Addressing the Barriers to Effective Pain Management and Issues of Opioid Misuse and Abuse

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Educational Learning Objectives

- Identify the negative impact of persistent pain on health and quality of life, methods to assess pain levels, appropriate use of opioid medications, and documentation required for compliance with regulatory policies.
- Integrate appropriate risk assessment strategies for patient abuse, misuse, and diversion of opioids into an overall management approach for acute and chronic pain.
- Describe the specific elements of new abuse deterrent technologies associated with opioid therapy, and assess their implications for clinical practice.
Multiple Types of Pain

A. Nociceptive
- Noxious Peripheral Stimuli

B. Inflammatory
- Inflammation

C. Neuropathic
- Multiple Mechanisms

D. Noninflammatory/Nonneuropathic
- Abnormal Central Processing

Examples

- Strains and sprains
- Bone fractures
- Postoperative
- Osteoarthritis
- Rheumatoid arthritis
- Tendonitis
- Diabetic peripheral neuropathy
- Post-herpetic neuralgia
- HIV-related polyneuropathy
- Fibromyalgia
- Irritable bowel syndrome

- Patients may experience multiple pain states simultaneously

Long-Term Consequences of Acute Pain: Potential for Progression to Chronic Pain

Surgery or injury causes inflammation

Peripheral Nociceptive Fibers

Sustained currents

Sensitization

Peripheral Nociceptive Fibers

Sustained Activation

CNS Neuroplasticity

Structural Remodeling

Hyperactivity

ACUTE PAIN

CHRONIC PAIN

Neuroplasticity in Pain Processing

Vicious Cycle of Uncontrolled Pain

- Pain
- Avoidance Behaviors
- Decreased Mobility
- Diminished Self-Efficacy
- Altered Functional Status
- Social Limitations

The cycle shows how uncontrolled pain can lead to avoidance behaviors, which in turn lead to decreased mobility, further diminishing self-efficacy and social limitations, creating a vicious cycle that affects functional status.
Breaking the Chain of Pain Transmission

5-HT = serotonin; NE = norepinephrine; TCA = tricyclic antidepressant

Components of Chronic Pain

- Chronic pain
  - Baseline persistent pain
  - Breakthrough pain (BTP)

Each component of chronic pain needs to be independently assessed and managed

# Opioid Formulations

<table>
<thead>
<tr>
<th>Type of Drug</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure $\mu$-opioid receptor agonists</td>
<td>Morphine, hydromorphone, fentanyl, oxycodone</td>
</tr>
<tr>
<td>Dual mechanism opioids</td>
<td>Tramadol, tapentadol</td>
</tr>
<tr>
<td>Rapid onset (transmucosal)</td>
<td>Fentanyl, alfentanil, sufentanil, diamorphine</td>
</tr>
<tr>
<td>Immediate release</td>
<td>Tramadol, oxycodone</td>
</tr>
<tr>
<td>Modified release (long acting)</td>
<td>Morphine, methadone, oxycodone</td>
</tr>
<tr>
<td>Available with co-analgesic</td>
<td>Oxycodone, tramadol, codeine</td>
</tr>
<tr>
<td>Only available with co-analgesic</td>
<td>Hydrocodone (until 2014)</td>
</tr>
</tbody>
</table>
Formulation Points to Consider

- Dose-limiting issues and toxicity with co-analgesics
  - 4 g/day acetaminophen limit
- Importance of titration
  - Risk of overdose, challenges of dose conversion during rotation
- Pharmacokinetics versus temporal patterns of pain
- Adherence
- Cost
- Convenience
- Caregiving issues
Domains for Pain Management

Outcome:
The 4 A’s

- Analgesia
- Activities of Daily Living
- Adverse Events
- Aberrant Drug-Taking Behaviors

Federation of State Medical Boards of the United States, Inc

Model Policy for the Use of Controlled Substances for the Treatment of Pain

FSMB Model Policy
Basic Tenets

• Pain management is important and integral to the practice of medicine
• Use of opioids may be necessary for pain relief
• Use of opioids for other than a legitimate medical purpose poses a threat to the individual and society
• Physicians have a responsibility to minimize the potential for abuse and diversion
• Physicians may deviate from the recommended treatment steps based on good cause
• Not meant to constrain or dictate medical decision-making

FSMB, Federation of State Medical Boards
New Illicit Drug Use United States, 2006

*533,000 new nonmedical users of oxycodone aged ≥ 12 years. Past year initiates for specific illicit drugs among people aged ≥ 12 years.
†LSD, lysergic acid diethylamide; PCP, phencyclidine.

### Definition of Terms

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Misuse</strong></td>
<td>Use of a medication (for a medical purpose) other than as directed or as indicated, whether willful or unintentional, and whether harm results or not</td>
</tr>
<tr>
<td><strong>Abuse</strong></td>
<td>Any use of an illegal drug&lt;br&gt;The intentional self administration of a medication for a nonmedical purpose such as altering one’s state of consciousness, eg, getting high</td>
</tr>
<tr>
<td><strong>Diversion</strong></td>
<td>The intentional removal of a medication from legitimate and dispensing channels</td>
</tr>
<tr>
<td><strong>Addiction</strong></td>
<td>A primary, chronic, neurobiological disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations&lt;br&gt;Behavioral characteristics include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, craving</td>
</tr>
<tr>
<td><strong>Pseudoaddiction</strong></td>
<td>Syndrome of abnormal behavior resulting from undertreatment of pain that is misidentified by the clinician as inappropriate drug-seeking behavior&lt;br&gt;Behavior ceases when adequate pain relief is provided&lt;br&gt;Not a diagnosis; rather, a description of the clinical intention</td>
</tr>
</tbody>
</table>

Rx Opioid Users Are Heterogeneous

## Risk Factors for Aberrant Behaviors/Harm

### Biological
- Age ≤ 45 years
- Gender
- Family history of prescription drug or alcohol abuse
- Cigarette smoking

### Psychiatric
- Substance use disorder
- Preadolescent sexual abuse (in women)
- Major psychiatric disorder (eg, personality disorder, anxiety or depressive disorder, bipolar disorder)

### Social
- Prior legal problems
- History of motor vehicle accidents
- Poor family support
- Involvement in a problematic subculture

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Stratify Risk

Low Risk
- No past/current history of substance abuse
- Noncontributory family history of substance abuse
- No major or untreated psychological disorder

Moderate Risk
- History of treated substance abuse
- Significant family history of substance abuse
- Past/comorbid psychological disorder

High Risk
- Active substance abuse
- Active addiction
- Major untreated psychological disorder
- Significant risk to self and practitioner

Opioid Treatment Agreement

Opioid (narcotic) treatment for chronic pain is used to reduce pain and improve what you are able to do each day. Along with opioid treatment, other medical care may be prescribed to help improve your ability to do daily activities. This may include exercise, use of non-opioid analgesics, physical therapy, psychological counseling or other therapies or treatment. Vocational counseling may be provided to assist in your return to work effort.

To the doctor: Keep signed originals in your file; give a photocopy to the patient. Renew at least every 6 months.

I ______________________________________________________________________ understand that compliance with the following guidelines is important in continuing pain treatment with Dr. ______________________________________________________________________.

1. I understand that I have the following responsibilities:
   a. I will take medications only at the dose and frequency prescribed.
   b. I will not increase or change medications without the approval of this doctor.
   c. I will actively participate in RTW efforts and in any program designed to improve function (including social, physical, psychological and daily or work activities).
   d. I will not request opioids or any other pain medicine from physicians other than from this doctor. This doctor will approve or prescribe all other medications.
   e. I will inform this doctor of all other medications that I am taking.
   f. I will obtain all medications from one pharmacy, when possible known to this doctor with full consent to talk with the pharmacist given by signing this agreement.
   g. I will protect my prescriptions and medications. Only one lost prescription or medication will be replaced in a single calendar year. I will keep all medications from children.
   h. I agree to participate in psychiatric or psychological assessments, if necessary.

2. I understand that in the event of an emergency, this doctor should be contacted and the problem will be discussed with the emergency room or other treating physician. I am responsible for signing a consent to request record transfer to this doctor. No more than 3 days of medications may be prescribed by the emergency room or other physician without this doctor’s approval.

3. I understand that I will consent to random drug screening. A drug screen is a laboratory test in which a sample of my urine or blood is checked to see what drugs I have been taking.

4. I will keep my scheduled appointments and/or cancel my appointment a minimum of 24 hours prior to the appointment.

5. I understand that this doctor may stop prescribing opioids or change the treatment plan if:
   a. I do not show any improvement in pain from opioids or my physical activity has not improved.
   b. My behavior is inconsistent with the responsibilities outlined in #1 above.
   c. I give, sell or misuse the opioid medications.
   d. I develop rapid tolerance or loss of improvement from the treatment.
   e. I obtain opioids from other than this doctor.
   f. I refuse to cooperate when asked to get a drug screen.
   g. If an addiction problem is identified as a result of prescribed treatment or any other addictive substance.
   h. If I am unable to keep follow-up appointments.

YOUR SAFETY RISKS WHILE WORKING UNDER THE INFLUENCE OF OPIOIDS:

You should be aware of potential side effects of opioids such as decreased reaction time, clouded judgment, drowsiness and tolerance. Also, you should know about the possible danger associated with the use of opioids while operating heavy equipment or driving.

SIDE EFFECTS OF OPIOIDS:

- Confusion or other change in thinking abilities
- Problems with coordination or balance that may make it unsafe to operate dangerous equipment or motor vehicles
- Breathing too slowly—overdose can stop your breathing and lead to death
- Nausea
- Constipation
- Sleepiness or drowsiness
- Aggravation of depression
- Vomiting
- Dry mouth

THESE SIDE EFFECTS MAY BE MADE WORSE IF YOU MIX OPIOIDS WITH OTHER DRUGS, INCLUDING ALCOHOL.

RISKS:

- Physical dependence. This means that abrupt stopping of the drug may lead to withdrawal symptoms characterized by one or more of the following:
  - Runny nose
  - Diarrhea
  - Sweating
  - Rapid heart rate
  - Difficulty sleeping for several days
  - Abdominal cramping
  - ‘Goose bumps’
  - Nervousness
- Psychological dependence. This means it is possible that stopping the drug will cause you to mass or crave it.
- Tolerance. This means you may need more and more drug to get the same effect.
- Addiction. A small percentage of patients may develop addiction problems based on genetic or other factors.
- Problems with pregnancy. If you are pregnant or contemplating pregnancy, discuss with your physician.

PAYMENT OF MEDICATIONS:

State law forbids L & I from paying for opioids once the patient reaches maximum medical improvement. You and your doctor should discuss other sources of payment for opioids when L & I can no longer pay.

RECOMMENDATIONS TO MANAGE YOUR MEDICATIONS:

- Keep a diary of the pain medications you are taking, the medication dose, time of day you are taking them, their effectiveness and any side effects you may be having.
- Use of a medication box that you can purchase at your pharmacy that is already divided in to the days of the week and times of the day so it is easier to remember when to take your medications.
- Take along only the amount of medicine you need when leaving home so there is less risk of loosing all your medications at the same time.

I have read this document, understand and have had all my questions answered satisfactorily. I consent to the use of opioids to help control my pain and I understand that my treatment with opioids will be carried out as described above.

Identifying Who Is at Risk for Opioid Abuse and Diversion

- Predictive tools
- Aberrant behaviors
- Urine drug testing
- Prescription monitoring programs
- Severity and duration of pain
- Pharmacist communication
- Family and friends
- Patients
Signs of Potential Abuse and Diversion

- Request appointment toward end-of-office hours
- Arrive without appointment
- Telephone/arrive after office hours when staff are anxious to leave
- Reluctant to have thorough physical exam, diagnostic tests, or referrals
- Fail to keep appointments
- Unwilling to provide past medical records or names of HCPs
- Unusual stories

However, emergencies happen: 
not every person in a hurry is an abuser/diverter

Drug Enforcement Administration. Don’t be Scammed by a Drug Abuser. 1999. 
Risk Assessment Tools

- **Addiction Behaviors Checklist (ABC)**
  - Evaluate and monitor behaviors indicative of addiction related to prescription opioids in patients with chronic pain.

- **Addiction Severity Index (ASI)**
  - Assess current and lifetime substance-use problems and prior treatment.

- **Current Opioid Misuse Measure (COMM)**
  - Periodically monitor aberrant medication-related behaviors in patients with chronic pain currently on opioid therapy.

Risk Assessment Tools (cont)

- **Drug Abuse Screening Test (DAST-10)**
  - Screen for probably drug abuse or dependence

- **Pain Medication Questionnaire (PMQ)**
  - Assess risk for opioid medication misuse in patients with chronic pain

- **Screening Instrument for Substance Abuse Potential (SISAP)**
  - Identify individuals with possible substance-abuse history

- **Opioid Risk Tool (ORT)**
  - Predict which patients might develop aberrant behavior when prescribed opioids for chronic pain

Risk Assessment Tools (cont)

- **Diagnosis, Intractability, Risk, Efficacy (DIRE)**
  - Predict the analgesic efficacy of, and patient compliance to, long-term opioid treatment in the primary care setting

- **Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R)**
  - Predict aberrant medication-related behaviors in patients with chronic pain considered for long-term opioid therapy
    - Empirically-derived, 24-item self-report questionnaire
    - Reliable and valid
    - Less susceptible to overt deception than past version
    - **Scoring:** $\geq 18$ identifies 90% of high-risk patients

**ORT Validation**

Mark each box that applies

1. Family history of substance abuse
   - Alcohol
   - Illegal drugs
   - Prescription drugs

2. Personal history of substance abuse
   - Alcohol
   - Illegal drugs
   - Prescription drugs

3. Age (mark box if 16-45 years)

4. History of preadolescent sexual abuse

5. Psychological disease
   - ADD, OCD, bipolar, schizophrenia
   - Depression

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
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<tbody>
<tr>
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<tr>
<td>2.</td>
<td>![ ]</td>
<td>![ ]</td>
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<tr>
<td>3.</td>
<td>![ ]</td>
<td>![ ]</td>
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<tr>
<td>4.</td>
<td>![ ]</td>
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<tr>
<td>5.</td>
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</table>

- Exhibits high degree of sensitivity and specificity
  - 94% of low-risk patients did not display an aberrant behavior
  - 91% of high-risk patients did display an aberrant behavior

N = 185
ADD, attention deficit disorder; OCD, obsessive-compulsive disorder.
Name: Chris Jackson  Date: 9/16/09

The following survey is given to all patients who are on or being considered for opioids for their pain. Please answer each question as honestly as possible. This information is for our records and will remain confidential. Your answers will not determine your treatment. Thank you.

Please answer the questions below using the following scale:

0 = Never, 1 = Seldom, 2 = Sometimes, 3 = Often, 4 = Very Often

1. How often do you have mood swings?
   - 0
   - 1
   - 2
   - 3
   - 4
   - [ ]

2. How often do you smoke a cigarette within an hour after you wake up?
   - 0
   - 1
   - 2
   - 3
   - 4
   - [ ]

3. How often have you taken medication other than the way that it was prescribed?
   - 0
   - 1
   - 2
   - 3
   - 4
   - [ ]

4. How often have you used illegal drugs (for example, marijuana, cocaine, etc.) in the past five years?
   - 0
   - 1
   - 2
   - 3
   - 4
   - [ ]

5. How often in your lifetime have you had legal problems or been arrested?
   - 0
   - 1
   - 2
   - 3
   - 4
   - [ ]

Please include any additional information you wish about the above answers. Thank you.

Mr. Jackson’s Score = 3

To score the SOAPP, add ratings of all questions. A score of 4 or higher is considered positive.
Risk Assessment Tools Highlights

- **ORT, SOAPP & DIRE**
  - Best assess abuse potential among those being considered for long-term opioid therapy

- **COMM & PMQ**
  - Characterize degree of medication misuse or aberrant behavior once opioids are started

- **DAST-10 & PMQ**
  - More suitable for assessing current alcohol and/or drug abuse than potential for such abuse

Urine Drug Testing

- When to test?
  - Randomly, annually, PRN
- What type of testing?
  - POC, GS/MS
- How to interpret
  - Metabolism of opioids
  - False positive and negative results
- What to do about the results
  - Consult, refer, change therapy, discharge
Positive and Negative Urine Toxicology Results

- Positive forensic testing
  - Legally prescribed medications
  - Over-the-counter medications
  - Illicit drugs or unprescribed medications
  - Substances that produce the same metabolite as that of a prescribed or illegal substance
  - Errors in laboratory analysis

- Negative compliance testing
  - Medication bingeing
  - Diversion
  - Insufficient test sensitivity
  - Failure of laboratory to test for desired substances

Urine Drug Testing

- Initial testing done with class-specific immunoassay drug panels
  - Typically do not identify individual drugs within a class

- Followed by a technique such as GC/MS
  - To identify or confirm the presence or absence of a specific drug and/or its metabolites

UDT Immunoassay Screening

- Lab Testing or POCT
  - Drug class
  - High sensitivity, low specificity
  - Rapid results
  - Not quantitative

POCT, point-of-care testing

Detection of Opioids

- Opiate immunoassays detect morphine and codeine
  - Do not detect synthetic opioids
    - Methadone
    - Fentanyl
  - Do not reliably detect semisynthetic opioids
    - Oxycodone
    - Hydrocodone
    - Buprenorphine
    - Hydromorphone

- GC/MS will identify these medications

UDT Laboratory-Based Tests

- GC/MS, LC/MS, ELISA
  - High sensitivity, high specificity
  - Expensive
  - Quantitative
  - 1-3 days for results

RESULTS OF CONTROLLED SUBSTANCE UDT: WORKPLACE

Donor Name: Jack
Donor ID #: 1897221
Specimen ID #: 1897221-112
Accession #: None assigned
Random
Date collected: 04/11/2008
Date received: 04/15/2008
Date reported: 04/15/2008
Reason for test:
Time collected: 1648

<table>
<thead>
<tr>
<th>Class or Analyte</th>
<th>Result</th>
<th>Screen Cut-Off</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMPHETAMINES</td>
<td>NEGATIVE</td>
<td>1,000 ng/ml</td>
</tr>
<tr>
<td>BARBITUATES</td>
<td>NEGATIVE</td>
<td>200 ng/ml</td>
</tr>
<tr>
<td>BENZODIAZEPINES</td>
<td>NEGATIVE</td>
<td>200 ng/ml</td>
</tr>
<tr>
<td>CANNABINOIDS</td>
<td>NEGATIVE</td>
<td>50 ng/ml</td>
</tr>
<tr>
<td>COCAINE</td>
<td>NEGATIVE</td>
<td>300 ng/ml</td>
</tr>
<tr>
<td>METHADONE</td>
<td>NEGATIVE</td>
<td>150 ng/ml</td>
</tr>
<tr>
<td>OPIATES</td>
<td>POSITIVE</td>
<td>100 ng/ml</td>
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<tr>
<td>OPIATES</td>
<td>POSITIVE</td>
<td>100 ng/ml</td>
</tr>
<tr>
<td>CREATININENORMAL</td>
<td>NORMAL</td>
<td>≥ 20 mg/dL</td>
</tr>
<tr>
<td>SPECIFIC GRAVITY</td>
<td>NORMAL</td>
<td>≥ 1.003</td>
</tr>
<tr>
<td>pH</td>
<td>NORMAL</td>
<td>4.6-8.0</td>
</tr>
</tbody>
</table>

ELISA, enzyme-linked immunosorbent assay; GC, gas chromatography; LC, liquid chromatography; MS, mass spectrometry.

Opioid Metabolism

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

Heroin → 6-MAM

C-6G → Codeine

Minor

Codeine → Morphine

Minor

Morphine → M-3G

Hydrocodone → Dihydrocodeine

Hydromorphone → Dihydromorphine

<table>
<thead>
<tr>
<th>Drug</th>
<th>Approximate Retention Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamines</td>
<td>• 48 hours</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>• Short-acting (eg, secobarbital), 24 hours</td>
</tr>
<tr>
<td></td>
<td>• Long-acting (eg, phenobarbital), 2–3 weeks</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>• 3 days if therapeutic dose is ingested</td>
</tr>
<tr>
<td></td>
<td>• Up to 4–6 weeks after extended dosage (≥ 1 year)</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>• Moderate smoker (4 times/week), 5 days</td>
</tr>
<tr>
<td></td>
<td>• Heavy smoker (daily), 10 days</td>
</tr>
<tr>
<td></td>
<td>• Retention time for chronic smokers may be 20–28 days</td>
</tr>
<tr>
<td>Cocaine</td>
<td>• 2–4 days, metabolized</td>
</tr>
<tr>
<td>Ethanol</td>
<td>• 2–4 hours</td>
</tr>
<tr>
<td>Methadone</td>
<td>• Approximately 30 days</td>
</tr>
<tr>
<td>Opiates</td>
<td>• 2 days</td>
</tr>
<tr>
<td>Phencyclidine</td>
<td>• Approximately 8 days</td>
</tr>
<tr>
<td></td>
<td>• Up to 30 days in chronic users (mean value = 14 days)</td>
</tr>
<tr>
<td>Propoxyphene</td>
<td>• 6–48 hours</td>
</tr>
</tbody>
</table>

Identifying and Managing Abuse and Diversion

- Assessing risk and aberrant behaviors
- Performing scheduled and random UDTs
- Utilization of PMPs
- Assessing stress and adequacy of pain control
- Developing good communication with pharmacists
- Receiving input from family, friends, and other patients
Pharmacologic
- Sequestered antagonist
- Bio-available antagonist
- Pro-drug

Aversive Component
- Capsaicin – burning sensation
- Ipecac – emetic
- Denatonium – bitter taste

Physical
- Difficult to crush
- Difficult to extract

Deterrent Packaging
- RFID – Protection
- Tamper-proof bottles

Prescription Monitoring
Abuse Deterrent Formulations

- FDA supports development of innovations that promote safe use of opioids
- Abuse deterrent properties cannot compromise attributes of medicine
- Must account for real world abuse
Guidance for Industry-Abuse Deterrent opioids, Evaluation and Labeling

- Issued January 2013 by FDA
- Abuse deterrent formulation have 4 tiers:
  - (1) product formulated with physicochemical barriers of abuse
  - (2) product is expected to reduce or block effect of opioid when manipulated
  - (3) Product expected to result in meaningful reduction in abuse
  - (4) product has demonstrated reduced abuse in the community.
- Some products developed with abuse deterrent properties prior to issuance of Draft guidance document (Nucynta, Opana)
Abuse Deterrent

- April 2013
  - Reformulation of OxyContin approved by FDA for Tier 3 claim
    - Determined that generic version of medication with abuse deterrent formulation could not be marketed due to safety concerns.
Physical Barrier Technology-Oxycontin

- Reformulated with polymer matrix providing physical barrier to tablet breaking and crushing.
- Exposure to water creates viscous gel
- Original formulation distribution stopped April 2010
- Multiple studies showed drastic drop in oral and non-oral abuse
- Same technology now being utilized by Perdue for extended release Hydrocodone product, Hysingla, expected to be released soon.
Physical Barrier Technology - Opana

- Reformulated to incorporate polyethylene oxide matrix designed to render resistant to crushing.
- Forms a gel when exposed to water
- 2013: FDA found original formulation was not withdrawn for safety reasons
  - Reformulated Opana resists crushing, but could be compromised when subjected to other forms of manipulation (cutting, grinding, chewing)
  - Post marketing investigations supporting ADF claim inconclusive
- Can be prepared for injection using available tools and methods
Physical Barrier Technology-Nucynta

- Nucynta ER approved 2011
- Confers resistance to crushing or extraction
- Shown that individuals who regularly tampered with original formulation liked new formulation much less
- 10 fold decrease in active ER tapentadol than original formulation could be extracted from newer tablets.
- Label does NOT include this.
Opioid agonist/antagonist combination—Suboxone

- Buprenorphine acts as partial opioid antagonist with diminished reinforcing effects in comparison to full opioid antagonist
- Suboxone approved in 2003, now available in tablet and film
- In multiple studies, suboxone showed reduced abuse liability compared to Buprenorphine
- Less likely to be injected
Pharmacologic Deterrent: Antagonist

- Oral formulation
- Sequestered antagonist
- Antagonist bioavailable only when agent is crushed for extraction
- SR morphine + naltrexone (Embeda®) FDA approved 2009

Incorporation of Aversive Agents-Oxecta

- IR oxycodone (Pfizer) that incorporates abuse deterrent properties to reduce non-oral abuse
- Oxycodone combined with sodium lauryl sulfate to deter insufflation (irritates nasal passage)
- Forms a gel when exposed to water
- Approved June 2011
What is NEW
Physical Deterrent: Viscous Gel Base

- SR oxycodone formulation: Remoxy™
  - Deters dose dumping
    - Accessing entire 12-h dose of CR medication at 1 time
  - Difficult to crush, break, freeze, heat, dissolve
    - The viscous gel-cap base of PTI-821 cannot be injected
    - Resists crushing and dissolution in alcohol or water
Targiniq ER (Purdue)

- Oxycodone:Naloxone in 2:1 ratio
- Approved many regions outside of US
- Indicated for treatment of pain and opioid induced constipation
Encapsulation of tamper resistant beads housing opioid that are enveloped in medium that confers ER properties.

Studies showed chewing, crushing, and extraction did not substantially alter drug release.

Solidifies upon cooling, prohibiting intake into syringe.

Formulation with oxymorphone and oxycodone in development.
NKTR-181 (Nektar)

- Currently in phase 2
- Molecule designed to be slowly absorbed through blood brain barrier, limiting rapid CNS exposure
- May limit euphoria
What we say to dogs

Okay, Ginger! I've had it!
You stay out of the garbage!
Understand, Ginger? Stay out of the garbage, or else!

What they hear

blah blah GINGER blah
blah blah blah blah
blah blah GINGER blah
blah blah blah blah...