Understanding Opioid Use Disorder and the Treatment Armamentarium

Edwin Salsitz, Mount Sinai Beth Israel
Lisa Alexander, PA Education Association & George Washington School of Medicine and Health Services

Join the conversation at #OUDTreatment #EndTheStigma
Understanding Opioid Use Disorder and the Treatment Armamentarium:

Neurobiology, Vulnerability, Stigma, Terminology

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No Disclosures
Drs. Dole, Nyswander, and Kreek

... “their Brain Lacks Something that Heroin Provides” V.D.

... “they Function Better on Heroin, than off Heroin” M.N
A Medical Treatment for Diacetylmorphine (Heroin) Addiction

A Clinical Trial With Methadone Hydrochloride

Vincent P. Dole, MD, and Marie Nyswander, MD

A group of 22 patients, previously addicted to diacetylmorphine (heroin), have been stabilized with oral methadone hydrochloride. This medication appears to have two useful effects: (1) relief of narcotic hunger, and (2) induction of sufficient tolerance to block the euphoric effect of an average illegal dose of diacetylmorphine. 

JAMA. 1965;193(8):646-650

JAMA Classics: Celebrating 125 Years
Methadone Maintenance 4 Decades Later
Thousands of Lives Saved But Still Controversial
Commentary by Herbert D. Kleber, MD
JAMA. 2008;300(19):2303-2305

From the Rockefeller Institute, and Manhattan General Division of Beth Israel Hospital, New York. 
Reprint requests to Rockefeller Institute, New York 10021 (Dr. Dole).
Reward Pathways

Frontal Cort.

Nuc. Acc.

VTA

DA pathways
Cerebral phosphorus metabolite abnormalities in opiate-dependent polydrug abusers in methadone maintenance

Fig. 3. Metabolite levels in control subjects (n=16) and in short- (n=7) and long-term (n=8) methadone maintenance treatment (MMT) subgroups. Shown are means±S.D. of percent metabolite measures.
From these data, we conclude that polydrug abusers in MMT have 31P-MRS results consistent with abnormal brain metabolism and phospholipid balance. The nearly normal metabolite profile in long-term MMT subjects suggests that prolonged MMT may be associated with improved neurochemistry.

Psychiatry Research: Neuroimaging
Volume 90, Issue 3, 30 June 1999, Pages 143-152
Figure 1. Activation Maps of Brain fMRI Response to Heroin-Related Stimuli in Methadone Maintenance Patients Before and After Daily Methadone Dose.

N=25
Mean=54mos

MMTP

Normalize & Stabilize the Brain, so that Rehabilitation Can Proceed.

V.Dole

Am J Psychiatry 2008; 165:390-394
Vulnerability to Addiction

- Genetic
- Environmental
- Cultural
- Stress
- Social Determinants/Syndemics
- Exaggerated Response
- Spotlight Euphoria
- Geriatrics
- Adolescents
- Privileged Upbringing
- Availability
“Exaggerated Response”

What Did It Feel Like The First Few Times You Used Opioids?

- “All My Problems Disappeared”
- “Felt Like There Was Sunshine on My Face”
- “Felt Like I Was Under a Warm Blanket”
- “Thought This is How Normal People Feel”
- “Forgot About All the Abuse”
- “Felt Like the World Was at Peace”
- “Totally Relaxed” “Not Shy”
- “Looking at a Beautiful Sunset”
- “I Was Energized!!”
- Liking an Opioid is Itself a Vulnerability
Rates of Opioid Overdose Deaths, Sales, and Treatment Admissions, United States, 1999–2010

Prescriber Vulnerability “Perfect Storm”
Opioid Agonist Therapy

Addiction
Regulatory
Pharmacology
Stigma
Destitution
Political
“My Wife’s Opinion Is that Methadone Maintenance Treatment Is As Close To Evil As You Can Get, Without Killing Someone.”

A “successful” methadone patient quoting his wife’s attitude toward methadone maintenance treatment.
Duration Barriers: Stigma

SM: You must be excited to see him when he comes back?
Mrs. Claus: By the time he stumbles in at 6AM, Chris has eaten roughly 2 Billion cookies, so he pukes for a solid day! She continues-
THEN HE SPENDS A WEEK IN A METHADONE CLINIC TO COME DOWN FROM THE SUGAR HIGH.

Aidy Bryant, Seth Meyers. SNL, 12/8/12
OAT Barriers: Terminology
A Way Out for Junkies?

By JOHN CLAUSON

In trials going on nationwide, buprenorphine "seems to block the cravings of heroin withdrawal"

W

hen heroin users smoked the controversial drug, they often linked it to a feeling of being numb, of being able to shut out the world. Now, instead of being able to shut out the world, heroin users are finding they may be able to escape the feeling of being numb.

"We still have some way to go," says John Clauson, a clinical psychologist who has been treating heroin addicts for more than 20 years. "But in the past year, I've seen a major shift in the way people feel about heroin. The feeling of being numb has been replaced by a feeling of being alive."}

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OAT Barriers: Terminology
OAT: Terminology

• OST: Opioid Substitution Therapy
• Commonly Used in Europe and Australia
• Leads To:
  “Substituting One Addiction For Another”
  “Substituting One Drug For Another”

MAT: A Misnomer For Many Patients
Why Not Call It: “Treatment for OUD” or
  “Pharmacotherapy for OUD”
OAT: Terminology

Physical Dependence Does Not Necessarily Equal Addiction

Courtesy A.W.
Opioid Agonist Therapy:
The Duration Dilemma

Based on 55 Years of Evidence,
With Consistently High Relapse Rates,
Indefinite Effective Treatment is the Safest Option
MEDICATION “ASSISTED” TREATMENT
“ADDICTION PHARMACOTHERAPY”

“All Treatments Work For Some People/Patients”

“No One Treatment Works for All People/Patients”

Alan I. Leshner, Ph.D
Former Director NIDA
Actor Philip Seymour Hoffman, 46 yo, who was found dead February 2, 2014 on the bathroom floor of his New York apartment with a syringe in his left arm, died of acute mixed drug intoxication, including heroin, cocaine, benzodiazepines and amphetamine, the New York medical examiner's office said Friday.

3 Children: 11, 8, 6, yo.
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The Evidence for Medication-Assisted Treatment of Opioid Use Disorder

Lisa Mustone Alexander EdD, MPH, PA-C
President
Physician Assistant Education Association
Objectives for Medication-Assisted Treatment

• Suppress signs and symptoms of opioid withdrawal

• Extinguish opioid-drug craving

• Block the reinforcing effects of illicit opioids (“blockade”)

• Treatment of OUD is part of a continuum of care that includes prevention, screening, treatment, and follow-up care
Basic Overview/Pharmacology

Methadone
- Daily dosing in supervised settings
- On WHO’s essential medicines list
- Synthetic opioid with long half-life

Buprenorphine
- Partial opioid receptor agonist; ceiling effect
- Combined with naloxone antagonist
- Available through treatment programs and in outpatient settings
- Requires special training to prescribe—DATA 2000 Waivers

Naltrexone
- Full opioid receptor antagonist
- Available through treatment programs and outpatient offices
- No special training to prescribe
Evidence for Use
Evidence for efficacy, effectiveness, and safety in OUD and other disorders

- Methadone Maintenance Treatment
  - 633 studies (1972)
- Buprenorphine AND opioid use disorder
  - 185 studies (1978)
- Naltrexone AND opioid use disorder
  - 104 studies (1981)

PubMed September 2018

Limits: “Clinical Trial” and “Humans”
Methadone

Systematic reviews demonstrate:

- Improved retention in treatment
- Reduced levels of criminality
- Reduced rates of injection drug use and blood-borne infections
- Reduced overall mortality

Innov Clin Neurosci. 2017; 14(7-8): 8-19
Cochrane Database of Systematic Reviews 2009, Issue 3, Art. No. CD002209
Proposal for the Inclusion of Methadone in the WHO Model List of Essential Medicines, 2004
Cochrane Database of Systematic Reviews 2003, Issue 3, Art. No. CD002208
Buprenorphine

Systematic reviews demonstrate:

- Increases time in treatment
- Reduces illicit opiate use
- Reduces use of other illicit substances

The Journal of Substance Abuse Treatment 2015; 48: 62-69
Cochrane Database of Systematic Reviews 2014, Issue 2, Art. No. CD002207
Naltrexone

Systematic reviews demonstrate:

- Assists in maintaining abstinence from illicit opioids
- Significantly reduces cravings for opioids

The Lancet 2018; 391: 309-318
JAMA Psychiatry 2017; 74: 1197-1205
CNS Drugs 2013; 27: 851-861
OUD Treatment Risks

• The primary risk for mortality with methadone treatment is during the first four weeks after induction and the first four weeks after cessation.

• The most lethal adverse reaction to methadone is QT-prolongation and the risk for fatal arrhythmia.

• The ceiling effect of buprenorphine obviates the risk of respiratory depression after induction however, risk of mortality increases after cessation (due to loss of tolerance).

• Diversion risk is reduced
  • By directly observed treatment in OTPs
  • Combining buprenorphine with naloxone or using the extended release IM formulation or implant.
Summary

• When used in appropriately selected patients, all three medications approved for the treatment of opioid use disorder are effective at:
  
  • Preventing relapse to illicit opioid use
  • Increasing retention in treatment

Harvard Review of Psychiatry 2015; 23: 63-75
Summary

Selected References


Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine Maintenance Versus Placebo or Methadone Maintenance for Opioid Dependence. *Cochrane Database of Systematic Reviews* 2014, Issue 2, Art. No. CD002207


Proposal for the Inclusion of Methadone in the WHO Model List of Essential Medicines, 2004


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