OUD and MAT 101: Understanding the Disorder and The Medications

A Training for Multidisciplinary Addiction Professionals

Module III

Revised May 2019

New England (HHS Region 1) ATTC Addiction Technology Transfer Center Network
Funded by Substance Abuse and Mental Health Services Administration

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Disclosures

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Goals for Module III

This module reviews the following:

- Overview of three medications used to treat opioid use disorders: Methadone, Buprenorphine and Vivitrol.
- The development and approval process
- Determining which medication would be most effective
- Phases of Treatment
  - Induction
  - Detoxification
  - Maintenance
  - Medically-Assisted Withdrawal

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Introductory Statement

- There are currently 3 approved medications for the treatment of Opioid Use Disorder:
  - Methadone
  - Buprenorphine
  - Naltrexone
- There is no medication that is 'good' for all; the choice needs to be the clients.
- Clients need unbiased information on all 3 to then make an informed decision.
- Some people can embrace a successful recovery without the use of medication.

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Agonist Therapy: Methadone

By the mid- and late 1960's, heroin related mortality was the leading cause of death for young adults between ages 15-35 in New York City.

In 1962, Dr. Vincent Dole received grant to study feasibility of opiate maintenance in NY/Rockefeller University

Dr. Nyswander and Dr. Mary Jeanne Kreek joined Dr. Dole's staff in 1964

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Agonist Therapy: Methadone

- No euphoric/analgesic effects
- Doses between 80-120mg held at level to block their euphoric and tranquilizing effects
- No change in tolerance level over time
- Could be taken once a day
- Relieved craving attributed to relapse
- Medically safe and nontoxic

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Agonist Therapy: Methadone

- Proper dose lasts between 24 - 36 hours
- Does not create euphoria, sedation or analgesia
- Duration of treatment individualized
- Most significant long term effects on health is marked improvement

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Side Effects

- Side effects usually subside within a month and may include:
  - Experience difficulty breathing or shallow breathing
  - Feel lightheaded or faint
  - Experience hives or a rash; swelling of the face, lips, tongue, or throat
  - Feel chest pain
  - Experience a fast or pounding heartbeat
  - Experience hallucinations or confusion

THESE SIDE EFFECTS REQUIRE MEDICAL ATTENTION

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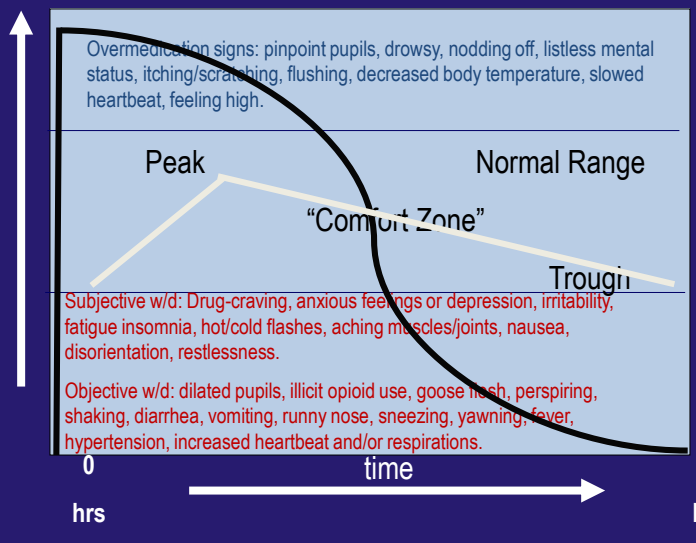
Agonist Therapy: Methadone



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Agonist Therapy: Methadone

- Indicated for use with pregnant and nursing mothers
- Women who are pregnant or breastfeeding can safely take methadone. When withdrawal from an abused drug happens to a pregnant woman, it causes the uterus to contract and may bring on miscarriage or premature birth.
- Undergoing methadone maintenance treatment while pregnant will not cause birth defects, but some babies may go through withdrawal after birth. This does not mean that the baby is addicted.
- Mothers taking methadone can still breastfeed. Research has shown that the benefits of breastfeeding outweigh the effect of the small amount of methadone that enters the breast milk.

- Learn more from the SAMHSA publication: *Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and Their Infants. 2018.*

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Agonist Therapy: Methadone

- Reduces crime rates, criminal behaviors
  - drug offenses decline
  - predatory crimes decline
  - legitimate employment rates increase

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Agonist Therapy: Methadone

- Improves quality of life
  - increased employment
  - improved family relationships
  - improved financial status
  - improved access to general health, dental and mental health care

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Agonist Therapy

- Effective prevention of infection from:
  - HIV disease
  - Hepatitis B/C
- Reduces needle use

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Agonist Therapy: Methadone

- Dose Determination:
  - History of use
  - History of last agonist treatment
  - Induction Period
  - Achievement of a steady state
  - Peak and trough

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Agonist Therapy: Methadone

DINOVAMP: An Assessment Tool for Dose Determination

- **D**rug abuse (may include inadequate methadone dose) Dose adequacy must be monitored.
- **I**nteractions (with other medications or herbal products may affect methadone potency.
- **N**euroleptics (Patients with psychiatric illnesses may require methadone dose adjustments
- **O**pioid withdrawal signs/symptoms
- **V**itamin C (Urinary acidifiers can cause more rapid elimination of methadone; **V**iral Infection (HCV will sometimes require dose increases)
- **A**tmosphere (Stress at home, work, etc. may foster a request for increase.
- **M**enopause (symptoms may mimic opioid withdrawal; **M**edical conditions may require special management
- **P**regnancy (affects methadone dose requirements; **P**lasma (serum levels) may need monitoring.

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Agonist Therapy: Methadone

Early Induction

- Early dose adjustments to get to "Comfort Zone"
- Half of today's dose will be added to tomorrow's dose resulting in increasing effects with no increase in dose, and so on until steady state is achieved.
- Steady State refers to lack of withdrawal symptoms and craving for the drug.

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Agonist Therapy: Methadone

Late Induction

Gradual continued dose adjustments beyond initial relief in order to:

- Establish adequate level of cross-tolerance or "Blockade"
- Provide a dose adequate to achieve the desired effect
- Prevent W/D, craving and relapse

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Agonist Therapy: Methadone

Blood Levels: The Peak and Trough

- Peak and Trough provides a clinical picture
- Ensures adequacy of dose
- Documents the need for a dose change
- Determines need for and effectiveness of split dose level

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Agonist Therapy Treatment Issues

- Program Choices
  - Short Term Detoxification
  - Long Term Detoxification
  - Methadone Maintenance (MMTP)
- Determinants
  - Length of addiction
  - Amount of opiates being used
  - Previous attempts

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How Can You Treat Opioid Addiction?

<u>Detox Protocols: Short Term vs. Long Term</u>

- Relieves withdrawal symptoms while patients adjust to a drug-free state
- Can occur in an inpatient or outpatient setting
- Typically occurs under the care of a physician or medical provider
- Serves as a precursor to behavioral treatment, because it is designed to treat the acute physiological effects of stopping drug use

(National Institute on Drug Abuse, 2009)

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Agonist Therapy: Methadone

Detoxification Programs

- No prior treatment
- Patient request
- Less than two Admissions to Detoxification Treatment Episodes in one year

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Agonist Therapy: Methadone

Length of Detoxification Programs

- Short term
  - 30 days or less
  - Entrée into treatment
  - Starting dose of 20-30mg

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Agonist Therapy: Methadone

Length of Detoxification Programs

- Long Term
  - 180 days or less
  - Can work with shorter drug abuse history, lower tolerance
  - Starting dose 20-40mg
  - Individual dosing schedule that will reach 0mg's no later than 180 days from initial dose.

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Agonist Therapy: Methadone

MMTP: Criteria for Admission

- Verified one year of addiction
- Voluntary choice and consent of patient
- Patient education
  - Duration of treatment
  - Adverse effects
  - Program expectations

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Agonist Therapy: Methadone

MMTP: Exceptions to current Addiction

- Recently released from correctional facility
- Recent discharge from chronic facility
- Pregnant patient
- Previously treated patients
- Minors

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Agonist Therapy: Methadone

Take-home Privileges

- Federal and State regulations provide the framework from which:
  - Take-home schedules are developed
  - OTP's requirements for earning privileges are outlined.
- Patients should be informed of take-home privilege requirements during orientation to the program

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Agonist Therapy: Methadone

MMTP: Indications for MSW

- Different from a Detox Protocol
- Indicators or readiness:
  - Self-motivation
  - Treatment Compliance
  - Support network in place
  - Psychiatric/medical stability
  - Women of child bearing age should be assessed for pregnancy
  - Commitment to abstinence from all mood-altering substances
  - Evidence of long term abstinence (usually six or more months)

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Partial-Agonist Therapy: Buprenorphine

- Buprenorphine is currently marketed for opioid treatment under the trade names:

Subutex® (buprenorphine)

Suboxone® (buprenorphine/naloxone)

Zubsolv

- Over 25 years of research
- Over 5,000 patients exposed during clinical trials
- Proven safe and effective for the treatment of opioid addiction

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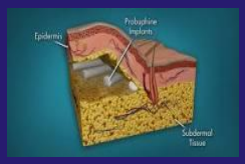
Partial-Agonist Therapy: Buprenorphine

- **Probuphine**: Implant designed for persons who are stable for 6 or more months. It is indicated for the maintenance treatment of opioid dependence in patients who have achieved and sustained prolonged clinical stability on low-to-moderate doses of a transmucosal buprenorphine-containing product (i.e., doses of no more than 8 mg per day of Subutex or Suboxone sublingual tablet or generic equivalent).
- Probuphine should be used as part of a complete treatment program to include counseling and psychosocial support.



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Partial-Agonist Therapy: Buprenorphine

- In November 2017, the FDA approved Indivior's **Sublocade**, an extended-release buprenorphine injection for the treatment of moderate-to-severe opioid use disorder (OUD) in adult patients who have initiated treatment with a transmucosal buprenorphine-containing product. With its approval, Sublocade became the first once-monthly buprenorphine injection for the treatment of OUD.

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Partial-Agonist Therapy: Buprenorphine

- The recommended dose of Sublocade following induction and dose adjustment with transmuscosal buprenorphine is 300 mg monthly by subcutaneous injection in the abdominal region for the first 2 months followed by a maintenance dose of 100 mg monthly.

  The maintenance dose may be increased to 300 mg monthly for patients who tolerate the 100 mg dose, but do not demonstrate a satisfactory clinical response, as evidenced by self-reported illicit opioid use or urine drug screens positive for illicit opioid use.

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Partial-Agonist Therapy: Buprenorphine

	Indication	Administration	Frequency	Generic Available[4]
Sublocade (buprenorphine)	Opioid dependence	SQ Injection	Monthly	N
Probuphine (buprenorphine)	Opioid dependence	Intradermal implant	6 months x 1 dose	N
Suboxone (buprenorphine and naloxone)	Opioid dependence	Sublingual tablet and film	Daily	Y (tablet), N (film)
Subutex (buprenorphine)	Opioid dependence	Sublingual tablet	Daily	Y
Zubsolv (buprenorphine and naloxone)	Opioid dependence	Sublingual tablet	Daily	N
Bunavail (buprenorphine and naloxone)	Opioid dependence	Buccal film	Daily	N
Buprenex (buprenorphine)	Pain	IM or IV injection	Varies	Y
Belbuca (buprenorphine)	Pain	Film	Twice daily	N
Butrans (buprenorphine)	Pain	Transdermal patch	7 days on, 3 weeks off	N

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Partial-Agonist Therapy: Buprenorphine

Clinical trials with opioid dependent adults have established the effectiveness of buprenorphine for the treatment of opioid addiction. Effectiveness of buprenorphine has been compared to:

- Placebo (Johnson et al., 1995; Kakko et al., 2003; Ling et al., 1998)
- Methadone (Fischer et al. 1999; Johnson, Jaffee, & Fudula, 1992; Schottenfield et al., 1997; Strain et al. 1994)
- Methadone and LAAM (levo-alpha-acetyl-methadol) (Johnson et al. 2000)

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Partial-Agonist Therapy: Buprenorphine

- Buprenorphine is as effective as moderate doses of methadone (Fischer et al., 1999; Johnson, Jaffee, & Fudula, 1992; Ling et al., 1996; Schottenfield et al., 1997; Strain et al., 1994).
- Buprenorphine is as effective as moderate doses of LAAM (Johnson et al., 2000).
- Buprenorphine's partial agonist effects make it mildly reinforcing, encouraging medication compliance (Ling et al., 1998).
- After a year of buprenorphine plus counseling, 75% of patients retained in treatment compared to 0% in a placebo-plus-counseling condition (Kakko et al., 2003).

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Partial-Agonist Therapy: Buprenorphine

- A synthetic opioid
- Described as a mixed opioid agonist-antagonist (or partial agonist)
- Available for use by certified physicians outside traditionally licensed opioid treatment programs

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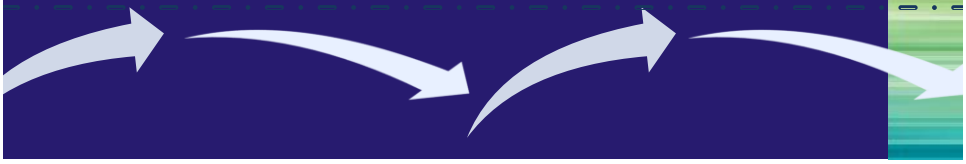
Partial-Agonist Therapy: Buprenorphine

- Partial Opioid Agonist
  - Produces a ceiling effect at higher doses
  - Has effects of typical opioid agonists—these effects are dose dependent up to a limit
  - Binds strongly to opiate receptor and is long-acting
- Safe and effective therapy for opioid maintenance and detoxification



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Partial-Agonist Therapy: Buprenorphine

1. Patient can participate fully in treatment activities and other activities of daily living easing their transition into the treatment environment
2. Limited potential for overdose (Johnson et.al, 2003)
3. Minimal subjective effects (e.g., sedation) following a dose
4. Available for use in an office setting
5. Lower level of physical dependence

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Partial-Agonist Therapy: Buprenorphine

- Discourages IV use

Diminishes diversion

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Partial-Agonist Therapy: Buprenorphine

1. Greater medication cost
2. Lower level of physical dependence (i.e., patients can discontinue treatment)
3. Detectable only in specific urine toxicology screenings

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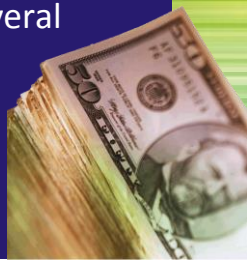
Partial-Agonist Therapy: Buprenorphine

- Medication costs are only one factor. Costs of providing treatment also include costs associated with clinic visits, staff time, etc. These costs are greater for methadone.
- While not yet studied in young adults, research on adult populations has demonstrated cost effectiveness of buprenorphine across several indicators.



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Partial-Agonist Therapy: Buprenorphine

- A cost effective comparison of buprenorphine versus methadone for opioid dependence both demonstrated increases in heroin-free days.
- There no statistical significance between the cost-effectiveness for buprenorphine and methadone.

(Doran et al., 2003)

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Partial-Agonist Therapy: Buprenorphine

- Treatment with buprenorphine-naloxone was associated with a reduction in opioid utilization and cost in the first year of follow-up (Kaur &McQueen, 2008).
- Systematic review found good studies supporting buprenorphine as a cost effective approach to opioid treatment (Doran, 2008).

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Use of Buprenorphine: Studies on Cost-Effectiveness, cont'

- Another study in Australia found buprenorphine demonstrated lower crime costs and higher quality adjusted life years (QALY), concluding the likelihood of net benefits from substituting buprenorphine for methadone.

(Harris, Gospodarevshaya, & Ritter, 2005)

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Why was Buprenorphine/Naloxone Combination Developed?

- Developed in response to increased reports of buprenorphine abuse outside of the U.S.
- The combination tablet is specifically designed to decrease buprenorphine abuse by injection, especially by out of treatment opioid users.

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Partial-Agonist Therapy: Buprenorphine

- Each tablet contains buprenorphine and naloxone in a 4:1 ratio
  - Each 8 mg tablet contains 2 mg of naloxone
  - Each 2 mg tablet contains 0.5 mg of naloxone
- Ratio was deemed optimal in clinical studies
  - Preserves buprenorphine's therapeutic effects when taken as intended sublingually
  - Sufficient dysphoric effects occur if injected by some physically dependent persons to discourage abuse

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Partial-Agonist Therapy: Buprenorphine

- Buprenorphine and naloxone have different sublingual (SL) to injection potency profiles that are optimal for use in a combination product.

SL Bioavailability	Potency
Buprenorphine 40-60%	Buprenorphine ≈ 2:1
Naloxone 10% or less	Naloxone ≈ 15:1

(Chaing & Hawks, 2003)

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Partial-Agonist Therapy: Buprenorphine

Abscesses due to injection of Subutex

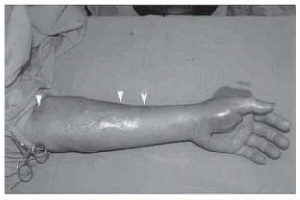

Fig. 1. Case 1, thenar intramuscular abscess. Several smaller subcutaneous abscesses are present along the line of the cephalic vein and in the cubital fossa (arrows).

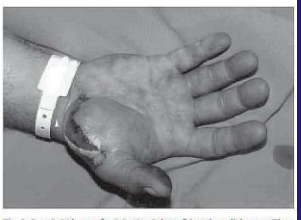

Fig. 2. Case 2, 24 hours after injecting Subutex® into the radial artery. There is fixed patchy mottling of the palmar skin similar to a "trash foot", due to micro-emboli. The tips of the thumb, index, middle and ring fingers are dusky, but the little finger is spared. This pattern may be due to an incomplete palmar arterial arch with separate supply from the ulnar artery to the little finger. Injection marks can be seen along the course of the radial artery at the wrist (arrows). Thenar fasciotomy has been performed.

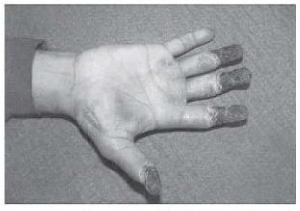

Fig. 3. Case 2, 2 weeks after injecting Subutex® into the radial artery. Dry gangrene of the tips of the thumb, index, middle and ring finger.

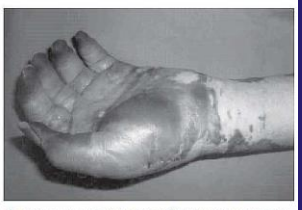

Fig. 4. Case 3, 2 months after injecting Subutex® into the brachial artery. There is wet gangrene of all the fingers, with blistering and fixed discolouration of the skin of the hand and forearm.

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Partial-Agonist Therapy: Buprenorphine

Induction

Maintenance

Tapering Off/Medically-Assisted Withdrawal

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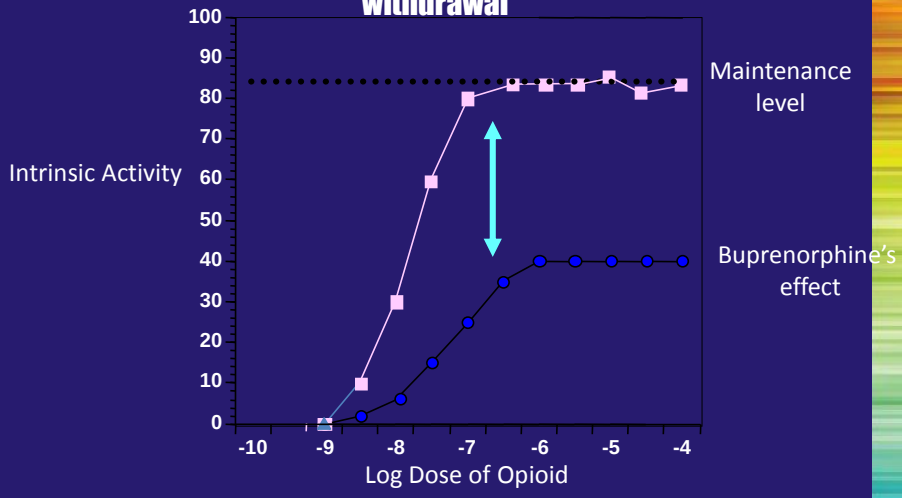
Partial-Agonist Therapy: Buprenorphine

If the patient needs a high level of medication to achieve maintenance, the ceiling effect of buprenorphine may result in withdrawal



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Partial-Agonist Therapy: Buprenorphine

Transferring Patients Onto Buprenorphine: 3 Ways Significant Withdrawal Could Occur

Dose too low?

Insufficient agonist effects

Not full agonist

May not fully replace

Precipitates Withdrawal

Ceiling effect

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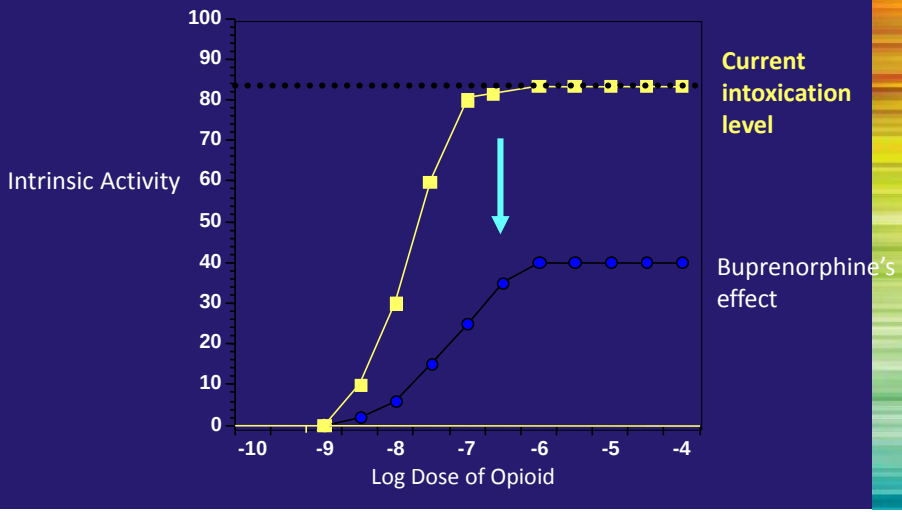
Partial-Agonist Therapy: Buprenorphine

Buprenorphine will replace other opioids at the receptor site; therefore the patient experiences withdrawal.



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Partial-Agonist Therapy: Buprenorphine

Direct Buprenorphine Induction from Short-Acting Opioids

- Ask patient to abstain from short-acting opioid (e.g., heroin) for at least 6 hrs. and be in mild withdrawal before administering buprenorphine/naloxone.
- When transferring from a short-acting opioid, be sure the patient provides a methadone-negative urine screen before 1st buprenorphine dose.

(Amass et al., 2004; Johnson et al., 2003)

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Partial-Agonist Therapy: Buprenorphine
Direct Buprenorphine Induction from Long-Acting Opioids

- Clinical experience has suggest that induction procedures with patients receiving long-acting opioids (e.g. methadone-maintenance patients) are basically the same as those used with patients taking short-acting opioids, except:
  - The time interval between the last dose of medication and the first dose of buprenorphine must be **increased.**
  - **At least 24 hrs should elapse** before starting buprenorphine and longer time periods may be needed (up to 48 hrs).
  - Urine drug screening should indicate no other illicit opiate use at the time of induction.

(Center for Substance Abuse Treatment, 2004)

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Partial-Agonist Therapy: Buprenorphine
Buprenorphine Withdrawal

- Working to provide a smooth transition from a physically-dependent to non-dependent state, with medical supervision
  - Medically supervised withdrawal (detoxification) is accompanied with and followed by psychosocial treatment, and sometimes medication treatment (i.e., naltrexone) to minimize risk of relapse.
- Medically- supervised withdrawal may lead to early treatment engagement (Brigham et al., 2007).

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Partial-Agonist Therapy: Buprenorphine
Medically-Assisted Withdrawal

- Outpatient and inpatient withdrawal are both possible
- How is it done?
  - Switch to longer-acting opioid (e.g., buprenorphine)
    - Taper off over a period of time (a few days to weeks depending upon the program)
    - Use other medications to treat withdrawal symptoms
  - Use clonidine and other non-narcotic medications to manage symptoms during withdrawal

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Partial –Agonist Therapy: Buprenorphine
and Pregnancy

- May be preferable for patients who are new to treatment because it is easier to transfer from buprenorphine to methadone (it can be very difficult to transfer from methadone to buprenorphine), who do not like or want methadone, or who have requested this medication.
- Approximately 50% of exposed neonates are treated for NAS; NAS may be milder with buprenorphine compared with full mu opioid agonists such as most opioid analgesics and methadone.
- Available research suggests there is not a linear cause and effect relationship between prenatal buprenorphine exposure and developmental problems when compared with other opioids; the research base is limited.

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Antagonist Medication: Vivitrol

- Approved for use in treatment for opioid use disorder on October 12, 2010.
- Approval followed a six-month clinical trial in which recovering adults were given either Vivitrol or a placebo.
- 36% of those on Vivitrol were still in treatment at the end of the study compared to 23% on the placebo.

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Antagonist Medication: Vivitrol

- Prior to approval for use with opioid use disordered persons, it was already being used to treat alcoholism [as was the shorter acting pill form: Naltrexone (trade name ReVia)].
- When used in conjunction with counseling, it was shown to reduce the number of drinking days and heavy drinking days as well as prolonging abstinence.

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Antagonist Medication: Vivitrol

- The recommended dose of VIVITROL is 380 mg delivered intramuscularly every 4 weeks or once a month. The injection should be administered by a health care professional as an intramuscular (IM) gluteal injection, alternating buttocks, using the carton components provided. VIVITROL must not be administered intravenously.
- If a patient misses a dose, he/she should be instructed to receive the next dose as soon as possible.
- Effectiveness in opioid treatment is related to:
  - Binding to opioid receptors in the brain,
  - Blocking neurotransmitters in the brain,
  - Eliminating pleasurable effects of recreational drugs such as alcohol, heroin and morphine.

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Antagonist Medication: Vivitrol

- Vivitrol is administered via intramuscular injection.
- Unlike most forms of methadone and buprenorphine which must be taken daily, Vivitrol is effective for 30 days.
- It can be prescribed by a Prescribing Nurse or Physician's Assistant like Methadone and Buprenorphine.

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Antagonist Medication: Vivitrol

- The following side-effects have been identified:
  - Nausea, dizziness and vomiting
  - Fatigue and decreased appetite
  - Joint pain, muscle cramps and headaches
  - Depression (including suicidal thoughts)
  - Rashes, hives and swelling around the face
  - Liver damage
  - Pnuemonia

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Antagonist Medication: Vivitrol

- For extreme stomach pain, vomiting or diarrhea, or if the area of injection becomes red or painful, prescriber should be notified.
- Also, persons should seek medical assistance if the following side-effects appear since they might be indicative of liver damage:
  - Dark or tea-colored urine
  - Bad stomachache
  - Light-colored bowel movements
  - Yellowing in the whites of the eyes or skin.

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Antagonist Medication: Vivitrol

- Few to no side-effects occur when administered 7-10 days after the last use of an opioid.
- Switching from Methadone or Buprenorphine to Vivitrol will require the 7-10 day abstinence in order to have no opioids in the person's system.
- If opioids are present when the injection occurs, the person will be put into withdrawal.
- The person can be prescribed medications to address w/d s/s.

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Antagonist Medication: Vivitrol

- Vivitrol blocks opioids from activating the opiate receptors in the brain, therefore it takes away the reward of getting high.
- It may not stop drug-craving. Person should be highly motivated to stay in recovery.
- Prior to the first dose, the person should have a physical examination in order to ensure that the liver will adequately and safely processed.

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Antagonist Medication: Vivitrol

- There are no withdrawal symptoms when a person stops taking Naltrexone, or misses his/her next injection.
- Some persons will take especially large amounts of opioids with the hope of being able to get high. This can lead to overdose and death.
- Naltrexone/Vivitrol will prohibit effectiveness of pain relieving narcotic medications.

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Antagonist Medication: Vivitrol

- The medication can be used for either detox protocols or maintenance.
- Length of stay on the medication is determined by the person, and can be used as long as need to prevent relapse.

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Antagonist Medication: Vivitrol
and Pregnancy

- There is insufficient information about the safety of extended-release injectable naltrexone during pregnancy and the effects of intrauterine exposure to this medication. The expert panel did not agree on whether women on naltrexone should continue to use it during pregnancy.
- Women stable on naltrexone can be offered treatment with buprenorphine or methadone to prevent return to substance use if they choose to discontinue naltrexone injections. However, this transition must be carefully managed because patients on long-acting naltrexone are no longer opioid tolerant and the falling naltrexone level will result in increasing agonist activity over time during cross-titration.

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Which Medication Makes Sense?

Comparison of OUD Medications to Guide Shared Decision-Making			
Category	**Buprenorphine**	**Methadone**	**Naltrexone**
Outcome; tx retention	Higher than without medication	Higher than without medication	Naltrexone: no difference. Vivitrol: higher that without medication.
Outcome; suppression of illicit opioid use	Effective	Effective	Effective
Outcome: overdose mortality	Lower for people in tx.	Lower for people in tx.	Unknown
Location/frequency of visits		6-7 days/wk until takehomes approved	Varies from weekly to monthly

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Which Medication Makes Sense (cont.)

Comparison of OUD Medications to Guide Shared Decision-Making			
Category	**Buprenorphine**	**Methadone**	**Naltrexone**
Misuse/diversion potential	Low in OTP's or other settings with observed administration Moderate for take-home doses	Low in OTP's or other settings with observed administration Moderate for take-home doses	None
Sedation	Low unless use of other substances	Low unless does titration is too quick or concurrent substance use	None
Risk of Respiratory Depression	Rare. Lower than with Methadone	Rare. May be elevated in first 2 weeks.	None
Risk of Precipitated W/D	Can occur if started too soon after recent use of other opioids	None	Severe w/d if abstinence inadequate before starting.
W/D sx's on discontinuation	Present; lower than methadone	Present	None
Common side effects	Constipation, vomiting, headache, sweating, insomnia, blurred vision.	Constipation, vomiting, sweating, dizziness, sedation	Difficulty sleeping, anxiety, joint pain, headache, injection site pain, toothache, liver enzyme elevation.

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Which Medication Makes Sense (cont.)

Comparison of OUD Medications to Guide Shared Decision-Making			
Category	**Buprenorphine**	**Methadone**	**Naltrexone**
Appropriate Clients	Typically for patients with OUD who are physiologically dependent on opioids.	Typically for patients with OUD who are physiologically dependent on opioids and who meet federal criteria for OTP admission.	Typically for patients with OUD who have abstained from short-acting opioids for at least 7–10 days and long-acting opioids for at least 10–14 days.
Pharmacology	Partial Agonist	Agonist	Antagonist
Client Education	•That they will need to be in opioid withdrawal to receive their first dose to avoid buprenorphine-precipitated opioid withdrawal. •About the risk of overdose with concurrent benzodiazepine or alcohol use, with injecting buprenorphine, and after stopping the medication.	•That their dose will start low and build up slowly to avoid oversedation; it takes several days for a given dose to have its full effect. •About overdose risk in the first 2 weeks of treatment, especially with concurrent benzodiazepine or alcohol use, and after stopping the medication.	That they will need to be opioid f ree for at least7–10 days for short-acting opioids and at least10–14 days for long-acting opioids before their first dose to avoid XR-NTX-precipitated opioid withdrawal (which may require hospitalization). •About the risk of overdose after stopping the medication.

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Which Medication Makes Sense (cont.)

Comparison of OUD Medications to Guide Shared Decision-Making			
Category	**Buprenorphine**	**Methadone**	**Naltrexone**
Administration	Daily (or off-label less-than-daily dosing regimens) administration of sublingual or buccal tablet or film. Subdermal implants every 6 months, for up to 1 year, for stable patients. Monthly subcutaneous injection of extended-release formulation in abdominal region for patients treated with transmucosal buprenorphine for at least 1 week.	Daily oral administration as liquid concentrate, tablet, or oral solution f rom dispersible tablet or powder (unless patients can take some home).	Every 4 weeks or once-per-month intramuscular injection.
Prescribing	Physicians, nurse practitioners (NPs), and physician assistants (PAs) need a waiver to prescribe. Any pharmacy can fill a prescription for sublingual or buccal formulations. OTPs can administer/ dispense by OTP physician order without a waiver.	SAMHSA-certified OTPs can provide methadone for daily onsite administration or at-home self-administration for stable patients.	Physicians, NPs, or PAs prescribe or order administration by qualified healthcare professionals.

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Which Medication Makes Sense (cont.)

- *Long-acting buprenorphine implants (every 6 months) for patients on a stable dose of buprenorphine are also available through implanters and prescribers with additional training and certification through the Probuphine Risk Evaluation and Mitigation Strategy (REMS) Program. Extended-release buprenorphine monthly subcutaneous injections are available only through prescribers and pharmacies registered with the Sublocade REMS Program.
- **Naltrexone hydrochloride tablets (50 mg each) are also available for daily oral dosing but have not been shown to be more effective than treatment without medication or placebo because of poor patient adherence.

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Module III – Summary

- Three effective medications are available.
- These medications have been proven to be safe and effective in the treatment of opioid addiction.
- The multidisciplinary team is critical in medication assisted treatment. Providing psychosocial and supportive treatment to patients maximizes the potential for success.

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