Opioid Dependence: the crossroads between pain and addiction

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Where are we?

The opioid problem today

Where are we?

- 1 out of 7 individuals will have a serious substance use problem (13.5% lifetime prevalence)
- 1 out of 3 Americans are directly affected by addiction
- Up to 50% of admissions to the ER are substance-related
- Addiction is a common problem among physicians and other health care providers

ER = emergency room.

Where are we?

• 2011: 420,000 ER visits from misuse or abuse of narcotic analgesics
• 1 in 32 of those receiving chronic opioids will die from an opioid related overdose

Opioid Addiction

- Currently about 2.5 million US Citizens actively addicted to opioids
  - 1.9 million to prescribed opioids (79%)
  - 517,000 to heroin (21%)
- Opioid societal costs: $55 billion/year (not including criminal)
- Opioid ODs 4× from 1999 to 2015
- December 2016, 91 people per day dying of Opioid OD
- Increased risk for HIV, Viral Hepatitis, Other...

How did we get here?

A brief history of opioid use

- Sumerians (3400 BC) – Cultivated... the “Joy Plant”
- Alexander the Great (330 BC) – Introduced opium to India
- Hua Tuo (220–264 AD) – Chinese surgeon used on patients before surgery
- Paracelsus (1527) – Swiss/German alchemist made opium pills
- Thomas Sydenham (1680) – “Father of English medicine” introduced laudanum (opium and wine or sherry)
- Late 17th Century – Opium began arriving in the United States by British, French, and Dutch traders
- 1804 – Morphine isolated from opium

How did we get here?

- 1800s Opioid Addiction – Hidden disease. Many women used for female problems such as menstrual cramps
- 1853 – Hypodermic syringe …morphine use increased
- 1861–1865 – Civil War vets addicted to laudanum and morphine
- 1874 – Heroin synthesized, promoted as “non-addictive alternative to morphine”
- 1880s – Sigmund Freud and other physicians advocated use of cocaine to treat alcoholism and opioid addiction
- 1880s – Multiple “cures” for ETOH and opium addiction produced – most contained ETOH, opium, morphine and/or cannabis
- 1898 Bayer – Commercial use of heroin: “wonder drug” – cough / pain

How did we get here?

- Early 1900s – St. James Society in the United States supplied free samples of heroin to help morphine addicts stop
- 1907–1913 – Wave of state laws passed calling for sterilization of “defectives” including addicts and alcoholics
- 1909 – Opium Exclusion Act barred import of opium for smoking
- 1914 – Harrison Act required physicians and pharmacists to pay nominal tax and registration to dispense opioids – Gatekeepers. Criminalization followed
- 1916 – Germans synthesized oxycodone. Believed it would “help pain and be less addicting”
- 1919–1924 – 40 communities establish maintenance clinics run by health departments and police departments to use morphine to treat narcotic addiction. Feds closed
- 1924 – Heroin Act made heroin illegal

Bayer 1890s commercialized heroin for cough, cold, and pain ... promoted heroin for use in children suffering from coughs/colds/teething/“irritation” as late as 1912
How did we get here?

- 1938 – Legislation gave FDA authority to see that medications were safe. Codeine, morphine, and oxycodone already in use were not affected
- 1951 – Boggs Act – mandatory minimum sentences
- 1956 – Narcotic Control Act increased length of sentences and death penalty for some drug offenses
- 1950s and 1960s – Many church programs developed
- 1970 – The Controlled Substances Act Scheduled Drugs (II-V)
- 1960 and 1970s – Recreational drug use increases
- 1970s – Under-treatment of acute pain; pain clinics detoxed patients with chronic pain as though they had addiction
- 1972 – Methadone approved to treat Opioid Addiction/particularly heroin. HIGHLY REGULATED, STIGMATIZED
- 1973 – Opioid receptor discovered leading to understanding of opioid effect and activity in brain

Gary D. Carr, MD, FAAFP, DFASAM (2016 presentation).

How did we get here?

- 1973 – DEA Created and Nixon proclaimed “The War on Drugs”
- 1980s belief that opioids were appropriate management for chronic pain. Letter to NEJM claiming lack of risk of addiction associated with opioid pain treatment. Joint Commission developed the “fifth vital sign” (it was thought that only those with substance use disorder are at risk for developing opioid use disorder) Other publications and studies conclude that opioid maintenance can be safe and humane, superior to surgery or intractable non-malignant pain.
- 1990s – Pain medicine / drug companies aggressively lobbied for increase use of opioids for non-cancer pain
- 2000s – Mechanisms of hypalgesia from chronic opioids analyzed and developed
- 2012 – 259 million prescriptions written for opioid analgesics (enough for every adult in the United States to have a bottle of pills)

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How did we get here?

- 2012 – 259 million prescriptions written for opioid analgesics (Enough for every adult in the United States to have a bottle of pills. THE INCREASE RATE IS NOT EXPLAINED BY UNDERLYING HEALTH PROBLEMS).
- 2016 – US Surgeon General declared the opioid epidemic, requested of physicians that they rationally prescribe accordingly, and the CDC gave guidelines for opioid prescribing, and also that medical school curriculum to include training on appropriate and rational opioid prescribing
- 2018 – American Society of Addiction Medicine will have a text available on Pain and Addictions, intended to be a guide for primary care providers

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Previous Medical Approaches to Addiction

- Benjamin Rush, MD used bleeding, blistering, and treatment with mercury laden calomel
- Drink wine in which eels suffocated
- Water Cures (hydrotherapy)
- Later half of 1800s various drugs: Cocaine, Morphine, Cannabis, Heroin, ETOH, Bromide
- Aversion Therapy: 1932 – present
- ECT, Insulin Shock, Psychosurgery 1940s – about 1960s
- Mid-1900s Drug Interventions: Sedatives, Tranquilizers, Amphetamine/Methamphetamine, LSD, Hallucinogens, Hormones, Co2

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New York State Inebriate Asylum 1864
Deemed a “Complete Failure” in 1979

ECT Treatment for Addiction > 1940s and 1950s
Continued into 1970s

- Federal Narcotic Farms:
  - Lexington, KY and Fort Worth, TX primary source of treatment, 1938–1950
- Long treatment (Voluntary vs Involuntary)
- Little or no family involvement
- Forced labor
- Relapse rate: VERY HIGH

The Modern Alcoholism Movement

- Alcoholics Anonymous – 1935, Big Book 1939
- Research Council on Problems of Alcohol
- Yale Center for Alcohol Studies
- National Committee for Education on Alcoholism

Does Abstinence-Based Treatment Work?

National Treatment Outcome Research Data on Opioid Addiction Patients

242 patients in residential treatment:
- 34% relapse w/in 3 days 45% relapse w/in 7 days
- 50% relapse w/in 14 days 60% relapse w/in 90 days

- Multiple “Studies consistently show 2/3 of patients in abstinence-based programs relapse”, Dr. Steven Batki, MD, Professor of Psychiatry, Upstate Medical Center Syracuse

Does Abstinence-Based Treatment Work?

- Studies of patients who complete abstinence-based treatment only 36% are sober at 1 year
- Why? Multiple reasons: Denial, Minimization, lack of support, co-occurring illness, no meetings, no sponsor, no monitoring, not followed medically like other chronic illnesses… etc.
- Bottom line: “It works if you work it”. Yet studies show only about 17% of people attending AA have actually worked all the 12 Steps

"Man’s First Duty is Escape" –(Unknown)

Success Rates Vary

- Depending on
  - The Individual
  - The Addiction
  - Comorbid conditions
  - Psychosocial/Family

Neurobiology

…or
Why isn't everyone that tries a drug addicted?
Neurobiology

- 40+ years of research have brought us to a new understanding of drug use and addiction, their complexity and their solutions
- Addiction is a primary chronic relapsing disease of the brain's reward cycle

Risk Factors for Dependence

- Genetics
- Gender
- Mental Illness

Risk Factors for Dependence

- Genetics
- Family History
- Drug use in family
- Peer Influences
- School Environment
- Stress

Neurotransmitter Pathways and Effect

- Serotonin Pathways
- Dopamine Pathways
- Ondansetron
- Aripiprazole
- Topiramate
- Bupropion
- Cannabinoids

Medication-Assisted Treatment/Recovery

- Topiramate
- Buprenorphine
- Ondansetron
- Aripiprazole

Brain Pathways

- Serotonin Pathways
- Dopamine Pathways
- Cannabinoids
- Ondansetron
- Aripiprazole

Pain Pathways

Pain

- Why does pain exist?
- Chronic vs Acute pain?
- Emotional pain (80% of pain is emotional)
- Why won’t pain go away?
- What makes pain better or worse?
- Will I ever be free of pain?
- Why do I have to do things that hurt in order to get better?
- Family involvement?
- Why do I hold on to my pain?

Pain

- 3 pathways/components of pain
  - Spino-Thalamic Tract – Awareness of sensation
  - Spino-Reticular Tract – Suffering aspect of pain
  - Spino-Mesencephalic Tract – Includes mood relatedness to pain, serotonin, and pain killing and inhibition with natural opioid secretion

Pain

- 2002: 14.6% of adults have current widespread or localized pain that lasted 3+ months
- 2012: 11.2% of adults report having daily pain
- Only 6% of patients with an initial 1-day prescription remained on an opioid 1 year later.
- The percentage more than doubles if the initial prescription is for ≥ 8 days – 5%
- When the prescription is for ≥ 31 days, the risk of chronic use jumps to just under 30%
- Long-acting opioids are also a risk factor. 25% of patients initially prescribed a long-acting painkiller continued use for a year, and 20% were still on an opioid at 3 years
- New persistent opioid use after surgery is common, not significantly different between minor and major surgical procedures but rather associated with behavioral and pain disorders
- 25% of patients in traditional pain management are non-compliant and potentially face discharge

Pain

- Beliefs and attitudes most important to change perceptions of pain and diminish suffering

References:


Pain

- Opioids for pain management:
  - If pain is not relieved within the first month, unlikely to be beneficial over longer intervals
  - “No strong evidence based foundation for the conclusion that long term opioid treatment of chronic nonmalignant pain is effective”
  - Opioid-induced hyperalgesia
    - A state of nociceptive sensitization caused by exposure to opioids
    - Frequently witnessed in people taking progressively higher doses of opioid analgesics
    - Loss of opioid efficacy

Non-Opioid Pharmacologic Treatment

- Anti-inflammatory
- Interventional
- Implantables
- Sensory nerve ablation
- Surgery

Non-pharmacologic Treatment

- Therapeutic involvement
  - Cognitive-Behavioral Therapy (CBT)
  - Acceptance and Commitment Therapy (ACT)
  - Mindfulness
  - Pacing worksheets
- Physical treatment
  - Physical therapy, occupational therapy, chiropractic, music therapy
  - Acupuncture
  - Exercise

CBT

- Thoughts cause feelings and behaviors
- Brief and time-limited
- Average # of sessions ~ 16 vs psychoanalysis = several years
- Emphasis placed on current behavior
- CBT is a collaborative effort between the therapist and the patient
  - Patient role: Define goals, express concerns, learn, and implement learning
  - Therapist role: Help patient define goals, listen, teach, encourage
- Teaches the benefit of remaining calm or at least neutral when faced with difficult situations. (If you are upset by your problems, you now have 2 problems: 1) the problem, and 2) your upsetedness)
- Based on “rational thought.” Fact not assumptions
- CBT is structured and directive. Based on notion that maladaptive behaviors are the result of skill deficits
- Based on assumption that most emotional and behavioral reactions are learned. Therefore, the goal of therapy is to help patients unlearn their unwanted reactions and to learn a new way of reacting
- Homework is a central feature of CBT

Pacing

- Pacing is a learned skill to allow one to consistently be active without causing extra pain.

A Middle Ground. Spending just enough time on an activity to get the most out of it, but without pushing too far. Increase fitness, less vulnerable to injury

Pacing Worksheet

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:15 (1) ok</td>
<td>10:15 (2) rested</td>
<td>10:15 (3) good</td>
<td>15:15 (1) tired</td>
<td>15:15 (2) better</td>
<td>15:15 (3) ok</td>
<td>20:15 (2) finished</td>
</tr>
</tbody>
</table>


Pacing Worksheet

Epigenetics

- Changes in gene expression
- Phenotype without changing genotype
- 3 systems affected:
  - DNA Methylation
  - Histone modification
  - Non-coding RNA gene silencing
- Naturally occurs (active vs inactive genes)
- Also influenced by
  - Age
  - Environment (stress, trauma)
  - Lifestyle (especially nutrition/exercise)
  - Disease state
  - Medications/Drugs

How to know who is at risk
Who is at Risk?

<table>
<thead>
<tr>
<th>Biology (genes/epigenetics)</th>
<th>Environment (stress/trauma)</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Family Hx of addiction or psychiatric Dx</td>
<td>• Current trauma experience or re-experiencing</td>
<td>• Other drug use</td>
</tr>
<tr>
<td>• Personal Hx of psychiatric Dx</td>
<td>• Abuse, violence, stressful home/work/school</td>
<td>• Polypharmacy</td>
</tr>
<tr>
<td>• Personal Hx of dependence</td>
<td>• Poor nutrition</td>
<td>• Multiple pharmacy use</td>
</tr>
<tr>
<td>• Childhood Hx of R/I/D etc. (likely low dopamine early)</td>
<td></td>
<td>• Multiple doctor use</td>
</tr>
<tr>
<td>• Immune/Inflammatory Dx</td>
<td></td>
<td>• &gt; 50 MME</td>
</tr>
<tr>
<td>• Hormone/Vitamin/Thyroid imbalances</td>
<td></td>
<td>• Response to certain drugs with dopamine spike</td>
</tr>
</tbody>
</table>

Biology: Genes/Epigenetics

• Family Hx of addiction or psychiatric Dx
• Personal Hx of psychiatric Dx
• Personal Hx of dependence
• Childhood Hx of R/I/D etc. (likely low dopamine early)
• Immune/Inflammatory Dx
• Hormone/Vitamin/Thyroid imbalances

Environment: Stress/Trauma

• Current trauma experience or re-experiencing
• Abuse, violence, stressful home/work/school
• Poor nutrition

Drug

• Other drug use
• Polypharmacy
• Multiple pharmacy use
• Multiple doctor use
• > 50 MME
• Response to certain drugs with dopamine spike

Rational Prescribing
Rational Prescribing

• Use sparingly and only when needed, but if treating, give the right dose (sometimes less is NOT better!)
• Treat symptoms to help patient stay in recovery and learn tools for long-term wellness
• Some medications may be long-term, but most will be short-term while neurogenesis and synaptogenesis and neural repair occur, especially in the first 3 to 24 months of recovery
• My whole philosophy is stabilizing until the foundation is built, then moving away from medications when possible


• Part of a whole treatment toolbox
• Office visits
• Accountability
• Building trust

**Treatment and Recovery**

**Biology (genes/epigenetics)**
- Family Hx of addiction or psychiatric Dx
- Personal Hx of psychiatric Dx
- Personal Hx of dependence
- Childhood Hx of Rx/D etc. (likely low dopamine early)
- Immune/inflammatory Dx
- Hormone/Vitamin/Thyroid imbalances

**Environment (stress/trauma)**
- Current trauma experience or re-experiencing
- Abuse, violence, stressful home/work/school
- Poor nutrition

**Drug**
- Other drug use
- Polypharmacy
- Multiple pharmacy use
- Multiple doctor use
- > 50 MME
- Response to certain drugs with dopamine spike

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**Biology: Genes/Epigenetics**
- Check labs
- Check SNPs/biomarkers?
- Treat psychiatric Sx: anxiety, depression, nightmares, sleep issues, mood instability...
- Treat inflammatory comorbidities
- Treat vitamin/cofactor deficiencies
- Acupuncture
- Physical Therapy
- Chiropractic
- Massage Therapy

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**Environment: Stress/Trauma**
- Stress management
- Mindfulness
- Individual/group therapy
- Eye Movement Desensitization and Reprocessing (EMDR)
- Exercise
- Nutrition
- Acupuncture
- Physical Therapy
- Chiropractic
- Massage Therapy

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**Treatment and Recovery**

**Biology**
- Genes
- Epigenetics
- IEM’s

**Stress**
- Especially Trauma

**Drugs**
- Prescribed Illicit

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**Risk of Abuse / Addiction**

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**Treatment and Recovery**

**Biology (genes/epigenetics)**
- SNP = single nucleotide polymorphisms.

**Environment (stress/trauma)**

**Drug**
- Check labs
- Check SNPs/biomarkers?
- Treat psychiatric Sx: anxiety, depression, nightmares, sleep issues, mood instability...
- Treat inflammatory comorbidities
- Treat vitamin/cofactor deficiencies
- Acupuncture
- Physical Therapy
- Chiropractic
- Massage Therapy
- Treat withdrawal
- Consider opioid partial agonist or antagonist
- If not, MME < 50
- No (few) benzodiazepines
- Prescription Monitoring Programs (PMP)
- Utx
- Decrease access
Drug

- Treat withdrawal
  - Supportive (clonidine/lamotrigine, plus comfort medications)
  - Buprenorphine (buprenorphine/naloxone sublingual film, buprenorphine/naloxone sublingual tablets, buprenorphine/naloxone buccal film)
- Consider opioid partial agonist or antagonist for short- or long-term maintenance
  - Buprenorphine (buprenorphine/naloxone sublingual film, buprenorphine/naloxone sublingual tablets, buprenorphine/naloxone buccal film)
  - Buprenorphine implant
  - Naltrexone
    - Oral; extended-release injectable suspension; implant
- If using full agonist, MME < 50
- No (few) benzodiazepines
- Prescription Monitoring Programs (PMP)
- Utox
- Decrease access


Treatment and Recovery

- Chronic care approach
- Multi-modal treatment is essential
- Treatment must address the multiple needs of the individual, not just the pain or just the addiction
- Multiple courses of treatment must be required for success
- Adequate time frame is needed—3 months to produce stable behavior change
- Relapse is likely

In Conclusion
