals with all patients. This should include realistic goals for pain and function. It will be discontinued if benefits do not outweigh risks.
5. Continue therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patients safety.
6. Before starting therapy and intermittently, clinicians should discuss with patients the known risks and realistic benefits of opioid therapy.

Opioid Selection, Dosage, Duration, Follow-up and Discontinuation.

1. Clinicians should use immediate release opioids instead of extended-release/long acting opioids.
2. Clinicians should prescribe the lowest effective dosage and reassess if increasing the dosage over 50 MME/day.
3. Avoid over 90 MME/day.
4. When prescribing for short term use, use less than 7 days supply.
5. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy. Re-evaluate every 3 months. If benefits do not overcome harms, taper to a lower dose.
Assessing Risk and Addressing Harms of Opioid Use.

1. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid harms.
2. Clinicians should incorporate into the management of opioid therapy, strategies to minimize risk.
3. Minimize benzodiazepine use.
4. Review the patient’s PMP data, to determine his MME’s.
5. Clinicians should use urine drug testing.
6. Avoid concurrent opioids and benzodiazepines.
7. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with Suboxone for patients with opioid use disorder).

How to Approach Before Treatment?

1. Conduct a thorough history, including substances.
2. Consider using empiric screening tools.
3. Evaluate known risk factors.
5. Enhance monitoring for patients.
6. Set treatment goals and discuss expectations with the patient before starting opioid therapy.

Before Prescribing

1. There needs to be comprehensive documentation of the patient’s pain condition, general medical condition, psychosocial history, psychiatric status, and substance use history of the patient and patient’s family.
2. Use a screening tool for opioid addiction
3. UDS
4. Informed consent
5. Taper benzodiazepines first
6. Obtain PMP
During Treatment

2. Routinely reassess the patient every 3 months. Document opioid therapy, efficacy, adverse effects, evidence of misuse, and evidence of benefits overshadowing risks.
3. Obtain PMP.
4. UDS
5. Address, evaluate and respond to questionable use, per policy.
6. Discontinue use of opioids if no benefit or risks overshadow benefits.
7. Evaluate behavior and determine course of action, if questionable use occurs.
8. Address questionable use with patient.
9. Re-evaluate benefits and risks.
10. Consider referral to an addiction specialist for consultation.
11. Initiate opioid taper if discontinuing; consider addiction consult if SUD is present.

History and Physical

- Should include the cause and the nature of the pain, past treatments, tests, medication trials.
- Estimate the pain level and the intensity.
- Psychological history, includes living arrangement, family/social support, work status, family obligations.
- The psychiatric status should include psychiatric disorders and treatments and family history of psychiatric disorders.
- Substance Use History – current, past, and family history of substance use and abuse, addiction, and treatment for addiction.
- Documentation. Documentation.
SOAPP - SF

- 0 – NEVER
- 1 – SELDOM
- 2 – SOMETIMES
- 3 – OFTEN
- 4 – VERY OFTEN

1. How often do you have mood swings?
2. How often do you smoke a cigarette within an hour after you wake up?
3. How often have you taken medication other than the way it was prescribed?
4. How often have you used illegal drugs in the last 5 years?
5. How often, in your lifetime have you had legal problems or been arrested?
6. Have you ever overdosed?

When Are Opioids Indicated?

1. Pain is moderate to severe.
2. Pain has significant impact on function.
3. Pain has significant impact on quality of life.
4. Non-opioid therapy and other therapies have failed.
5. Patient is agreeable to have opioid use closely monitored, and understands the risks and benefits.
6. You, the prescriber determine that the risk is not elevated!!!!

Evidence of CNCP Efficacy

- Tramadol – Fibromyalgia
- Opioids
  - Diabetic neuropathy
  - Peripheral neuropathy
  - Post-herpetic neuralgia
  - Phantom Limb Pain
  - Spinal cord injury with pain below level of injury
  - Lumbar radiculopathy
  - Osteoarthritis and Rheumatoid Arthritis
  - Low back pain
  - Neck pain
Opioid Prescribing Guidelines

- Medical Practice Act of Mississippi
- Mississippi Code 1972
- MSBML website - Outlined in the Jurisprudence Handbook
- Http://www.msbml.ms.gov/msbml/web.msf

Patient Record

- H&P – Good faith
- Evaluation
- Treatment
- Documented diagnosis
- Reason for prescribing
- Date
- Name, dose, strength, and quantity of drug and refills
- Patient record maintained 7 years

Lack of “Good Faith”

- Physician allows the patient to “name the desired drug.”
- Dispensing drugs “when the physician knew or should have known the patients were addicts.”
- Repeated refills, despite non-compliance (failure to take correct dosage).
- Physician endorses non-therapeutic uses of drugs.
- Physician prescribes contradicted medicines, resulting in therapeutic conflicts.
Administrative Code Definition of Chronic Pain

- Patients receiving controlled substances for more than six months.
- Does not refer to Terminal Disease Pain, i.e., those with life expectancy less than six months.
- Physicians may use controlled substances to treat chronic pain, with caution.

Requirements

- Conduct appropriate risk/benefit analysis.
- Review prior records and treatment.
- Proof of indicated need for long-term therapy.
- Documentation of complete medical history, examination, and treatment plan.
- Review and document every 3 months or less, including modification of therapy dependent on completion of treatment objectives and referrals and consultations as necessary.

Written Treatment Plan

- Stated objectives as a measure of treatment.
- Planned diagnostic evaluations.
- Informed consent that details risks and benefits.
- Use of one physician and one pharmacy, if possible.
- Use of UDS when requested.
- PMP
- The four A’s of every visit:
  - Analgesia
  - Activity
  - Adverse events
  - Aberrant behavior
Aberrant Medication Behavior –
Yellow Flags
- Complaints about the need for more medication
- Hoarding drugs
- Requesting specific medicine
- Openly acquiring medicines from other providers.
- Occasional unsanctioned dose escalation.
- Non-adherence to other recommendations.

Aberrant Medication Behavior –
Red Flags
- Deterioration in functioning at work or socially
- Illegal activities – selling, forging, buying on street
- Injection or snorting drug
- Multiple episodes of "lost" or "stolen"
- Resistance to change therapy despite adverse effects
- Refusal to comply with random drug screens
- Concurrent use of alcohol or illicit drugs
- Use of multiple physicians and pharmacies.
- Using adulterants or someone else’s urine.

Monitor for Misuse
- Use Agreement
- Monitor Behavior
- Monitor for Adherence, Addiction, and Diversion
- Initially small quantities and frequent visits.
- PMP
- Discuss monitoring with family.
Pearls from Years of Practice

- People with pain who are treated with small amounts of narcotics get better quicker.
- People with addiction do not notice any small increase in amounts.
- If it looks like an addict, asks for more drugs, and even demands, it is an addict.
- If their dog ate the medicine — did the dog die?
- Concurrent use of recreational drugs with pain meds is usually the mark of a polysubstance abuser.
- Anxiety is treated with anti-depressants, not benzos.
- The later in the day or closer to the weekend the patient calls for more, the more likely he is abusing.
- There are no shy bladders amongst drug abusers.

Pearls

- Lots of little old ladies make their living off the Rx. that you are writing them! Be suspicious.
- Excuses are what will get your DEA taken away.
- Do not write opioids for a patient after an overdose.
- Find a nurse who knows your patient base and has a nose for BS.
- Use your PMP and UDS.
- Patients who have received Suboxone are probably opioid addicts.

References

- Principles of Addiction Medicine – Fifth Edition
- Prescription Drug Abuse Crisis: Mississippi Prescriber’s Response – Dr. Scott Hamilton MD
- Utah Clinical Guidelines on Prescribing Opioids – Utah Dept. of Health
- FDA Blueprint for Prescriber Education for ER and LA Analgesics
- Prescribing for Pain – Daniel P. Alford MD, Boston University School of Medicine
- Substance Abuse – A Comprehensive Textbook – Fourth Edition
- CDC Guidelines for Prescribing Opioids for Chronic Pain – MAMR – March 15, 2016
When Things Go Wrong

- Evaluate behavior and determine course of action if questionable use occurs
- Address questionable use with the patient
- Evaluate benefit of continuing opioid therapy
- Consider referral to an addiction specialist for consultation

Perspective

<table>
<thead>
<tr>
<th>No Evidence of Addiction</th>
<th>Evidence of Addiction</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Control over medication use</td>
<td>- No control over medication</td>
</tr>
<tr>
<td>- Improved quality of life</td>
<td>- Worsened quality of life</td>
</tr>
<tr>
<td>- Concern about medical problems</td>
<td>- Requests dose increase despite side effects</td>
</tr>
<tr>
<td>- Adheres to treatment plan</td>
<td>- Lack of concern about medical problems</td>
</tr>
<tr>
<td>- Concern of pain relief greater than opioids</td>
<td>- Non-adherence to tx. Plan</td>
</tr>
<tr>
<td>- Some increase of tolerance</td>
<td>- Concern over opioids is greater than pain relief</td>
</tr>
<tr>
<td>- Some increase in amounts</td>
<td></td>
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</tbody>
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Lecture Summary: The CDC has stated that the United States is in the midst of the worst drug epidemic in the history of our nation. An underlying contributing factor to the inappropriate use of controlled substances is the lack of proper education about addiction as a brain disease. This lecture helps to address this issue.

Objectives: Upon completion of this lecture, attendees should be better prepared to:

- Discuss epidemiology of addiction.
- Describe the brain disease model of addiction.
- Describe the Physician Health Program (PHP) management of addictive disorders as a potential template for management of patients with addictive disorders in the general population.

NOTES:
Addictive Disorders: Management Principles & the MPHP Approach

Scott Hambleton, M.D.
Medical Director

Southern Medical Association:
Prescribing Controlled Substances
Hattiesburg, MS
June 17, 2016

Disclosures

I have no disclosure of conflicts of interest

Objectives

- Discuss epidemiology of addiction
- Describe the brain disease model of addiction.
- Describe Physician Health Program (PHP) management of addictive disorders as potential template for management of patients with addictive disorders in the general population
Addiction Facts

- Lifetime prevalence: 10-12%
- 31 million Americans and <12% receive treatment. (SAMHSA, 2013 NSDUH)
- 40-60% of people relapse after drug and alcohol treatment. (NIDA)
- 80% relapse rate with opioid dependence. (NIDA)

Addiction Facts, contd.

- Causes 20% of all deaths per year
- Costs in excess of $600 Billion per year
- 1/3 of all hospital in-patient costs are addiction related (SAMHSA, 2013 NSDUH; Ries, et al., 2014)
- 25% of primary care patient visits (Jones et al., Am. Fam. Physician, 2003)

WHEN SHOULD YOU START TREATMENT???
WHEN SHOULD YOU START TREATMENT???

Melanoma
WHEN SHOULD YOU START TREATMENT???

Rats Self-administer Heroin

Rats Self-administer Cocaine
Sagittal Plane View of Brain:

Human

Rat

Virtually Identical Reward Circuit

“Lizard Brain”

prefrontal cortex

nucleus accumbens

VTA

Brain Reward Pathway
Opioid binding sites (green)

Reward Pathway (orange)

EXCELLENT ARTICLE: BRAIN DISEASE MODEL


STAGES OF ADDICTION

Binge & Intoxication

Preoccupation & Anticipation

Withdrawal & Negative Affect

(Volkow et al., 53)
Neuroplasticity refers to the potential that the brain has to reorganize by creating new neural pathways to adapt. Behaviors during the three stages of addiction change as person transitions from experimentation to addiction.

(Volkow et al, 2016)

Progressive behavior change during process of becoming addicted represents compromised neurocircuitry, i.e., disruption of the dopamine and glutamate systems and the stress-control systems of the brain affected by corticotropin-releasing factor and dynorphin.

(Volkow et al, 2016)

Neuroplastic changes triggered by drugs have been uncovered in various regions of the brain: Nucleus accumbens (brain-reward), Dorsal striatum (encoding of habits and routines), Amygdala (emotions, stress, and desires), Hippocampus (memory), Prefrontal cortex (self-regulation and salience attribution[the assignment of relative value]).

(Volkow et al, 2016)
“The alcoholic at certain times has no effective mental defense against the first drink.”
*Alcoholics Anonymous, 4th Ed*

**47,055 Deaths (All O.D. Deaths)**

CDC, Web-based Injury Statistics Query and Reporting System (2014)

**Opioid Prescriptions Dispensed per Year (Oxycodone and Hydrocodone)**
Adverse Selection

Patients with mental health and substance abuse co-morbidities are more likely to receive chronic opioid therapy than patients who lack these risk factors. (Edlund MJ, et al., 2010)

CDC Guideline for Prescribing Opioids for Chronic Pain

No evidence shows a long-term benefit of opioids in pain and function versus no opioids for chronic pain with outcomes examined at least 1 year later (with most placebo-controlled randomized trials ≤6 weeks in duration)

http://www.cdc.gov/drugoverdose/prescribing/resources.html

CDC Guideline for Prescribing Opioids for Chronic Pain

Extensive evidence shows the possible harms of opioids (including opioid use disorder, overdose, and motor vehicle injury)

http://www.cdc.gov/drugoverdose/prescribing/resources.html
Extensive evidence suggests some benefits of nonpharmacologic and nonopioid pharmacologic treatments compared with long-term opioid therapy, with less harm.

http://www.cdc.gov/drugoverdose/prescribing/resources.html

12 Recommendations:

Three Areas

Determining when to initiate or continue opioids for chronic pain.

Opioid selection, dosage, duration, follow-up, and discontinuation.

Assessing risk and addressing harms of opioid use.

http://www.cdc.gov/drugoverdose/prescribing/resources.html
What is a “Distressed Physician”???

Challenges of Practicing Medicine

- Reimbursement hassles
- Electronic medical records
- Prior authorization
- Maintenance of certification
- Scope of practice
- The prescription drug crisis!!!

Culture of Medicine

- “Suck it up and get it done!”
- Resilience is not taught, it is expected
- Asking for help is stigmatized and not praised
- Psychiatric issues are not considered “real” illnesses
Characteristics of Medical Work

- Long hours
- Intense involvement
- Emotionally charged interactions
- Requirement for complex decision making
- Ambiguous and frustrating solutions/outcomes
- Requirement for constant “giving” (e.g., time, knowledge, empathy)
- Breeding ground for distress

Distressed Physician: Outcomes

- Healthy coping skills: resolution of problem
- Unhealthy coping skills: potential harm to patients
  1. Substance abuse/addiction
  2. Anxiety, depression, burnout
  3. Suicide
  4. Professional boundary violations/misconduct
  5. Disruptive behavior
  6. Impairment

Burnout: Syndrome Triad

1. Emotional Exhaustion (feelings of emotional overextension and fatigue)
2. Depersonalization (negative, cynical attitudes and feelings about patients; dehumanized perception of others)
3. Reduced Sense of Personal Accomplishment

Maslach Burnout Inventory: Manual, 3rd Edition
**Emotional Exhaustion**

- I feel emotionally drained from my work.
- I feel fatigued when I get up in the morning.
- Working with people all day is really a strain for me.

*Higher rating associated with burnout*

**Depersonalization**

- I feel I treat some patients as if they were impersonal objects
- I've become more callous towards people since I took this job
- I don't really care what happens to some patients

*Higher rating associated with burnout*

**Personal Accomplishment**

- I deal very effectively with the problems of my patients
- I feel I'm positively influencing other people's lives through my work
- I feel exhilarated after working closely with my patients

*Lower rating associated with burnout*
**Burnout Triad:**
Reported by Physicians

- 46-80% report moderate levels of **emotional exhaustion**
- Up to 93% report moderate to high levels of **depersonalization**
- Up to 79% report low to moderate levels of **personal achievement**
  
  (S. Chopra et al, *JAMA*, 2004)

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**Effects of Burnout**

- Highly statistically significant association between burnout and alcohol abuse or dependence.
- Highly statistically significant association between burnout and suicidal ideation.
- We know that burnout and depression often go hand in hand.
- We know that alcohol abuse has a strong association with medical errors.
  
  (Shanafelt, et al., 2014)

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**Physician Addiction**

- ≈ 12% (8%-13%) lifetime prevalence
- Physician illicit drug use < general population
- Physician alcohol abuse > general population (14-15%)
- Physician benzodiazepines & opiates use > > general population
  
  (Ries, et al., 2014; Oreskovich et al., 2012)
What is MPHP?

- 501 (c) 3 non-profit, charitable organization incorporated in 1978
- Subsidiary of the Mississippi State Medical Association
- Empowered by a Memorandum of Understanding with the Mississippi State Board of Medical Licensure

What is the Purpose of MPHP?

To provide a confidential, non-punitive alternative to disciplinary sanctions for licensees who may be suffering from potentially impairing conditions or illnesses.

Purpose, cont’d

- Early detection, intervention, and long term, intensive management of physicians with potentially impairing conditions
- Primary focus on potential impairment from substance use disorders
- End result: facilitation of a return to healthy, safe and productive medical practices
History of PHPs

- MPH originally created by Ellis and Nina Moffitt and MSMA in 1978 and incorporated as a 501(c)3 charitable organization
- By 1980 all but 3 Medical Societies had authorized or implemented impaired physician programs
- FSPHP created in 1990

MPHP Monitoring

- MPH evaluation
- Blood/urine drug screens
- Work place monitoring
- Recovery support group attendance
- MPH Case Manager: check-ins/visits
- Medication monitor
- QR to MSBML
- Level II and III relapse reported within 24 hours

Contingency Management: The “Stick”

- MSBML
  - Executive Director
  - Full Medical Board: Hearing/action/order/public record
  - Practicing medicine is much more difficult with Medical Board orders/restrictions
  - Loss of Specialty Board certification
  - Malpractice coverage
Contingency Management: The “Carrot”

- MPHP Confidentiality/anonymity:
  - PHPs referrals: exponentially increase when confidentiality is respected by Medical Boards
  - Decreases stigma of treatable conditions (addiction)
  - Promotes early intervention (days-to-weeks)
  - Promotes physician health
  - Contingent on full cooperation/compliance
  - Avoids costly legal battles
  - Protects the public

Without Confidentiality...

- Licensees more likely to “fight” the process
- Intervention is delayed: months-to-years instead of days-to-weeks
- Addiction is stigmatized: treatment is discouraged
- Addiction is enabled
- Increased risk of public harm

Limits to Confidentiality

- Defined in the Memorandum of Understanding (MOU) with the MSBML
- Anonymous cases are reported to the MSBML as a number, and not by name
- All relapses are reported to the MSBML
- The MSBML is the final authority and is not bound by any recommendations by the MPHP
California Diversion Program

- Discontinuation in 2008 by the California Medical Board
- Firestorm of negative publicity led by charges of hiding “physicians on drugs” by a Citizen Advocacy Group

Unequivocal Success of PHPs

- 5-year abstinence rates: 78%-84%
- Return to work rates: 96%
- Virtually no risk of harm to patients treated by participating physicians
- 45 States and District of Columbia have PHPs

Patient Safety?

- Project Blueprint: One (1) Report of Patient Harm (Overprescribing)
  (McLellan, AT et al. 2008)
- Consistent with another study of 259 physicians monitored over 11 years that failed to document even one case of patient harm.
  (Domino, 2005)
Addictive Disorders: Management Principles

- Longitudinal contingency management is best
- Residential, abstinence based treatment is best
- Encourage 12 step fellowship participation
- Expect denial, minimization and cognitive distortion
- Maximize leverage, encourage family involvement

- Minimum quantities + short duration
- Avoid controlled substances for chronic, non-terminal conditions
- Do not prescribe controlled substances to patients with addictive disorders, unless unavoidable

Thank You!
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Lecture Summary: It is estimated that 80 percent of benzodiazepine abuse occurs within a pattern of polysubstance abuse, with the highest correlation occurring with concurrent addiction to opioids and alcohol. Abuse is frequently associated with adolescents and young adults who take the drug orally or crush it up and snort it to get high. Abuse is particularly high among heroin and cocaine abusers.

Objectives: Upon completion of this lecture, attendees should be better prepared to:
- Learn the clinical uses of benzodiazepines.
- Understand the pharmacology and physiology of sedative hypnotics.
- Understand toxicity and side effects.
- Understand trends in abuse and misuse

NOTES:
Sedative Hypnotics and Their Use and Misuse

John C. Mutziger DO, FAOAAM
January 24, 2015

Prevalence of Abuse

NIH 2011 - 2014

- 12th graders – 68.2% alcohol
  - 38.1% cigarettes
  - 17.2% smokeless tobacco
  - 50.4% illicit drugs
  - 4.5% cocaine
  - 7.6% hallucinogens
  - 7.7% tranquilizers
  - 11.1% opioids
Barbiturates

- Synthesized originally in 1864 by von Bayer
- 1903 Barbital was synthesized (Veronal)
- 1912 Phenobarbital was synthesized
- These were the drug of choice during days leading up to the development of Benzodiazepines
- Benzodiazepines were developed in the 1950's
- 1954 Dr. Leo Sternback found chlordiazepoxide

Barbiturates

Types of Barbiturates

- Ultrashort
  - methohexital
  - thiopental
- Short acting
  - pentobarbital
  - secobarbital
  - amobarbital
- General Therapy
  - General anesthesia
- Sedation
  - Seizures
- Hypnotic
Types of Barbiturates

- Intermediate
  - butabarbital
  - butalbital
- Long Acting
  - phenobarbital
  - meprobamatral

Barbiturates

- Are highly lipid soluble
- Are excreted through hepatic metabolism and then renal excretion
- Favored through alkalization of the urine
- Half-lives are increased in pregnancy and in patients with chronic liver disease
- Depresses respiratory drive
- Hepatic metabolism is responsible for tolerance by induction

Benzodiazepines

- Next in 1963 diazepam was developed (Valium)
- Thereby leading to the Age of Anxiety – 20th Century
- These were used for many uses – sedative, hypnotic, anxiolytic, amnesic.
How Do They work?

- Both the benzodiazepines, barbiturates and the new non-benzodiazepines are modulated at the GABAa receptor.
- GABAa is a ligand-gated Cl- channel
- When stimulated it gives a fast inhibitory postsynaptic potential- therefore is allosterically activated by benzodiazepines; it reduces the probability of generation of an active potential

GABA beta

- This is a G protein coupled receptor that acts as a dimer- Increases permeability to K+ and decreases Ca++ conductance
- For barbiturates there is a positive modification of GABAa via allosteric mechanism that increases its effect; in other words, it is a direct GABAa agonist and prolongs the opening of the Cl- channel, esp. at B2 and B3 subunits
GABAa Receptor

How Benzos Work

This diagram shows how benzos act on the GABA receptor. As shown, the drugs allow the receptor to be kept open and the GABA to enter its receptor.
Non-benzodiazepines

- Zolpidem (Ambien)
- zalepom (Sonata)
- Zopidone (Lunesta)
- These may act through overlapping binding sites at alpha and beta subunits
- These drugs inhibit flumitrazepam

Benzodiazepines

- Rx. peaked in 1975 – 10% of all prescriptions
- They are prescribed mainly for anxiety and insomnia now
- They are relatively safe with rare OD’s
- Are addicting
- Are taken with other drugs

Clinical Uses of Benzodiazepines

- Anxiety disorders
  – Acute anxiety
  – Generalized anxiety disorder
  – Panic disorder
  – Phobias (social, simple)
  – PTSD
  – Obsessive-compulsive Disorder
Clinical Uses of Benzodiazepines

• Insomnia
• Anxiety associated with medical illness
  – Cardiovascular
  – Gastrointestinal
  – Somatoform disorder

Clinical Uses of Benzodiazepines

• Convulsive Disorders
• Acute status epilepticus
• Neonatal seizure disorders
• Preeclampsia
• Tetanus
• Adjunct to other anticonvulsants
• Amnestic (before surgery or procedure)

Clinical Uses of Benzodiazepines

• Spastic disorders and other types of acute muscle spasm – cerebral palsy, multiple sclerosis, paraplegia secondary to spinal trauma
• Involuntary movement disorders – restless leg syndrome, akathisia associated with neuroleptic use, choreiform disorders and myoclonus
Clinical Uses of Benzodiazepines

- Detoxification from alcohol and other substances
- Agitation or anxiety associated with other psychiatric conditions – acute mania, psychosis, anxiety with depression, impulse control disorder, catatonia or mutism
- Other adjunctive uses – surgery, dentistry, diagnostic procedures, cardioversion, chemotherapy

Toxicity and Side Effects

- With the introduction of chlordiazepoxide (Librium) in 1960, these agents replaced barbiturates as sedative-hypnotics.
- They cause significantly less respiratory depression and are rarely lethal by themselves in an overdose.

Toxicity and Side Effects

- Drowsiness, lethargy
- Ataxia, muscle incoordination
- Seizures, if abruptly discontinued
- Hypotonia, dysarthria, dizziness, and even hyperactivity
Characteristics of Benzodiazepines

• High Potency
  – Alprazolam (Xanax)
  – Lorazepam (Ativan)
  – Trizolam (Halcion)

• Drugs with a long half life
  – Clonazepam (Klonopin)
  – Chloradiazepoxide (Librium)
  – Clorazepate (Tranxene)
  – Diazepam (Valium)
  – Flurazepam (Dalmane)

Characteristics of benzodiazepines

• Drugs with a short half-life
  – Oxazepam (Serax)
  – Temazepam (Restoril)
Mechanisms of Abuse

- Hedonic uses
- Tolerance
- Withdrawal syndrome
- Benzodiazepines with rapid onset have the greatest risk for this type of abuse
- Tolerance causes patients to escalate the dose
- Withdrawal syndrome appears on decreasing dosage or discontinuation

Mechanisms of Abuse

- Tolerance develops as decreased responsiveness to GABAa receptors to Benzos
- Some evidence too that mRNA involved with the synthesis of alpha1 part of the GABAa site are reduced during long exposure to Benzos
- Glutamatergic system may also play a role in the withdrawal syndrome

Abuse Liability

- Benzodiazepines occupy an intermediate position of abuse liability
- Barbiturates and methaqualone had a greater risk of liability
Toxicity

• When used alone – low risk
• However when used with other types of medications, they act synergistically with other CNS depressants, sedating antidepressants, neuroleptics, anticonvulsants, antihistamines and alcohol, with and without opiates

Toxicity and Drug Interactions

• Psychomotor retardation – drowsiness, poor concentration, ataxia, dysarthria, motor incoordination, muscle weakness, vertigo and mental confusion.
• Memory impairment – Benzos induce anterograde amnesia. This appears separate from sedation as an effect.

Toxicity and Drug Interactions

• Paradoxical Disinhibition – Increased excitement, irritability, aggression, hostility, and impulsivity may occur.
• This paradoxical disinhibition may in rare cases result in attacks of rage or violence or other antisocial behaviors. They are more common in children and the elderly
Toxicity and Drug Interactions

• Depression and emotional blunting – there is an association between Benzos use and depressive symptoms, and in some cases the emergence of suicidal ideation.
• Dependence – may appear as early withdrawal or protracted withdrawal in patients.

Abuse of benzodiazepines

• Approximately 80% is polydrug abuse
• Rarely alone
• Usually with opioids
• 3-41% abuse with ethanol

Abuse of Benzodiazepines

• Increased risk of abuse
  – High potency
  – Short duration of action
  – High purity
  – Water solubility
  – High volatility
Benzodiazepine Overdose

- Dizziness
- Confusion
- Drowsiness
- Blurred vision
- Unresponsiveness
- Anxiety
- Agitation

Trends in Drug Use

Physical Exam Findings

- Nystagmus
- Hallucinations
- Slurred speech
- Ataxia
- Coma
- Hypotonia
- Weakness
- Amnesia
- Paradoxical excitation
- Respiratory depression
- Hypotension
Diagnosis

• Immunoassay screening
• Get ABG’s, CXR, Pregnancy test
• Serum electrolytes
• Glucose
• Bun
• Cr
• Ethanol level
• Acetaminophen level

Pearls

• Benzodiazepine risk increases with age
• Women are as twice as likely to receive a benzodiazepine Rx.
• ¾ of all Rx. for benzodiazepines are for long acting
• Men are more likely to abuse with opioids

Withdrawal Symptoms

• Insomnia
• Gastric problems
• Tremors
• Agitation
• Fearfulness
• Muscle Spasms
Withdrawal Symptoms

- Less likely
  - Irritable
  - Depersonalization
  - Derealization
  - Hypersensitive to stimuli
  - Suicidal behavior
  - Depression
  - Psychosis
  - DT’s
  - Seizures

Contraindications to Use

- Respiratory depression
- Myasthenia gravis
- Sleep apnea
- Bronchitis
- COPD
- Caution: Personality disorders, depression, pregnancy, elderly

Pharmacokinetics

<table>
<thead>
<tr>
<th>Drug</th>
<th>½ Life</th>
<th>Speed of onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>12-15 hrs</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Clordiazepoxide</td>
<td>10-30</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>18-50</td>
<td>Slow</td>
</tr>
<tr>
<td>Diazepam</td>
<td>20-80</td>
<td>Fast</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>10-20</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Oxazepam</td>
<td>5-10</td>
<td>Slow</td>
</tr>
<tr>
<td>Prazepam</td>
<td>50-200</td>
<td>Slow</td>
</tr>
</tbody>
</table>
Drug Interactions

• With drugs metabolized by cytochrome P450 enzymes
• With drugs metabolized through glucuronidation
• Oral contraceptives, some antibiotics, antidepressants, antifungal agents inhibit the cytochrome enzymes in the liver
• Carbamazepine and phenytoin accelerate many benzodiazepines.

Drug Interactions

• Common
  – Ketoconazole
  – Itremazole
  – Macrolide antibiotics
  – Fluoxetine
  – Nefozodone
  – Cimetidine

Benzodiazepine Use and Risk of Alzheimer’s Disease

• On Sept 9, 2014 published in the BMJ by Sophie Billioti de Gage et al
• Conclucion – Benzodiazepine use is associated with an increased risk of Alzheimer’s Disease. “The stronger the association observed for long term exposures reinforces the suspicion of a possible direct association, even if benzodiazepine use might also be an early marker of a condition associated with an increased risk of dementia. Unwarranted long term use of these drugs should be considered as a public health concern.”
Benzodiazepine Use and Risk of Alzheimer’s Disease

• Use of benzos significantly associated with an increased risk of Alzheimer’s Disease.
• 1.52 odds ratio for any use
• 1.85 odds ratio for long term use (6 months or more)
• 1.72 for use of benzos with a long half life.
• This was a case-control study; not a randomized, controlled trial.

Guidelines for the use of benzodiazepines in Office Practice

• Contra-indications:
  – Pregnancy and risk for pregnancy
  – Active substance abuse, including alcohol
  – Medical and mental health problems that may be aggravated by benzos— including fibromyalgia, chronic fatigue syndrome, bipolar disorder, ADHD, kleptomania and other impulse control disorders. Sleep apnea, COPD, CHF.
  – Pt.s being treated with opioids for chronic pain or replacement therapy for narcotic addiction.
  – Grief reactions.

Indications for short-term treatment with Benzos

• Short term treatment of anxiety disorders – 2-6 weeks.
• Insomnia- short term 1-2 weeks.
• Muscle relaxant- short term 1-2 weeks.
• Urgent treatment of acute psychosis and agitation.
• Treating alcohol detoxication
• Seizures
• Sedation
Indications for long term use of Benzodiazepines

- May be used longer in the terminally ill
- Certain neurological disorders
- Severely handicapped

Tapering Benzodiazepines

- A long term project
- Start slow, starting with ½ of a tablet every 2 weeks (or 10% of the daily dose of the BZD)
- May switch to an equivalent dose of a long acting BZD or phenobarbital and then taper off
- Counseling should be available
- Carbamazepine, valpoate, and gabapentin can be used to facilitate more rapid withdrawal.

Special Considerations

- Care to not taper alprazolam too quickly...more prone to withdrawal seizures
- Patients with other addiction problems or on high doses or taking other opiates will be more difficult to withdraw. Consider consult.
- As patients age, they become more sensitive to the same dose of BZD.
- There is risk to operating machinery even with stable doses of BZD's.
Equivalence Table

- **Alprazolam (Xanax)**: 0.5 mg.
- **Chlordiazepoxide (Librium)**: 25 mg.
- **Clonazepam (Klonopin)**: 0.5 mg.
- **Diazepam (Valium)**: 10 mg.
- **Lorazepam (Ativan)**: 1 mg.
- **Temazepam (Restoril)**: 20 mg.
- **Zolpidem (Ambien)**: 20 mg.
- **Zaleplon (Sonata)**: 20 mg.
- **Eszopiclone (Lunesta)**: 3 mg.

Bibliography

- Substance Abuse – Fourth Edition
- Principles of Addiction – Fifth Edition
- The Pharmacological Basis of Therapeutics - Goodman and Gilman
- Drug Information Service – University of Texas Health Center at San Antonio and the College of Pharmacy at Austin
CME Conference Calendar

July 18-21, 2016
Focus on the Female Patient Conference
Kiawah Island Golf Resort, East Beach Conference Center
Kiawah Island, SC
http://sma.org/female-patient

August 25, 2016
The Red, White and Blue of Prescribing Controlled Substances: Risks, Wisdom and Balance
Pickwick Landing State Park
Counce, TN
Call 800-423-4992, ext. 164 for additional information

November 3, 2016
Psychiatry Pearls for the Primary Care Provider
The Chattanoogan Hotel
Chattanooga, TN
Call 800-423-4992, ext. 164 for additional information

November 3-5, 2016
SMA Annual Scientific Assembly
The Chattanoogan Hotel
Chattanooga, TN
http://sma.org/assembly

December 16-18, 2016
Medical Dilemmas in Patient Care
Westin New York Times Square
New York, NY
Visit http://sma.org/medical-dilemmas for updates or to register.