

**Treating the Addicted Brain –
Advances in the Treatment of
Addictive Disorders**

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What is Common in this Slide?

- | | |
|------------------------------|--------------|
| • Beer | Amphetamines |
| • Double Chloride
of Gold | Morphine |
| • Carbon Dioxide | Cardiazol |
| • ACTH | Metrazol |
| • Benzodiazepines | LSD |
| • Barbiturates | Insulin |
| | Apomorphine |

Name the Drug?

“There is no longer any doubt that for the first
time in history a substance and methods have
been found to halt or control the drinking of the
toughest alcoholics known”

Hoffer and Osmond

“The Paths to Recovery are Many”

Bill Wilson
The Founder of AA

Unique Issues with Addiction

- Endless speculation on the causes of addiction
- No clear consensus on the etiology
- Is it a biological disease?
- Characterological disease?
- Moral and spiritual failing?
- Is medical intervention helpful?
- Stigma and shame

Dark History of Past Treatments

- Eugenics – involuntary sterilizations
- Water therapy – mineral water injections
- Convulsive therapies – drug and ECT
- Psychosurgery – lobotomy era
- Inebriate asylums
- Miracle and fraudulent cures with patent medicines
- Morphine maintenance clinics

Dependence-Producing Medications of the Past and Present

- Beer to treat alcoholism
- Opium and morphine for alcoholism
- LSD to treat alcoholism
- Benzodiazepines to treat alcoholism
- Heroin to treat morphine addiction
- Methadone to treat opioid addiction
- Buprenorphine to treat opioid addiction
- Nicotine to treat smoking

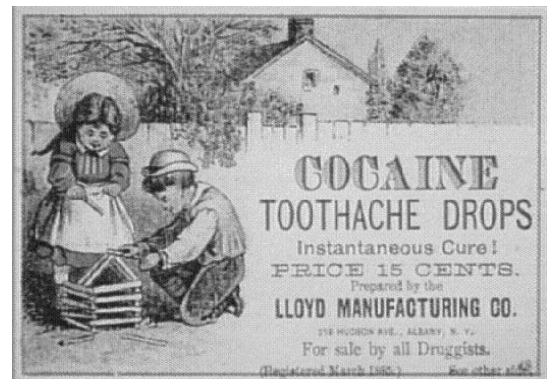
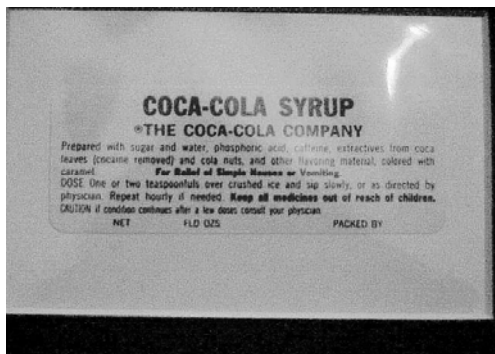
Definition of Dependence-Producing Drug

- Causes euphoria or 'high'
- Habit-forming and/or addicting
- Abuse potential
- Tolerance
- Diversion
- Street value
- Overdose and death

Why Dependence-Producing Drugs?

- Rapid attenuation of cravings
- Ease of administration
- Good safety
- Positive mood state or 'high'
- High compliance
- Reduction in drug-seeking behavior
- Reduction in high-risk behaviors

There were three types of medicines often containing cocaine—topical anesthetics such as toothache powders, catarrh medicines for relieving head and chest congestion, and medicinal (probably also recreational) cocaine-containing wines advocated for their numerous beneficial effects.



AFFECTIONS DE LA GORGE

ANTISEPSIE ANESTHESIE

DRAGEES ANTISEPTIQUES AU MENTHOL

BORATE DE SOUDE ET OHL DE COCAINE
Calment instantanément les maux de gorge, toux, enrouement, etc. — Restituent aux cordes vocales leur souplesse et leur élasticité.
Indispensables aux chanteurs, professeurs et orateurs.

DOSE : 8 à 10 dragées par jour; laissez fondre doucement dans la bouche

V. VANDERBROEK PHARMACIEN
6, Place Verte, ANVERS. Téléphone :

VIN MARIANI

FOR BODY AND BRAIN

Most popular and best-selling tonic in the world. It is the only tonic that is both a tonic and a stimulant. It is the only tonic that is both a tonic and a stimulant. It is the only tonic that is both a tonic and a stimulant.

NOURISHES FORTIFIES REFRESHES

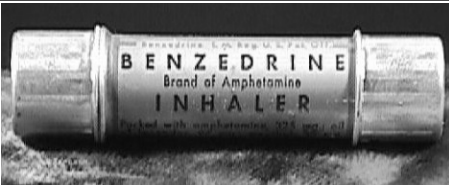
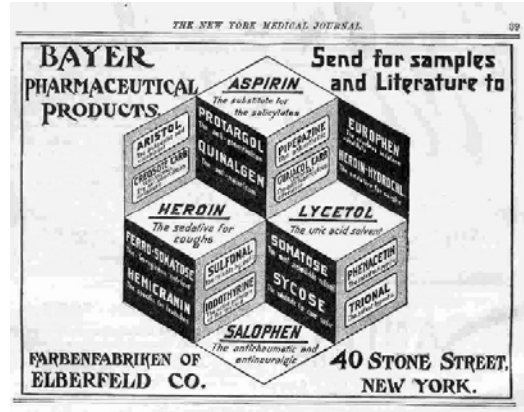
It is the only tonic that is both a tonic and a stimulant. It is the only tonic that is both a tonic and a stimulant. It is the only tonic that is both a tonic and a stimulant.

SPECIAL OFFER — Now, only 10¢ per bottle, a saving of 10¢ per bottle. It is the only tonic that is both a tonic and a stimulant. It is the only tonic that is both a tonic and a stimulant. It is the only tonic that is both a tonic and a stimulant.





Students at the University of Heidelberg take a break from their studies while smoking opium (c. 1900). I suppose it makes the accordion music even more enjoyable.



Benzedrine (racemic amphetamine) inhalers were available over-the-counter until the early 1950s. Some airlines even gave them out to passengers to minimize discomfort when the plane was landing and taking off. The Smith, Kline, and French advertisement proudly proclaims that over 10 million Benzedrine inhalers had been shipped by 1938, only 7 years after the product's introduction. This may have even outpaced McDonald's hamburger sales during their early expansion (Remember the "over x million hamburgers sold" signs on the golden arches?).

Dependence-Producing Drugs in Clinical Use

- Methadone
- Buprenorphine
- LAMM (not currently used)
- Benzodiazepines
- Nicotine – patches, gum etc.
- Barbiturates

Unintended Consequences of Using Dependence-Producing Drugs

- Distrust of science and medical community
- Pharmacophobia - ETOH treatment
- Pharmacohegemony - opioid treatment
- Domination of the field by people in recovery
- Marginalization of drug and alcohol treatment
- Lack of parity with mental illness
- Continued stigma for the disease and some treatments e.g. methadone

Why the Stigma?

- Unsocial/criminal behavior
- Embarrassment to self and family
- 'Free Will' Issue
- Lack of Self-control
- Moral/Spiritual failing
- No personal responsibility
- Repeated treatment failures

Stigma, Stigma Everywhere

Before, During and After Recovery

- Patients, family, friends
- Medical community, hospitals
- Employers, insurance companies
- Media
- Pharmacies
- Lawmakers

Evolution of the Non-Dependence Producing Drugs

Lexington Addiction Treatment Experiment

- Heroin addicts housed at center for three months
- Intense psychotherapy and psychoanalysis to curb addiction
- Patients reported no cravings, desire or thoughts for drugs
- Both patients and therapist considered the treatment a success

Lexington Addiction Treatment Experiment

- High relapse rates when patients returned home
- Many patients experienced symptoms similar to acute withdrawal despite being drug-free for three months
- Failure completely baffled and disappointed researchers

Dr. Abraham Wikler's Prophetic Quote

“Psychotherapy and psychoanalysis are complete failures in the treatment of addictions because there are forces at work that neither the therapist nor the patient is aware of”

What are these Forces?

Conditioned Abstinence Syndrome

- Symptoms similar to acute withdrawal
- “Sui Generis”
- Caused by the addiction getting embedded into the memory, emotional and motivational centers through neuro-circuitry changes
- Will last a lifetime
- Major cause of relapse

Recommendations of a Safe, Effective Antagonist in 1971

- Ability to antagonize the euphoric high of opiates
- Absent or low-agonistic effects, especially unpleasant ones
- Does not cause physical dependence
- Does not exhibit increasing tolerance to its antagonistic actions
- Absence of serious side effects and toxicity even in chronic use
- Absence or low abuse potential

Recommendations Continued

- Reversible effects in case of medical emergencies
 - High potency to allow administration of small amounts in a biodegradable vehicle
 - Easily Available and inexpensive
 - Therapeutic efficacy in the treatment of narcotic addictions
- By late 1972 compound EN-1639 fulfilled the criteria and the drug was NALTREXONE – the first non-dependence producing drug used clinically for opioid addiction

Classification of Opioid Drugs

- Agonist – Occupy and activate the opiate receptors
Heroin, methadone, oxycodone, hydrocodone
- Antagonist – Occupy but do not activate the receptors
Naloxone, naltrexone, nalmefene
- Partial Agonist – occupy but activate receptor in a limited way and may block some agonists
Buprenorphine

Opiate Receptor Activation

- Analgesia
- Euphoria
- Sedation
- Cough center suppression
- Breathing center suppression
- Miosis
- Emesis
- Histamine release

Principle of Opiate Receptor Affinity

- Stronger the affinity – stronger the analgesia
- Stronger the analgesia – stronger the euphoria
- Stronger the euphoria – stronger the addiction

EUPHORIA CANNOT BE DELINKED FROM THE ADDICTION

Drugs with High Opiate Receptor Affinity

- Heroin
- Morphine
- Oxycodone
- Hydromorphone
- Fentanyl
- Methadone

Definition of Non-Dependence Producing Drugs

- No euphoria or 'high' or other subjective effects
- No withdrawal symptoms when drug is discontinued
- No tolerance
- Non-habit-forming; non-addicting
- Non-abusable
- No fear of diversion
- No street value

Clinical Issues with Non-Dependence Producing Drug

- Patients unfamiliar with the drugs
- Miss the 'high' or 'buzz'
- Ambivalence about quitting and taking medications
- Misinformation about the drug
- Increased role for therapist, counselors, nurses
- POOR MEDICATION COMPLIANCE

Partial List of Non-Dependence Producing Drugs

- Acamprosate (alcohol)
- Baclofen (cocaine)
- Amantidine (cocaine)
- Disulfiram (alcohol, cocaine)
- Topiramate (alcohol)
- Vigabatrin (cocaine, methamphetamine)
- Ondansetron (alcohol)
- Naltrexone (alcohol, opioids)
- Nalmefene (alcohol, opioids)
- Rimonabant (obesity, smoking)
- Bupropion (smoking)
- Varenicline (smoking)

Non-Dependence Producing Drugs Approved by the FDA for Addictions

- Acamprosate
- Bupropion
- Disulfiram
- Naltrexone
- Nalmefene
- Varenicline

Creating the Treatment Paradigm for Non-Dependence Producing Drugs

- Lessons from the failure of naltrexone
- Medication compliance
- Medication administration site for injection, surgical implants etc.
- Training counselors, therapists, psychologist on the benefits of the newer medications
- Creating the treatment team

Other Critical Factors

- Cost of medications
- Support from insurance companies, EAPs etc.
- Developing a disease management program similar to other chronic diseases like diabetes, asthma etc.
- Contingency contracting, e.g. vouchers
- Creating virtual clinics
- Expanding the role of nurses, pharmacists, therapists etc.

Long Term Benefits of Utilizing Non-Dependence Producing Drugs

- Improved treatment outcomes
- Reduce the stigma associated with the disease and drugs
- Treat psychiatric and addictive symptoms simultaneously
- Changing societal views on addictions
- Bridging the treatment divide
- Reducing the hostility towards medications
- Broaden treatment choices
- Bring treatment of addictions into the mainstream of medicine

The Future Belongs to Non-Dependence Producing Drugs

How prepared are we?

- Much needs to be done
- Medical schools
- Residency Training
- Schools of social work
- Working with existing treatment centers, hospitals and professionals