



Opioids for Chronic Pain: Striking a Balance

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April 11, 2006

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I. LEARNING OBJECTIVES

You'll be able to describe:

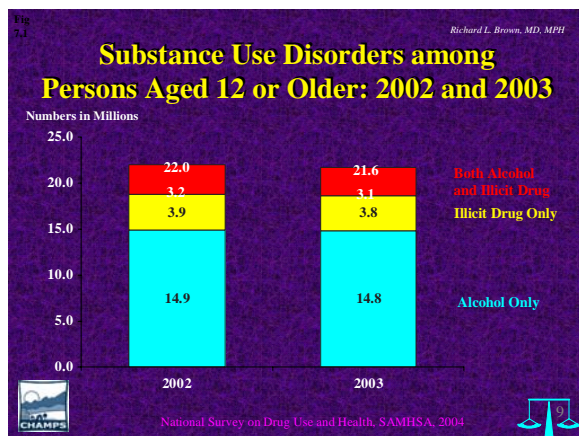
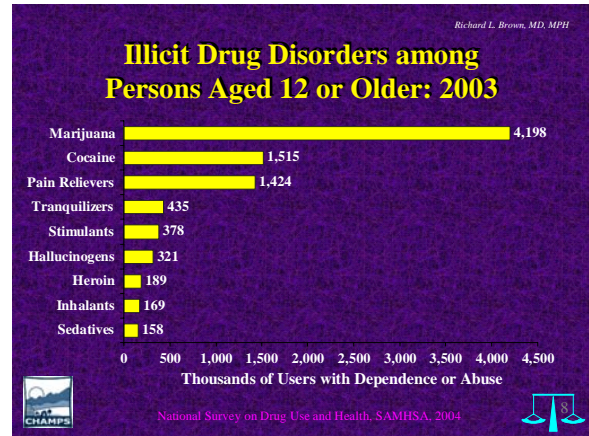
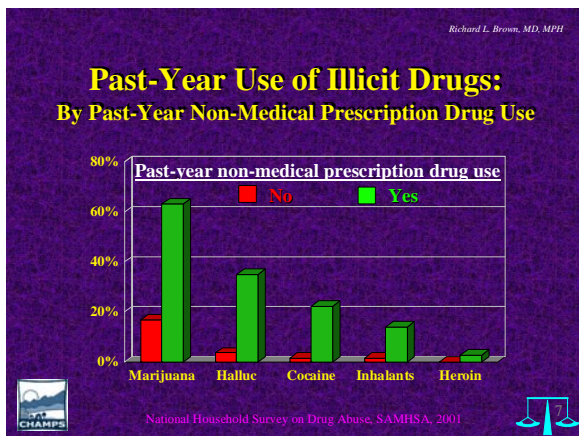
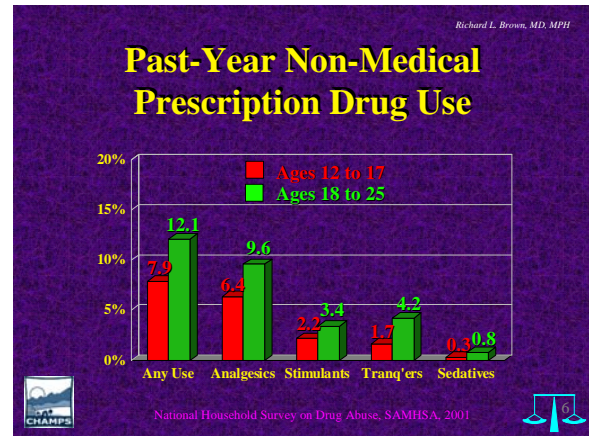
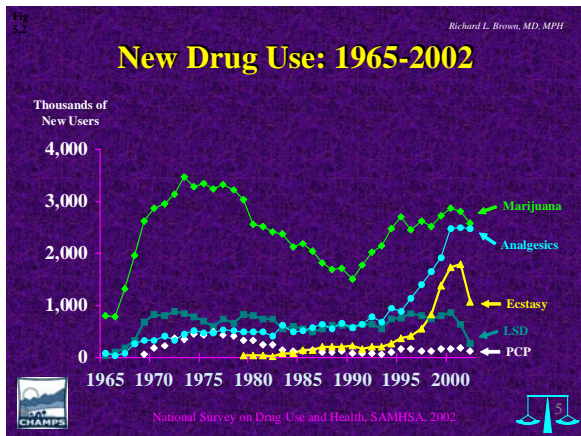
- 1. Epidemiology of prescription drug misuse and dependence
- 2. Therapeutic use and pharmacology of commonly misused prescription drugs
- 3. Detox and treatment for patients with prescription drug dependence

You'll be able to discuss:

- 4. The concept of balancing benefit and risk in prescribing potentially addictive medicines
- 5. Ways that prescribers and non-prescribers can optimize benefit and reduce abuse, addiction, and diversion

II. PRESENTATION SLIDE TEXT (NOTES PAGES)

1. EPIDEMIOLOGY OF PRESCRIPTION DRUG MISUSE AND DEPENDENCE



THE ELDERLY

- Prescription drugs may be the most commonly abused drugs
- The elderly often take drugs incorrectly
- Benzodiazepines are often prescribed unsafely
- Sedatives/tranquilizers are especially dangerous for alcohol users

2. THERAPEUTIC USE AND PHARMACOLOGY OF MISUSED PRESCRIPTION DRUGS

Categories of drugs

Opioids • Stimulants • Benzodiazepines

Information

Indications

Benefits

Adverse effects

OPIOIDS

Examples:

Hydrocodone (Vicodin, Lortab)

Oxycodone (Percocet, Roxicet, OxyContin)

Codeine (Tylenol #3, Robitussin AC)

Morphine (MS-IR, MS Contin) Hydromorphone (Dilaudid, Palladone)

Meperidine (Demerol)

Diphenoxylate (Lomotil)

Indications:

pain, cough, diarrhea

Short-term effects:

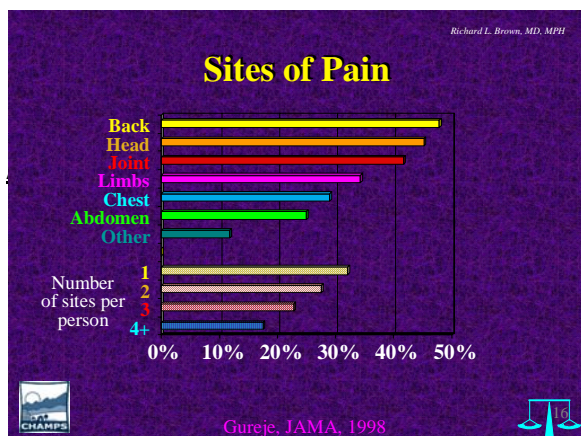
analgesia, cough suppression, constipation, nausea, drowsiness, cognitive blunting, respiratory depression

Long-term effects:

no organ damage

PREVALENCE OF CHRONIC PAIN

- Definition of chronic pain
 - Moderate to severe pain on ≥ 180 days/yr
 - Functional interference
 - Sought medical care
 - Surveyed consecutive primary care patients
 - Response rate = 96%
 - N = 373
 - Prevalence = 9.4% in men, 21.2% in women
- Gureje, JAMA, 1998



OPIOIDS FOR CHRONIC PAIN: EFFECTIVENESS AND RISK OF ADDICTION

- No long-term randomized trials
- Several case series studies suggest effectiveness
- Rates of opioid disorders vary from 2% to 45%
- Prior substance use disorders are the major risk factor for abuse and addiction
- Aberrant medication-related behaviors are common and often are not associated with abuse, addiction, and diversion

Passik SD, Pain Medicine, 2003; Vallerand AH, NCNA, 2003

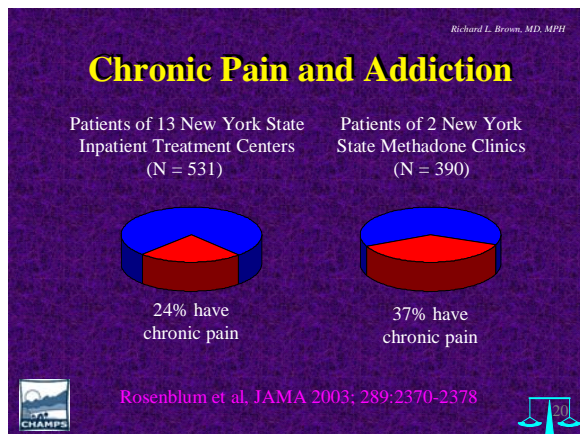
ENDORSEMENT OF OPIOIDS FOR TREATING CHRONIC PAIN

- American Pain Society
- American Society of Addiction Medicine
- Federation of State Medical Boards
- US Drug Enforcement Agency
- Wisconsin Medical Society

UNDERTREATMENT OF PAIN

- 40% to 50% of patients with chronic pain do not attain sufficient relief
- 50% of patients change physicians to seek more relief. Reasons include:
 - Failure to take the pain seriously
 - Insufficiently aggressive treatment
 - Apparent lack of knowledge

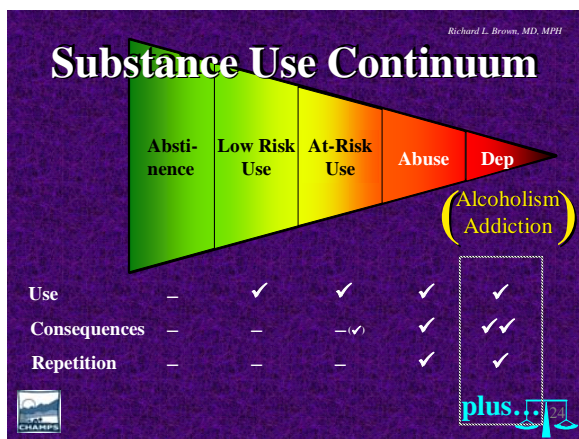
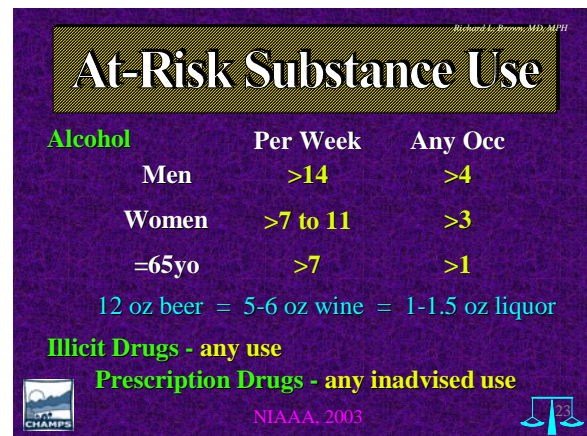
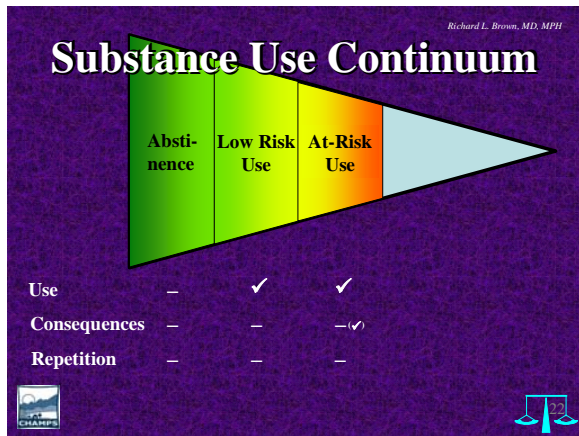
Glajchen, J Am Bd Fam Prac, 2001



CLINICIAN BARRIERS TO EFFECTIVE OPIOID PRESCRIBING

- Limited training, knowledge, and skills
- Fear of prescribing opioids
- Fear of prescribing sufficient doses
- Demographic stereotypes
- Misunderstanding of addiction-related terminology and issues

Glajchen, J Am Bd Fam Prac, 2001



ADDITIONAL SYMPTOMS OF SUBSTANCE DEPENDENCE

- Physical dependence (±)
- Compulsive Use
- Preoccupation with obtaining the substance
- Loss of control (???)

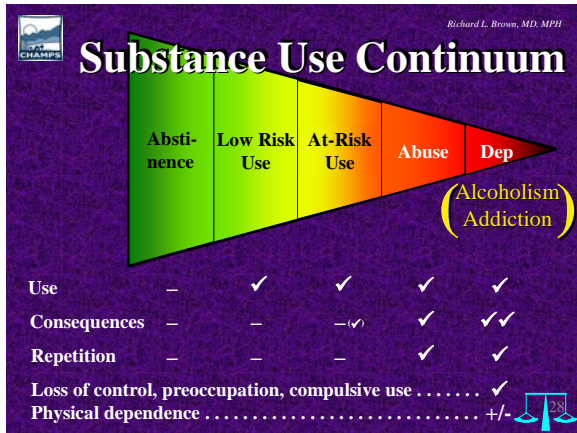
EFFECT OF COCAINE ON RAT VENTRAL TEGMENTUM

	Cytoplasmic Enzyme Activity	DNA Transcription
Baseline		
3 wk +		
3 mo +		
3 mo +; 3 mo -		

After Nestler E

LOSS OF CONTROL

- A hijacking of the pleasure/reward machinery of the brain
- Drives to eat and procreate instead become drives to obtain and use substances
- It is extremely difficult to resist these drives consistently over time



ADDICTION VS. PSEUDOADDICTION

Addicts

- Use substances initially to alter mood
- Later, for cravings and physical dep.
- Preoccupied with obtaining drugs

Pseudoaddicts

- Use solely for symptom control
- Doctor-shop, manipulate, hoard, etc., because of undertreatment

Weissman, 1989

3. DETOX AND TREATMENT FOR PRESCRIPTION DRUG DEPENDENCE

DETOXIFICATION

- Precedes addiction treatment
- Relieves withdrawal symptoms
- Prevents complications from withdrawal

OPIOID DETOXIFICATION

- Not life-threatening
- Can be very uncomfortable
- Tapering doses of a long-acting opioid (methadone) are best
- May use clonidine, NSAIDs, anti-diarrheals, hypnotics

TREATMENT

- Behavioral treatments are the mainstay
 - Individual counseling
 - Cognitive-behavioral therapy
- Relapse prevention
- Psychoeducation
- Family counseling
- Group counseling
- Self-help groups

NIDA, 2001

TREATMENT

- When available, pharmacologic treatment can help
- A combination of behavioral and pharmacologic treatment is best
- Methadone or buprenorphine is effective for opioid analgesic dependence

NIDA, 2001

4. BALANCING BENEFIT AND RISK IN PRESCRIBING

JEAN - INITIAL PRESENTATION

- 33-year-old divorced truck company dispatcher
- Back pain since MVA 4 years ago
 - Bilateral L/S spine and paralumbar areas, non-rad.
 - Negative X-rays and MRI scan
- Initial treatment
 - PT - ultrasound, heat/cold, exercises
 - Chiropractic - helped initially, then ineffective
 - Ibuprofen 600mg tid (3 other NSAIDs were no better)
 - 8 oxycodone 5mg/acet 325mg per day - hard to taper
- Returned to work 3 months after MVA

JEAN - LAST 3 YEARS

- Baseline pain - 2 to 3 on 0-to-10 scale
- Continues on ibuprofen 600 mg qd to tid
- Two exacerbations; no apparent cause
 - Tender lumbosacral spine
 - Paralumbar tenderness and palpable spasm
 - No radiation, normal neurologic exam
 - Treated with PT, oxycodone/acetaminophen 5mg/325mg qid, again hard to taper
 - Returned to work in 4 weeks

JEAN – TODAY

- Exacerbation x 10 weeks, same hx/PE
- Tried PT 3 times - too painful
- Had been taking 8 oxycodone/acet. per day
- Opioids discontinued 2 weeks ago - diarrhea, agitation, sleeplessness
- Pain had been 5 to 8, now 7 to 9
- "I'd really want to go back to work, but if I can't get some relief I'm going to have to go on disability."

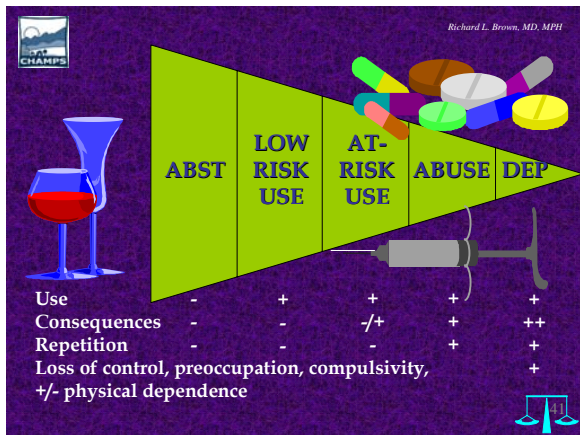
JEAN - SUBSTANCE USE AND PSYCHIATRIC HISTORY

- Drank heavily until MVA/DWI 4 years ago
- Completed mandated intensive outpatient tx.
- Usually 4 twelve-ounce beers on Fri & Sat + 2 beers twice a week; now 3/day due to pain
- Used marijuana regularly until age 25; now once or twice a month
- Tried cocaine once - "That was way too good; I definitely could have gotten hooked on that."
- No psychiatric history

QUESTION 1 - OPIOID DIAGNOSIS

Jean's recent opioid withdrawal and the difficulty discontinuing opioids suggest a DSM-IV diagnosis of:

1. Opioid abuse
2. Opioid dependence
3. Neither



JEAN AND SUBSTANCE USE

Opioids

- Recent physical dependence
- No neg. consequences or loss of control
- Difficulty in tapering due to pain

Alcohol

- Prior alcohol abuse, ? dependence
- Current - at least risky use

QUESTION 2 - INDICATIONS FOR OPIOIDS

Opioids should be considered for patients with chronic pain who have:

1. Moderate to severe pain
2. 1 + inadequate response to other treatments
3. 1 + 2 + significant functional disability
4. 1 + 2 + 3 + no active substance abuse/dep
5. 1 + 2 + 3 + 4 + no prior substance abuse/dep

INDICATIONS FOR OPIOIDS

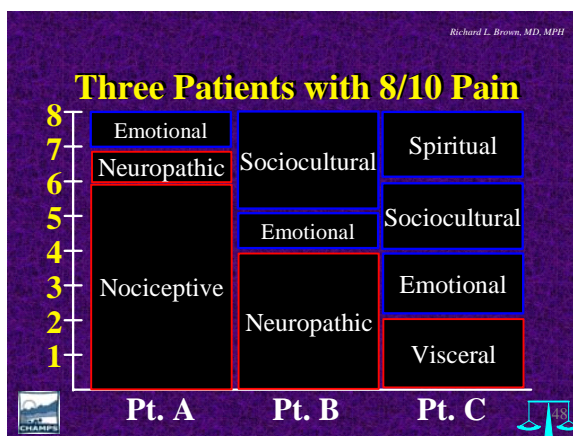
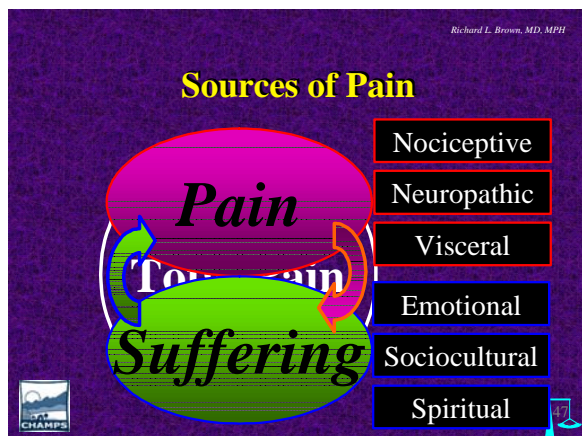
- Chronic pain of moderate to severe intensity
- Significant functional disability
- Inadequate response to other treatments

PAIN ASSESSMENT - INTENSITY

- Use standard scale such as 0 to 10 scale
0 = no pain 10 = worst pain imaginable
- Accept patients' reports
- Objective signs of acute pain are extinguished with chronic pain

ACUTE VS. CHRONIC PAIN

- Older definition
- Newer Definition
- Useful - Signals problem
- Harmful - Is the problem



ASSESSING FUNCTION

- Validated functional assessment tools
 - Chronic Pain Grade (VonKorff M et al. *Pain* 50:133-49,1992.)
 - Quebec Back Pain Disability Scale (Kocec JA et al. *J Clin Epidemiology* 49:151-61,1996.)
- Questions
 - Bed days, missed work, curtailed activities
 - Activities patient can do / misses
- Appearance: dress, grooming, affect

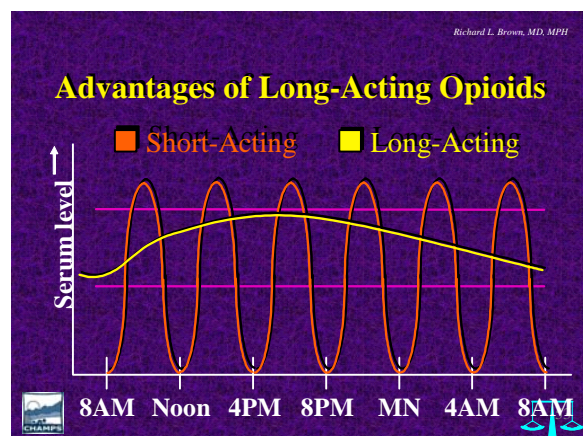
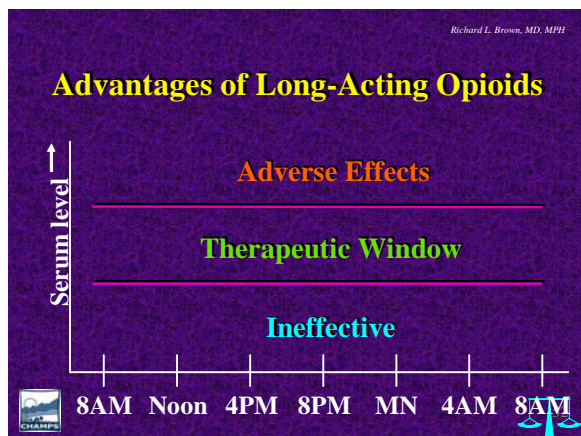
ATTEMPTING OTHER TREATMENTS

- The treatment with most evidence of effectiveness for CLBP is exercise
- Adjunctive meds may be helpful
- Treat for psychiatric disorders, stress
- Distraction, relaxation, coping skills
- TENS/PENS
- Invasive interventions
- CAM may be useful: massage, chiropractic, acupuncture, others
- NSAID's do not relieve severe pain
- COX-2 inhibitors are no more effective than other NSAIDs

QUESTION 3 - WHICH OPIOIDS?

The safest and most effective opioids for treating chronic pain include:

1. Propoxyphene and pentazocine
2. Hydrocodone and immediate release oxycodone
3. Morphine sulfate-extended release tablets and transdermal fentanyl
4. All of the above



ADVANTAGES OF LONG-ACTING OPIOIDS

- More consistent analgesia
- Fewer adverse effects
- More tolerance to adverse effects
- Better sleep → better daytime function
- Less euphoria, addiction, diversion

OPIOID REGIMEN FOR CHRONIC PAIN

- Long-acting opioid for baseline pain:
 - Hydromorphone-ERT
 - Oxycodone-ERT
 - Morphine-ERT
 - Transdermal fentanyl
 - Methadone
- Short-acting opioid for breakthrough pain:
 - Hydrocodone
 - Oxycodone
- Avoid:
 - Partial agonists: Pentazocine & Propoxyphene
 - Meperidine (Demerol®)

QUESTION 4 - MAXIMUM DOSE

What is the maximum recommended daily dose of opioid for chronic non-cancer pain?

1. 200 mg oral morphine or equivalent
2. 600 mg oral morphine or equivalent
3. 1200 mg oral morphine or equivalent
4. 2400 mg oral morphine or equivalent
5. As much as is necessary to control pain

TITRATING OPIOID DOSE

- Start at 50% to 100% of the recommended dose for acute or cancer pain
- At low doses, reassess weekly until titrated
- At higher doses (morphine equivalent $\geq 300\text{mg}$), increase by $\leq 20\%$ per month
- Start lower and increase more slowly with:
 - Impaired renal or hepatic function
 - Methadone

QUESTION 5 - PREVENTING ADDICTION

When treating chronic pain with opioids, the LEAST helpful strategy for preventing opioid addiction is:

1. Prescribing only long-acting opioids
2. Limiting the dose of opioids
3. Ensuring that opioids improve function
4. Using and enforcing written medication agreements (sometimes called contracts)

MEDICATION AGREEMENTS

- One prescriber and one pharmacy
- Prescriptions must last as intended
- No after-hours refill requests
- Lost prescription policy
- Random urine drug screens
- Possible responses to violations
- Safe activities when drowsy
- Additional required care

JEAN – TODAY

- Agreed to limit drinking - 1 beer/day
- Rx: transdermal fentanyl 25 $\mu\text{g/hr}$,
Apply 1 every 3 days, #2 patches

JEAN – TODAY, CONTINUED

- Transdermal fentanyl has:
 - Long duration of action - usually 3 days
 - Favorable impact on sleep
 - Low tamperability and diversion
 - Low incidence of constipation

MONITORING OPIOID RECIPIENTS

Analgesia
Adverse Effects
Activity
Adherence
Passik, 2002



QUESTION 6 - SIX DAYS LATER

Six days later, Jean’s pain has decreased to 5 to 7 out of 10. There have been no adverse effects. Her function is unchanged. She used the medicine as directed. At this time, you would:

1. Discontinue fentanyl
2. Continue fentanyl 25µg/hr
3. Increase fentanyl to 50µg/hr
4. Change to another long-acting opioid
5. Change to oxycodone/acetaminophen

INDICATIONS TO INCREASE OPIOID DOSE

Analgesia	Inadequate
Adverse Effects	Tolerable
Activity	Better or no worse
Adherence	Good

JEAN - 6 DAYS LATER

Analgesia	Pain ratings are 3 to 5
Adverse Effects	Mild sedation, resolving
Activity	Doing more housework
Adherence	Good

Asks to retry physical therapy

JEAN - TWO MONTHS LATER

Analgesia	Pain ratings are 0 to 3
Adverse Effects	None
Activity	Back to work x 1 mo, doing well in PT
Adherence	Good

Wishes to discontinue fentanyl

JEAN - TAPERING PLAN

- Transdermal fentanyl 25 µg/hr, #2, then discontinue
- Clonidine .1 mg, 1 to 2 tabs qid prn

Additional options:

OTC anti-diarrheal
OTC NSAID for muscle/joint pain
Sleeping aid

QUESTION 7 - LONG-TERM TREATMENT

If Jean had continued to require a long-acting opioid for adequate pain relief and return to work, you would have:

1. Insisted on a taper in 3 months
2. Insisted on a taper in 6 to 12 months
3. Referred Jean to an addiction or pain specialist
4. Continued the opioid indefinitely

LONG-TERM OPIOIDS

- Chronic pain is a chronic disease requiring ongoing treatment
- No tissue toxicity or documented harm with long-term opioids
- Most patients have no problem with tolerance to the analgesic effects
- For tolerance, consider opioid rotation

WITH OPIOIDS, CONSIDER:

- Non-opioid analgesics
- TCA's, anti-convulsants
- Exercise and other physical therapies
- Relaxation and distraction exercises
- Complementary/alternative modalities
- Treatments for suffering

5. RECOMMENDATIONS FOR PRESCRIBERS AND NON-PRESCRIBERS

OPTIMIZING PRESCRIBING

- Assessment
- Treatment planning
- Patient selection for potentially addictive medications
- Medication selection for patients
- Medication titration
- Patient monitoring / Follow-up
- Documentation

ASSESSMENT

- Symptoms
- Function - physical, psychosocial
- Past treatments and results
- Other past history
- Psychiatric history, stresses, supports
- Substance use - current and prior
- Health care resources
- Physical examination
- Criminal justice and prescribing databases, where available

TREATMENT PLANNING

- Negotiate appropriate treatment goals
- Address the primary problem and related conditions
- Consider multiple treatment modalities serially or in parallel
- Assemble treatment team
- Ensure communication among treatment providers
- Set follow-up

PATIENT SELECTION FOR POTENTIALLY ADDICTIVE DRUGS

- Failure of non-addictive drugs and non-pharmacologic modalities
- Access to non-pharmacologic modalities
- Severity of symptoms
- Severity of functional impact
- Urgency of addressing symptoms
- Substance use history
- Potential for safe self-administration
- Safety-sensitive occupations/child care
- Willingness to adhere to medication agreement

SELECTION OF POTENTIALLY ADDICTIVE DRUGS

- Consider emphasizing slow-onset, long-acting, medicines for baseline symptoms
- Consider the security of the delivery system
- Consider epidemiology of substance use
- Consider ease of monitoring
- Consider affordability
- Weigh considerations in light of risks and benefits

SAFER POTENTIALLY ADDICTIVE DRUGS

- Opioids for Chronic Pain:
Fentanyl patch (Duragesic)
Extended-release morphine
(MS-Contin, Oramorph, Avinza, Kadian)
Methadone
- Sedatives for Anxiety: clonazepam (Klonopin), clorazepate (Tranxene)
- Stimulants for ADD: Ritalin-SR, Adderal-SR

MEDICATION TITRATION

- Increase dose as needed on a timely basis
- Anticipate and manage side effects
- Try other medicines as needed
- Manage advance in activities

FOLLOW-UP

- Assess symptoms
- Assess function
- When possible, obtain confirmatory information from multiple sources
- Perform urine drug screens as appropriate
- Identify and manage aberrant behaviors

Kirsch, Clinical Journal of Pain, 2002

REGULATORY SCRUTINY

Poor documentation is the most common reason for discipline

Document:

- Through initial assessment
- Follow-up assessments - outcomes regarding symptoms and function
- Barriers that preclude optimal treatment

Another common reason for discipline is continued prescribing despite poor outcomes and violations of medication agreements.

- Document aberrant behaviors and management
- When abuse or addiction are possible, refer for substance abuse assessment
- Discontinue potentially addictive medicines for continued poor outcomes and aberrant behaviors

NON-PRESCRIBERS

- Most treatment team members are non-prescribers
- Help by:
 - Sharing observations
 - Contributing to problem-solving
 - Identifying other helpful resources
- For concerns about prescribing:
 - Speak with prescriber
 - Share current literature
 - Speak again with prescriber and request a referral
 - Consider report to medical board

SUMMARY

- Prescription drug misuse, abuse, and dependence are increasing
- Treatments are similar to those for other substance use disorders
- Potentially addictive medicines are legitimate, effective treatments
- For those who need such treatments, measures can be taken to minimize addiction, abuse, and diversion

III. Biography of Richard L. Brown, MD, MPH

Richard L. Brown, MD, MPH, completed medical school at Brown University, a family medicine residency at Overlook Hospital/Columbia University in Summit, New Jersey, a Robert Wood Johnson Foundation research fellowship at the University of Washington, and a substance abuse fellowship program sponsored by the National Institutes of Health and the Society of Teachers of Family Medicine. He joined the faculty of the Department of Family Medicine at the University of Wisconsin Medical School in 1990 and is now a tenured associate professor. His clinical practice emphasizes management of chronic pain and alcohol and drug disorders. He has lectured and conducted workshops on these topics, plus prescription drug abuse and motivational interviewing, around the US and in Europe and Asia. His NIH-funded research has focused on primary care screening and intervention for substance use disorders. Dr. Brown is a past president of the Association for Medical Education and Research in Substance (AMERSA). He received AMERSA's McGovern Award for excellence in medical education in 2002. He was the founding director of Project Mainstream (www.projectmainstream.net), a federally funded program to improve substance abuse education for fifteen health professions.

IV. Description of CHAMPS

CHAMPS, the Community Health Association of Mountain/Plains States, is a non-profit organization dedicated to providing a coordinating structure of service to non-profit primary health care programs whose primary purpose is to serve the medically indigent and medically underserved of Region VIII (CO, MT, ND, SD, UT, and WY). CHAMPS also serves the Region VIII State Primary Care Associations that assist those nonprofit primary health care programs (CCHN, MPCA, CHAD, AUCH, and WYPCA). Currently, CHAMPS programs and services focus on education and training, collaboration and networking, policy and funding communications, and the collection and dissemination of regional data for Region VIII Community Health Centers and Primary Care Associations.

For more information, please visit www.champsonline.org or call (303) 861-5165.