Methadone Maintenance Treatment for the Opioid Dependent Patient

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Outline Key Points

- What is the history of methadone treatment? Why is it so regulated?
- How does methadone work: what are the pharmacokinetics and pharmacodynamics?
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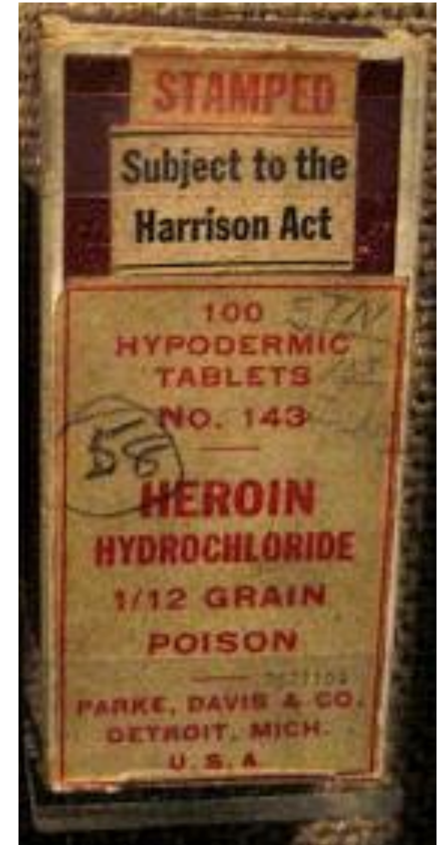
Early Treatment Efforts

- 1906: Pure Food and Drug Act (assure purity)
- 1914: Harrison Narcotic Act (opiates restricted)
- 1929: Congress established US Public Health Service Hospital (Lexington Kentucky). Detox and prison hospital – 93-97% relapsed
- Mid-late 1960's: Heroin related mortality - the leading cause of death for young adults, serum hepatitis, arrests for drug related crimes, over crowded jails
- No effective medical treatment



http://opiophilia.blogspot.com/2013/03/origins-of-methadone-part-ii-narcotic.html

Methadone Maintenance Treatment Timeline

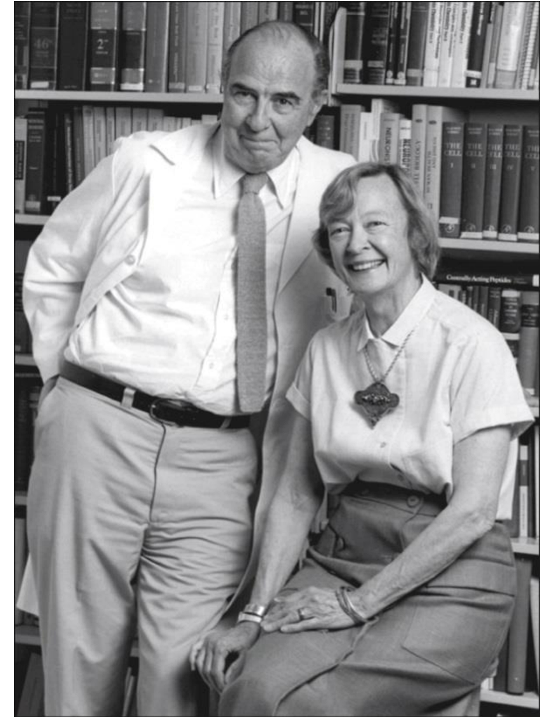
1947 Methadone FDA approved as an analgesic and antitussive

1963-1964 President Kennedy's Advisory Commission: determine the effectiveness of dispensing narcotics to addicts. Drs. Dole/Nyswander MMT research Rockefeller University.

1965 Dole/Nyswander MMT research published in *JAMA*

1972 FDA Federal Methadone Regulations established

1974 Narcotic Addiction Treatment Act defined MMT



Drs. Vincent Dole and Marie Nyswander at Rockefeller University

http://jamanetwork.com/journals/jama/article-abstract/1719708

Methadone Maintenance Treatment Timeline (2)

1981 AIDS detected in CA and NY

1984 HIV identified as cause of AIDS

1985 AIDS-related illnesses identified as major cause of MMT patient deaths

1990 GAO report issued; HCV (Hepatitis C) test was developed

1992 Congress created CSAT within ADAMHA (which was the precursor to SAMHSA)

1995 IOM "Federal Regulation of Methadone Treatment" report issued

Methadone Maintenance Treatment Timeline (3)

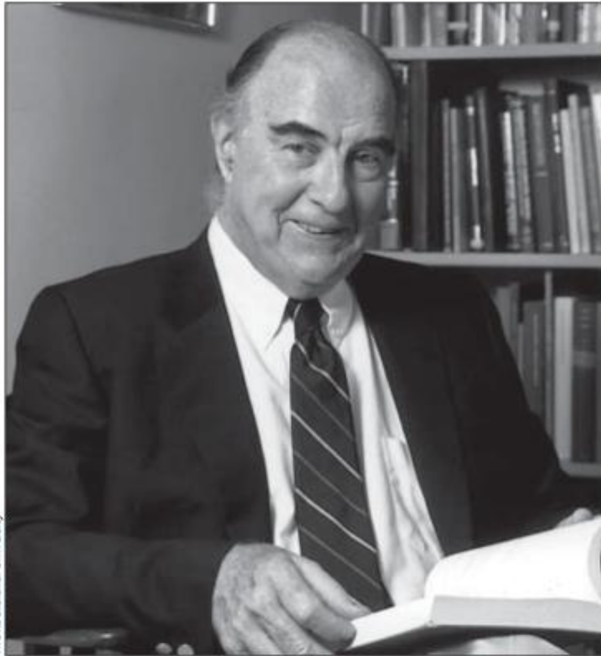
1997 NIH Consensus Statement issues calling for expansion of MMT

2001 Fed Regulations revised to include accreditation process

2002 Buprenorphine approved

2015 50th anniversary of MMT

Early Methadone Maintenance Research



The Rockefeller University

Dr. Vincent Dole

http://atforum.com/2015/08/retrospective-vincent-dole-would-be-disappointed-in-the-stigma-mmt-patients-face-today/

"The treatment is corrective, normalizing neurological and endocrinologic processes in patients whose endogenous ligand-receptor function has been deranged by long-term use of powerful narcotic drugs... there seems to be a specific neurological basis for compulsive use of heroin by addicts and that methadone taken in optimal doses can correct the disorder."

– Vincent Dole, 1988

Goals for Opioid Medication Treatment with Methadone

- Prevention or reduction of drug craving
- Prevention or reduction of withdrawal symptoms
- Prevention of relapse to use of addictive drug
- Restoration to or toward normalcy of any physiological function disrupted by drug use

Early Methadone Maintenance Research (1)

- Relieved narcotic craving or hunger
- Medically safe
- Minimal side effects:
    - constipation
    - sweating
    - decreased libido
    - weight gain
- Female patients resumed menses after years of amenorrhea.

Early Methadone Maintenance Research (2)

- Patients functioned normally without anxiety associated with drug craving
- Findings:
  - Patients did not experience the euphoric, tranquilizing, or analgesic effects of short-acting opiates
  - 80-120 mg blocked euphoria if patient self-administered opiates by injection or smoking
  - No change in tolerance over time.

Impact of Maintenance Treatment

- Reduction death rates (Grondblah, ’90, Gibson 2008, Clausen 2008)
- Reduction IVDU (Ball & Ross, ’91,)
- Reduction crime days (Ball & Ross, ’91, Lind 2005)
- Reduction rate of HIV seroconversion and infection
  (Bourne, ‘88; Novick ‘90; Metzger ’93, Ward, 1998, Gowing 2004)
- Reduction relapse to IVDU (Ball & Ross,‘91)
- Improved employment, health, & social function
- Increased retention in treatment vs. drug-free alternatives (Breen, Kimber 2009)

Why Methadone Maintenance

- Goal is rehabilitation, not abstinence
- 24-36 hr. duration w/o significant sedation, analgesia, euphoria, side effects.
- Opioid cross-tolerance or blockade
- Replaces a short-acting, illegal, poor quality, expensive, injectable drug with a long-acting, oral, legal, quality-controlled medication
- Dose of 80-120 mg/day most successful
- Best results occur with concomitant psychosocial treatment.

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Methadone – How Does it Work?

Actions

- Mu agonist
- Long acting (elimination half-life: 24-36 hours)
- Oral administration (80% bioavailability)
- 5-7.5 days (4-5 half-life) to achieve steady state (amount of drug entering the body = the amount excreted)

Indications

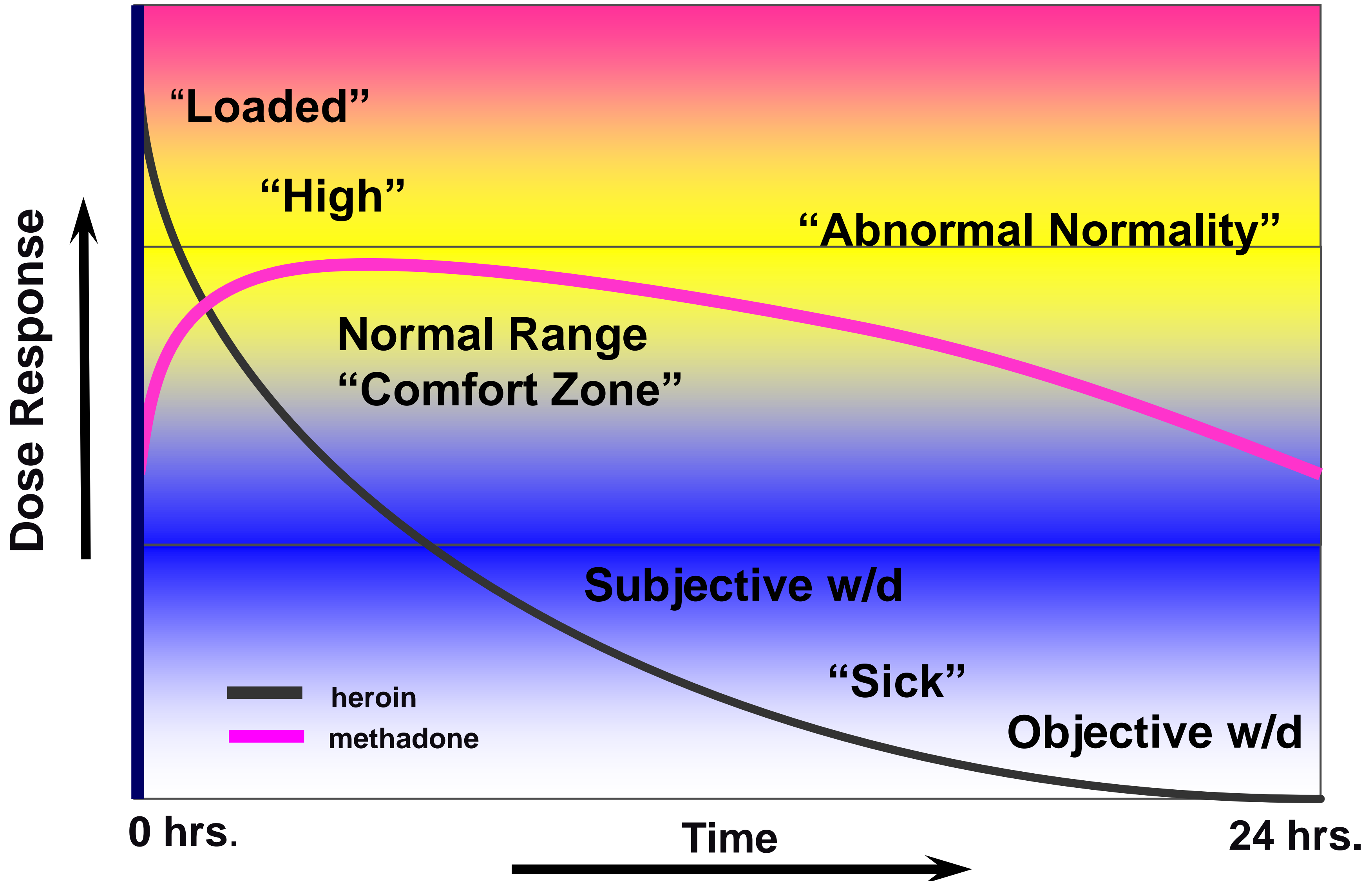
- Detox – under 180 days
- Maintenance – chronic relapsing opioid dependence

http://ph.parker.com/us/en/automated-liquid-methadone-dispensing-system-labtec

Induction/Dosage Determination

- Initial dose 20-30 maximum
- ≤40 mg first 24 hours (regulation)
- Daily COWS (objective & subjective) assessment titrate slowly over 7-10 days.
- Titrate slowly until elimination of objective & subjective withdrawal and craving to achieve steady state.
- It takes 5-7.5 days (4-5 half-life) to achieve steady state (amount of drug entering the body = the amount excreted)

24-hour Dose Response in Heroin-Tolerant and Methadone Steady-State Patients



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Methadone Caution/Contraindications: What We've Learned

- Rapid onset/cumulative effect: slowly increase to avoid over-sedation
- Interactions with alcohol, benzodiazepines, sedatives
- Gabapentin, Pregabalin, Seroquel, promethazine, clonidine common risky combination.
- Pregnancy–dose adjustments often needed in the 3rd trimester.
- Increased risk of QTc prolongation/Torsades de Pointes in higher doses and when used in combination with other medications.

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Eligibility Criteria for Methadone Maintenance Treatment

- Currently addicted to an opioid drug
- Became addicted at least 12 months prior to admission
    - < 1 year eligible for 180 detoxification treatment
- Exceptions:
    - Released from correctional institutions within 6 months
    - Pregnant
    - Previously treated up to 2 years after discharge
- Under 18 yo
    - 2 documented unsuccessful attempts at short-term detox or medication-free treatment within a 12 month period
    - Parental/guardian consent

Who Are Our Patients?

- Multiple substance-use disorders
- Prescription opioids initially, progressed to heroin
- Oral and intranasal use; some no reported IV use
- Psychiatric co-occurrence (anxiety, depression, and trauma)
- Serious medical problems (HIV, STDs, hepatitis, diabetes, endocarditis, soft tissue infections)
- Failed buprenorphine treatment
- Younger patients entering treatment
- White suburban young adults
- Returning veterans
- Coping with serious injuries (accidents & falls)
- Older patients living with chronic illness
- Disabled
- Chronic pain

Our Patients Are Also….

- Drug- and alcohol-free on take-home medication
- Bagging your groceries
- Working professionals
- Parents caring for children
- Working in addiction treatment programs

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How Do Patients Get Referred?

- Most self-referred—word of mouth
- Hospitals
- Acute Treatment Services (Detox)
- Courts
- Sterile syringe exchanges
- Law Enforcement
- Buprenorphine prescribers
- Primary Care

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Comprehensive Care: Core Services (1)

- Psychosocial assessment
- Initial and annual physical exam and blood work
- Daily medication dispensing (Take-home options)
- Toxicology screening (urine, saliva)
- Prescription Drug Monitoring Program: admission, annually, medication PRN (as needed)
- Peak & trough
- Required counseling (individual, group, family) addresses all substance use

Comprehensive Care: Core Services (2)

- Assessment and management of co-occurring disorders including pharmacotherapy
- Coordination of care for: chronic pain patients
- Pregnancy
- Provisions for tobacco, HIV, HCV testing & education, counseling and referral
- Case management

Treatment Domains

- Alcohol, illicit and prescription drug misuse
- Medical health concerns
- Co-occurring psychiatric disorders
- Employment, formal educational, and other income-related issues
- Family relationship and other social supports
- Legal problems

* Type, frequency, duration and structure of treatment designed by phase of treatment

Phases and Goals of Treatment

Phases of Treatment	Primary Treatment Goal
Acute	Stabilization on methadone; eliminate illicit use of opioids & reduction of other drug use
Rehabilitative	Learn skills to cope with major life problems
Supportive	Continued pharmacotherapy, medical care & resume primary responsibility for their life; eligible for take-home medication
Medical Maintenance	2 years of continuous stability in all domains, extended take-home privileges, reduction in frequency of clinic attendance
Medically Supervised Withdrawal & Readjustment	Stability in all domains; gradual reduction in medication Readmission for relapse

Take-Home Medication: Federal Eight-Point Criteria

- Length of time in comprehensive maintenance treatment
- Absence from all drug and alcohol misuse (including misuse of prescription medication)
- Regular attendance to Opioid Treatment Program (OTP) Absence of behavioral problems at the OTP
- Absence of criminal activity
- Stable home environment & social relationships
- Benefits of decreased attendance outweigh the potential risk of diversion
- Assurance of safe storage of take-home medication

Medically Supervised Withdrawal: For Whom?

- The highly motivated patient, if the patient wants to
- No alcohol/drug use/misuse (> 6 mo.)
- Stable living/social/employment situation
- No illegal activities, warrants, or cases pending
- Relative psychiatric/medical stability
- Friends and associates from outside drug culture
- Non-drug related hobbies, interests, and pursuits
- Support system and continuing care in place
- The risk of continued methadone treatment outweighs the benefits

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SAMHSA/CSAT Regulations: "The Rules"

- Only licensed/accredited opioid treatment programs (OTPs) can treat opioid use disorder with methadone.
- OTPs cannot treat patients for a primary diagnosis of chronic pain.
- Methadone maintenance requires one year of documented physiological dependence/addiction.
- Methadone can be used in acute care inpatient hospital settings when opioid use disorder is not the primary admission.
- Can treat pain with opioids in a patient with a known opioid use disorder.
- Caution when using methadone to treat pain for a patient with a known opioid use disorder.

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Stigma and Methadone Treatment? (1)

Medical community

- Methadone treatment isolated from mainstream medicine
- Lack of knowledge
- Encouraging taper in lieu of maintenance
- Inadequate pain management (methadone covers pain)
- Labeling patients “addicts”

Patients

- Stereotyped and misunderstood
- Estranged from families
- Isolated from self-help supports
- Lost jobs, restricted licenses
- Receive poor medical care

Stigma and Methadone Treatment? (2)

Opioid Treatment Programs –

- Some poorly run programs - “Juice bars”
- Loitering
- Diversion
- Use of pejorative language – “dirty” tox screens, “addicts,” “substitution therapy,” “liquid handcuffs”
- Clinician transference/countertransference
- Poor public relations

Here’s what you can do in your own practice:

- Become educated about ALL the evidence-based treatments for opioid use disorder
- Become knowledgeable about the resources in your community
- Work to create affiliations with programs that offer treatment for opioid use disorder in your community
- Provide education to your patients and work with them to access treatment appropriate to their level of readiness for change and needs
- Become a vehicle for education and advocacy in the community for patients with opioid use disorders

Unit Resources:

- Origins of Methadone, Part II. The Narcotic Clinics (Opiophilia.blogspot.com)
- Addiction Treatment Forum - Retrospective: Vincent Dole Would Be Disappointed In the Stigma MMT Patients Face Today
- Clinical Opiate Withdrawal Scale
- SAMHSA - Federal Guidelines for Opioid Treatment Programs (2015)
- SAMHSA TIP 43: Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs
- Federal Guidelines for Opioid Treatment
- ONDCP Guidance - Changing the Language of Addiction