

An aerial photograph of the University of Chicago campus, showing various academic buildings with red-tiled roofs and Gothic-style architecture. In the background, the Chicago skyline is visible, including several prominent skyscrapers like the Willis Tower. The sky is clear and blue.

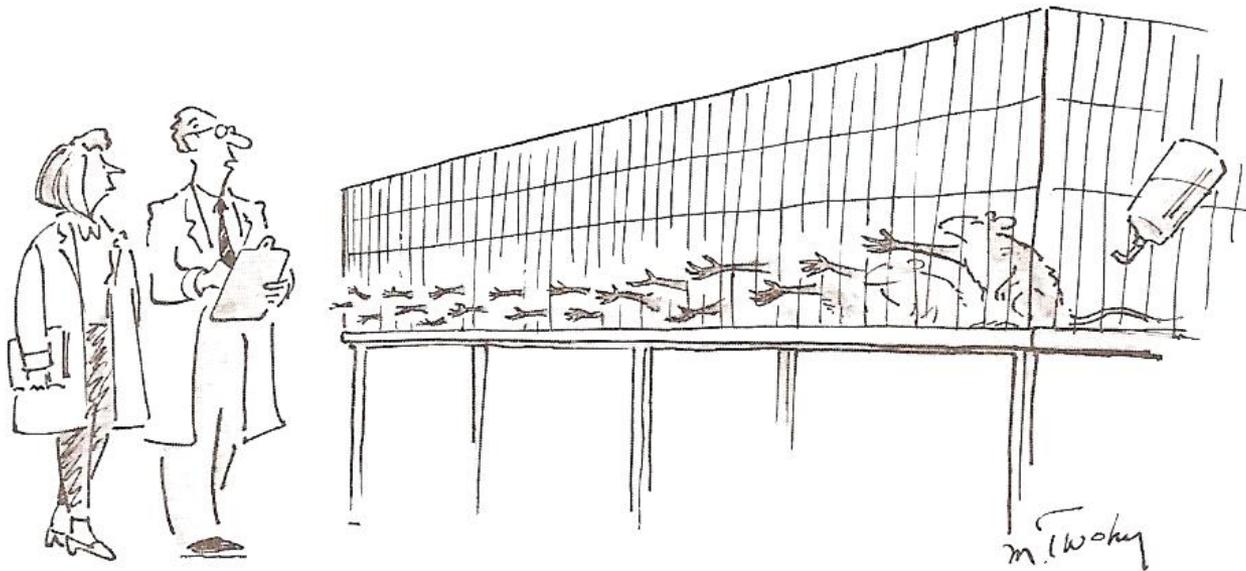
Opioid Addiction: Understanding a Global Epidemic

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Disclosure Information

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"At this point, we know it's addictive."

What is Addiction?

- ❧ Addict (verb) - “to devote or give (oneself) habitually or compulsively”; from Latin *addicere* - bound to or enslaved
- ❧ Core Components of Addiction
 - ❧ Continued Behavior Despite Adverse Consequences
 - ❧ Diminished or Lost Control / Compulsive Engagement
 - ❧ Craving or Urge State Component

Motivational Neural Circuits

- ❧ Multiple brain structures underlying motivated behaviors.
- ❧ Motivated behavior involves integrating information regarding internal state (e.g., hunger, sexual desire, pain), environmental factors (e.g., resource or reproductive opportunities, the presence of danger), and personal experiences (e.g., recollections of events deemed similar in nature).

Role of Dopamine



- ❧ Dopamine release into the nucleus accumbens - translates motivated drive into action - a “go” signal
- ❧ Dopamine release associated with rewards and reinforcing
- ❧ Dopamine release - maximal when reward is most uncertain, it plays a central role in guiding behavior during risk-taking situations.

Biochemistry – Opioid System

- ❧ The endogenous opioid system influences the experiencing of pleasure.
- ❧ Opioids modulate mesolimbic dopamine pathways via disinhibition of GABA input in the ventral tegmental area.

Opioid Use Disorder



A problematic pattern of opioid use leading to clinically significant impairment or distress (manifested by at least 2 of the following within a 12-month period):

1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain opioids, use them, or recover from its effects.
4. Craving, or a strong desire or urge to use opioids.

5. Recurrent use resulting in a failure to fulfill major role obligations.

6. Continued use despite having persistent or recurrent social or interpersonal problems



7. Important social, occupational, or recreational activities are given up or reduced because of use.

8. Recurrent use in situations in which it is physically hazardous.

9. Use continued despite knowledge of having a persistent or recurrent physical or psychological problem.

10. Tolerance

11. Withdrawal

What Are Opioids?



- ❧ Opioids are natural or synthetic substances that act on the brain's opiate receptors.
- ❧ Opioids dull pain and relieve anxiety that comes from thinking about pain.
- ❧ People abuse opioids because they provide a feeling of euphoria (a "rush").

Opium History



- ❧ **Between 400 -1200 AD Arab traders introduced opium to China.**
- ❧ **14th century Ottoman Empire-opium used to treat headache and back pain.**
- ❧ **15th century China- first officially recorded use of opium as a recreational drug.**
- ❧ **1874- heroin developed**
- ❧ **1898-heroin marketed by Bayer as safe pediatric cough suppressant**

Heroin



- 1874-first synthesized by an English chemist
 - Diacetyl-morphine
- 1897-resynthesized by Felix Hoffman working for Bayer trying to produce codeine
- 1898-1910-marketed as a cough suppressant and non-addictive morphine substitute
 - Then discovered it was metabolized to morphine
- 1914 Harrison Narcotics Act banned sale and distribution
- 1924 became a Schedule 1 drug

BAYER
PHARMACEUTICAL
PRODUCTS.

Send for
samples and
Literature to

ASPIRIN
The substitute for
the salicylates

HEROIN
The sedative for
coughs

LYCETOL
The uric acid solvent

SALOPHEN
The antirheumatic and
antineuralgic

AKSTOL
The substitute for
the salicylates

PROTARGOL
The substitute for
the salicylates

QUINALGEN
The substitute for
the salicylates

PIPERAZINE
The substitute for
the salicylates

EUROPHEN
The substitute for
the salicylates

HEROIN HYDROCHL.
The substitute for
the salicylates

FERRI SOMATOSE
The substitute for
the salicylates

SULFONAL
The substitute for
the salicylates

SOMATOSE
The substitute for
the salicylates

HEMICRANIN
The substitute for
the salicylates

IODOTHYRINE
The substitute for
the salicylates

SYCOSE
The substitute for
the salicylates

PHENACETIN
The substitute for
the salicylates

TRIONAL
The substitute for
the salicylates

**FARBENFABRIKEN OF
ELBERFELD CO.**

**40 STONE ST
NEW YORK.**

Opiates & Opioids



***Opiates* = naturally present in opium**

‣ e.g. morphine, codeine, thebaine

***Opioids* = manufactured**

‣ Semisynthetics are derived from an opiate

‣ heroin from morphine

‣ buprenorphine from thebaine

‣ Synthetics are completely man-made to work like opiates

‣ methadone

How did we get here?



1990s

☞ Under-treatment of pain

☞ Early data that opioid risks were low, some of which intentionally minimized

☞ Ease of medications for treatment

Epidemiology of Addictions



Epidemiology

∞ Prescription opioids

∞ National Survey on Drug Use and Health

- ∞ > 12 million reported non-medical use of prescription opioids
- ∞ Estimated 1.6 million met criteria for prescription opioid abuse or dependence

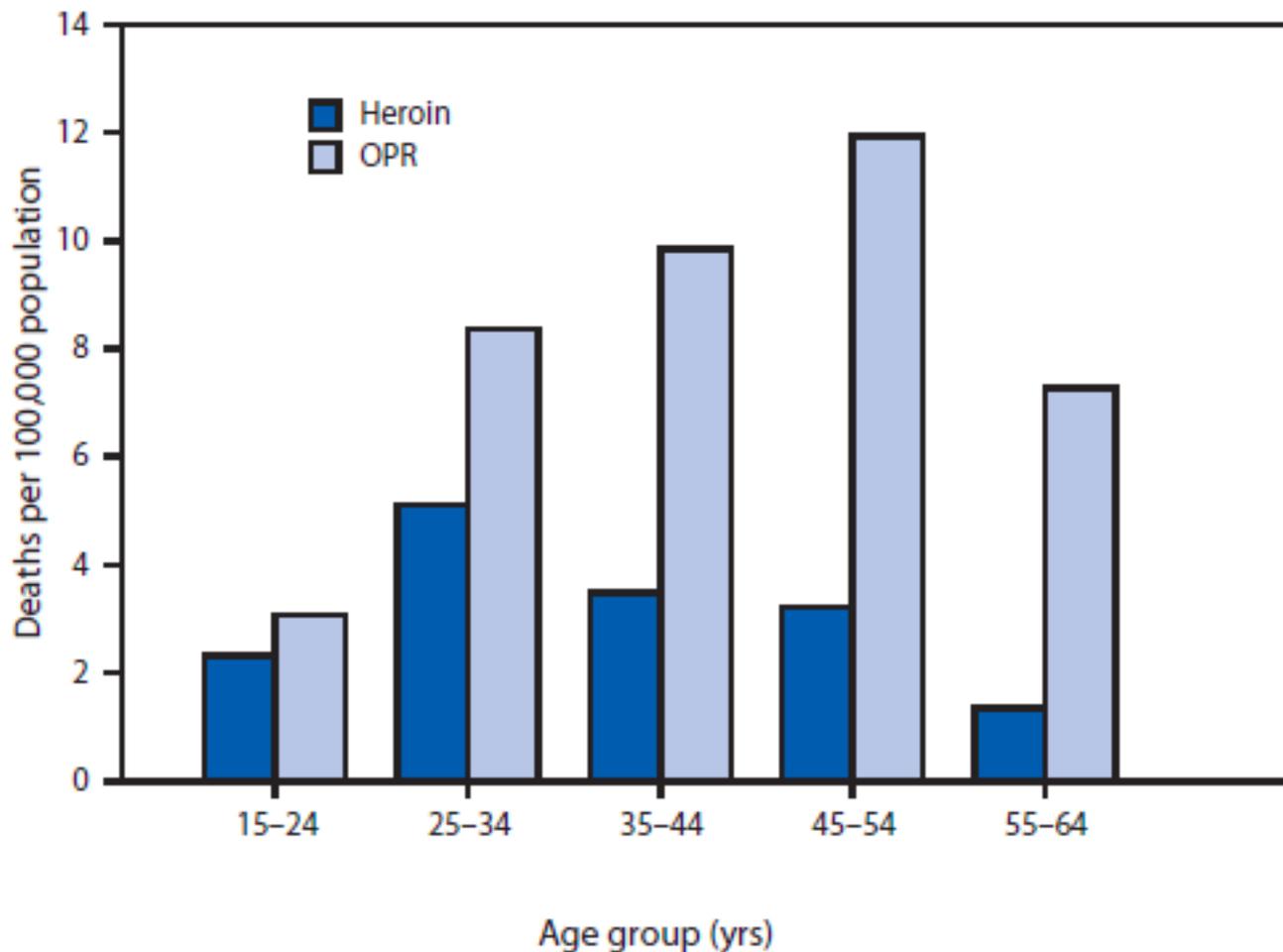
∞ Heroin

∞ National Household Survey on Drug Abuse

- ∞ > 500,000 reported past year heroin use
- ∞ Approximately 323,000 individuals met criteria for heroin abuse or dependence

∞ Combined, 2 million opioid dependent in U.S.

Death rates from overdoses of heroin or prescription opioid pain relievers (OPRs), by age group



SOURCE: CDC. *Increases in Heroin Overdose Deaths — 28 States, 2010 to 2012*
MMWR. 2014, 63:849-854

Chronic Pain

Pain lasting most of the day during most days for > 3 months

Point prevalence in U.S. adults: 15-20%

Lifetime prevalence in U.S. adults: 50-75%

Pain is most often-reported symptom in office visits after upper respiratory infections

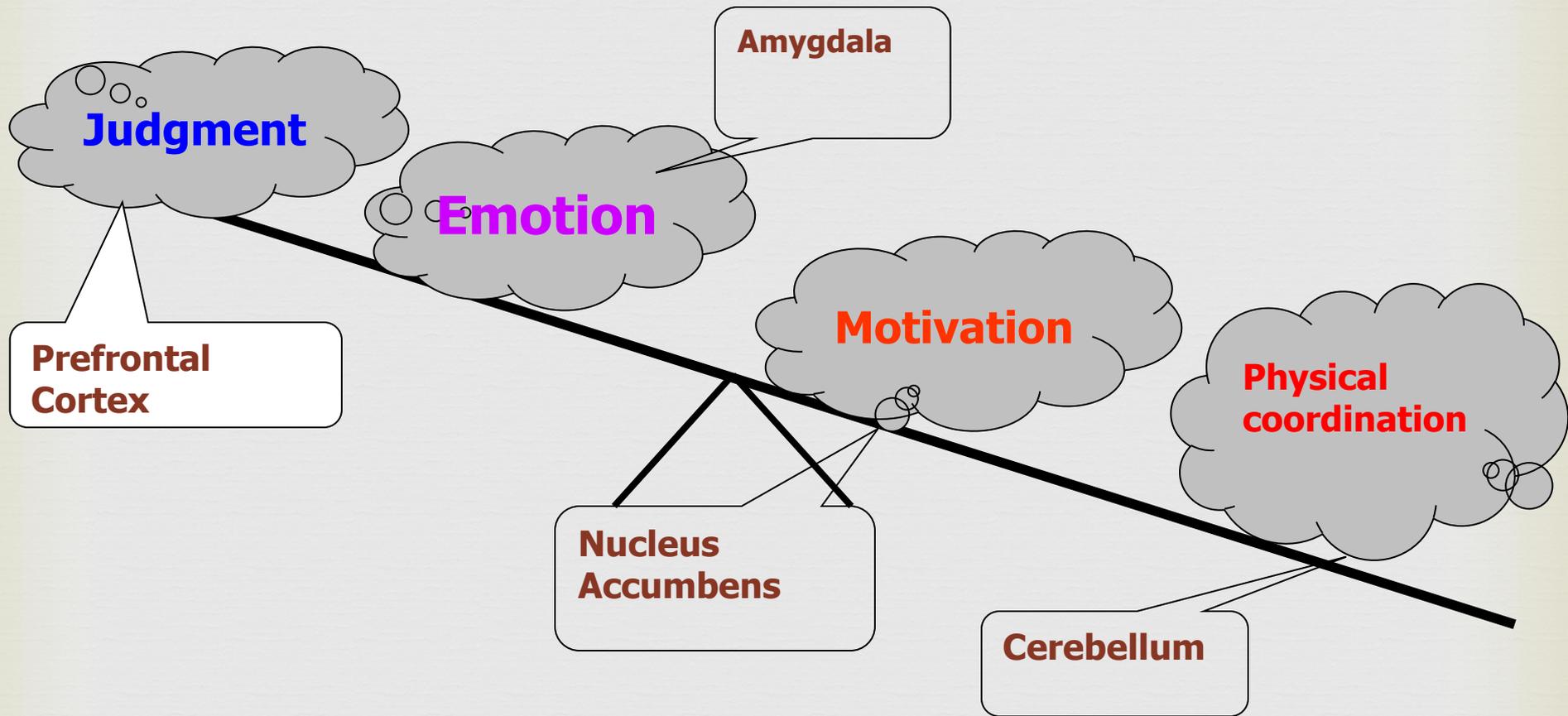
Multi-faceted disorder that, by definition, is bio-psycho- social

Developmental Biology

- Addiction generally starts in young adulthood.
- Environmental and genetic influences - vulnerability to and expression of addictive disorders
- Changes in brain structure and function during adolescence might influence the motivation to engage in risk-taking behaviors.

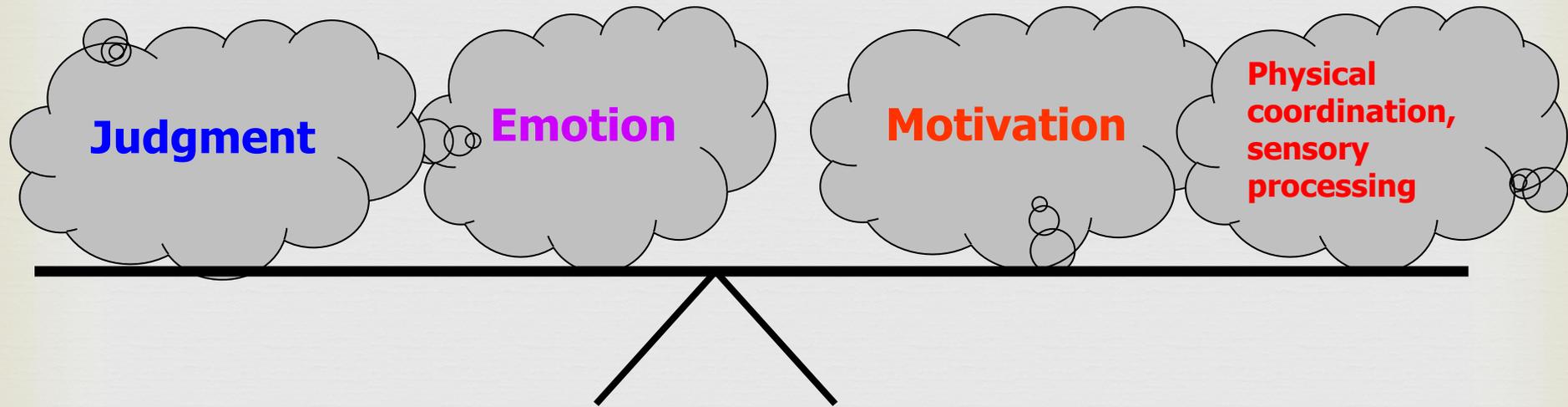
Brain Development

- **During late childhood, neurons increase their number of connections.**
- **But around 11 – GIRLS; 12¹/₂ - BOYS:**
 - **Some of these connections are pruned off.**



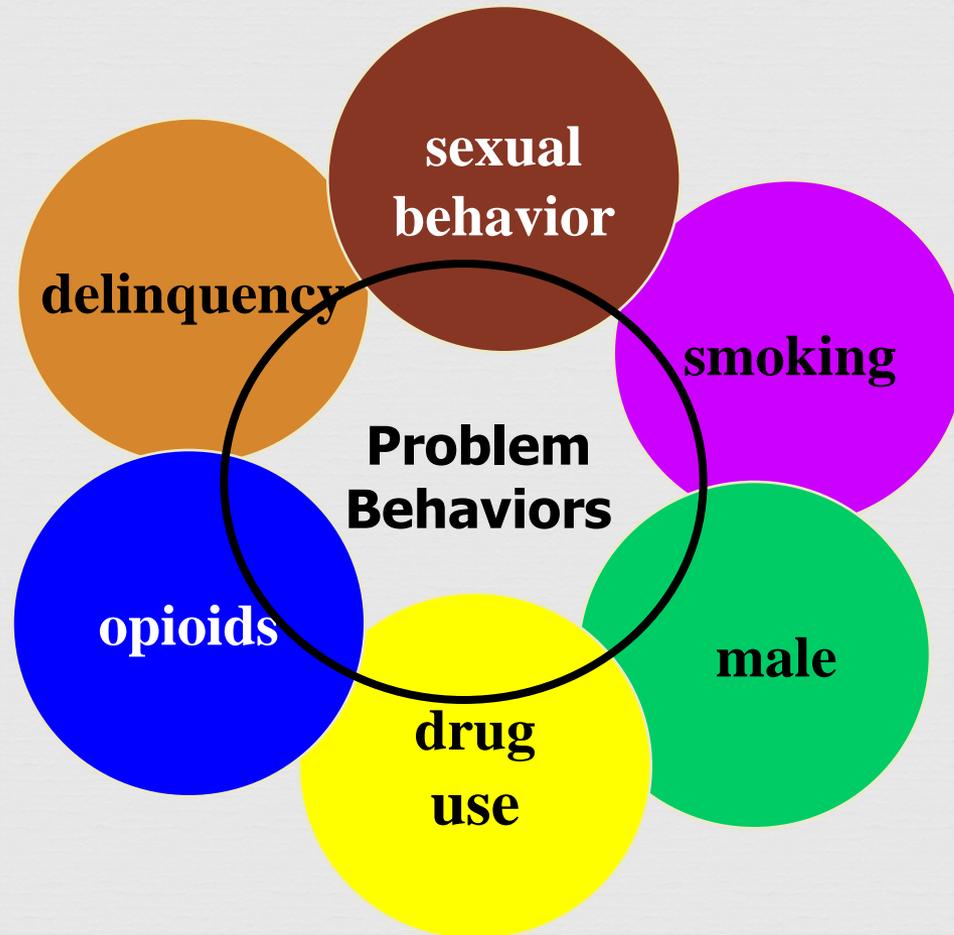
Notice: Judgment is last to develop!

Age 24



Balance

Youth Problem Behaviors



Opioid Withdrawal Symptoms



- Pupillary dilation
- Watery eyes
- Runny nose
- Muscle spasms (“kicking”)
- Yawning, sweating, chills, gooseflesh
- Stomach cramps, diarrhea, vomiting
- Restlessness, anxiety, irritability

Usually result in further use to quiet symptoms

Changes in Neurobiology

Repeated exposure to short acting opioids leads to neuronal adaptations

- ∞ Mesolimbic dopaminergic system
- ∞ adaptations in G protein-coupled receptors
- ∞ changes in transcription and translation

Adaptations

- ∞ Mediate tolerance, withdrawal, craving, self-administration
- ∞ Provide insight into the chronic and relapsing nature of opioid dependence

Consequences

Drug-seeking Behavior → requests for opioid medications for the purpose of getting high

Aberrant Behaviors → among patients on opioids for chronic pain, behaviors that may be indicative of misuse or addiction

- ∞ Early refills
- ∞ Frequent phone calls
- ∞ Doctor shopping
- ∞ Prescription forgery

Consequences



∞ HIV

∞ Hep C

∞ Infections

∞ Overdose

∞ Death

Treatment



A

Thoughts/
Feelings

B

C

**Antecedent
(Triggers)**

Behavior

Consequence

Particular people
Environment
Feelings
e.g., urges,
argument with
spouse,
boredom, anxiety

Alternate behavior
e.g., I drove by the bar, next
think I knew it was last call
Abstinence
e.g., I thought about the effect
it would have on my family,
and took a different route
home

Positive
e.g., I used and I forgot
about that argument with
my wife
Negative
e.g., the next day, I felt
like I'm a failure.

Contingency Management



- Re-arranging the reinforcers in a person's environment
- Incentives or rewards to encourage specific behaviors
 - Vouchers, prizes, group acknowledgements, take-home dosing privileges, family privileges

Pharmacologic Treatment



Pharmacologic withdrawal - “detoxification”

Opioid antagonist treatment

☞ Naltrexone

Opioid agonist/partial agonist treatment

☞ Methadone

☞ Buprenorphine

Methadone



- ⌘ Federally licensed facility
- ⌘ Daily observed dosing
- ⌘ Authoritative review of 11 randomized clinical trials with 1,969 patients
- ⌘ Conclusion methadone is superior to placebo in:
 - Retaining patients in treatment
 - Reducing illicit opioid use

Advantages of Methadone



- 70% or more treatment retention at 1 year
- Treats craving
- Blocks illicit opioid use
- Over 40 years of research and treatment experience demonstrating effectiveness
- Significantly reduces risk for addiction related death and health problems
- Medication cost is minimal

Limitations of Methadone



- Full agonist with abuse potential
- Potential for dangerous interactions with other drugs when misused
- Highly regulated resulting in limited access to care
- Strong physical dependence results in difficult withdrawal
- Significant stigma in the community
- Heavy burden on patients for compliance

Buprenorphine



- Review of 24 randomized clinical trials with 4,497 patients
- Conclusion buprenorphine is superior to placebo and to moderate dose methadone:
 - Retaining patients in treatment
 - Reducing illicit opioid use

Advantages of Buprenorphine



- Less severe dependency allows for easier transitions between recovery with and without medication
- Partial agonist is safer with less overdose potential
- Lower abuse potential
- People live a normal life free from craving and withdrawal
- SAVES LIVES

Limitations of Buprenorphine

- Not a full agonist and does not retain people in treatment as well as full agonist
- Has diversion potential and may be misused
- Medication is expensive and access is limited
- Stigma in the recovery community

Advantages of Naltrexone



- Safe to use, no abuse potential
- Blocks the effects of opioids
- Reduces danger of accidental overdose
- No physical dependence
- Little or no stigma in the recovery community

Limitations of Naltrexone



- No reinforcing effects to support retention in treatment
- No withdrawal symptoms to prevent treatment drop-out
- May not control cravings
- Must be opioid free for induction, indication is for relapse prevention

Therapy and Medication



Pharmacotherapies

Detoxification

Maintenance and stabilization

Reduce reinforcement

Reduce craving/prevent relapse

Treat coexisting disorders

Behavioral therapies

- Set motivation to stop use
- Develop alternatives to drug use
- Teach coping skills
- Improve interpersonal functioning
- Enhance affect management
- Enhance compliance with medication

Limitations of single approaches

Variable efficacy

Some not helped

Partial effects

Side effects may limit compliance

Effects fall off with treatment cessation

Treatment efficacy limited to single drug class

Multidimensionality of addicts' problems



High attrition

No clear superiority of a single approach

Don't address physiologic aspects of addiction

Variable fidelity

What do we know so far?

- ❧ Prescription opioid users tend to have better outcomes than heroin users
- ❧ Most dropout occurs early (first month)
- ❧ Early opioid/cocaine positive urines strong negative predictor of retention/success
- ❧ Dropout usually associated with very poor outcomes
 - ❧ Hence reasonable to focus on retention as indicator of better outcomes, but not the whole story

Neurocognition in Behavioral Addictions

∞ Executive function deficits are greater in those with behavioral addictions than in control subjects, including:

∞ Planning

∞ Cognitive flexibility

∞ Inhibition

QUESTIONS?



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