



OPIATES AND ADDICTION MEDICATIONS

NEW YORK STATE OFFICE OF ALCOHOLISM AND SUBSTANCE ABUSE SERVICES

Workbook prepared by:

Steven Kipnis MD, FACP, FASAM

Joy Davidoff, MPA

Reviewed by:

OASAS Methadone Planning and Policy Bureau

OASAS Methadone Treatment Program Task Force Members

Thomas Schmidt, Ph.D, CASAC

John A. Galea, Deputy Director, New York City Relations & Section
Chief, Epidemiology, Ethnography & Trend Analysis



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DEFINITIONS



Papaver Somniferum
"Poppy Plant"

- Opium
 - Fluid obtained from the poppy plant
- Opiate
 - a substance derived from opium
- Opioid
 - substance with morphine-like actions, but not derived directly from the poppy plant



OPIATES

- OPIUM COMES FROM THE POPPY PLANT - PAPAVER SOMNIFERUM
 - An erect herbaceous annual or biennial which grows in 3 major areas of the world: Southeast Asia, Middle East, and Latin and South America
 - 50 to 150 cm tall
 - Stems are slightly branched
 - Leaves are large, erect, and oblong
 - Petals are 4 - 8 cm in length
 - Petal colors are white, pink, purple and violet



PROCESS OF DERIVING OPIUM FROM POPPIES



Papaver somniferum Pod

Photo by Eric Clausen, © 2000 Erowid.org



After flowering, the petals drop in a few days leaving bulbous green capsules atop the stalks. These are the seed pods.



PAPAVER SOMNIFERUM



Incisions are made in the pods and the milky fluid that oozes out is air dried. This must be done while the pods are still green.



OPIATES ARE DERIVED FROM THE POPPY PLANT

- CONTENTS OF THE POPPY
- POD FLUID:
- Morphine 4 - 21 %
- Codeine 1 - 25%



*There are at least 20 other alkaloids, such as Thebaine, in the fluid.



OPIATES ARE DERIVED FROM THE POPPY PLANT EXCEPT IN

- New “No-Morphine” plant
 - Called TOP1 or Norman
 - Thebaine and Oripavine are produced in increased concentrations



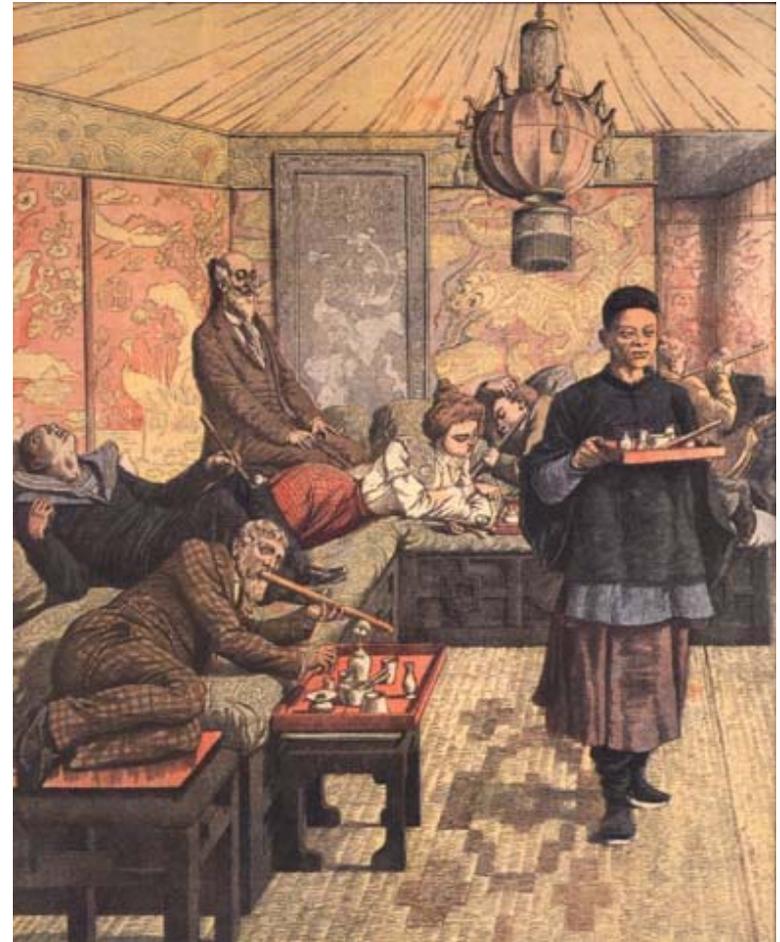
OPIUM HISTORY

- 4000 – 2000 BC: Opium believed to be discovered in the Mediterranean area.
- 1500 BC: Egyptian papyri list opium as one of 7000 remedies.
- 1st century AD: Opium poisoning described.
- 1655: Portuguese physician, Acosta, wrote of withdrawal sickness.
- 1701: British physician, John Jones, advocated moderation in the use of the drug in order to avoid the discomforts with its continued use.
- 1805: Morphine isolated as the main active ingredient in opium.

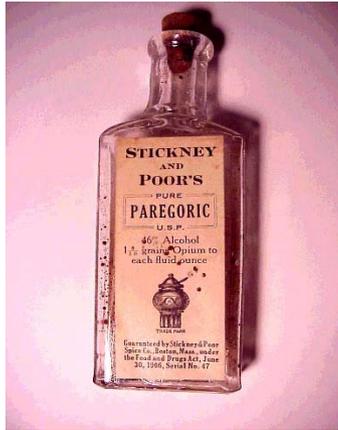


OPIUM HISTORY

- 1850 – 1865 thousands of Chinese laborers immigrated to the US and brought the habit of opium smoking with them (Opium Den shown on right)
- Civil war soldiers became opioid dependent through medical treatment – referred to as “army disease” or “soldier’s disease”
- It was estimated that the total number of opium users in the U.S. in 1868 was 100,000
- Heroin was first synthesized in 1874 by the chemist, C.R. Alder Wright
 - First commercial production in 1898 by the Bayer Pharmaceutical Company
 - 1898: Heinrich Dreser announced that tests confirmed heroin was ideal for treating bronchitis, emphysema, asthma, tuberculosis, and was a cure for opium and morphine dependence



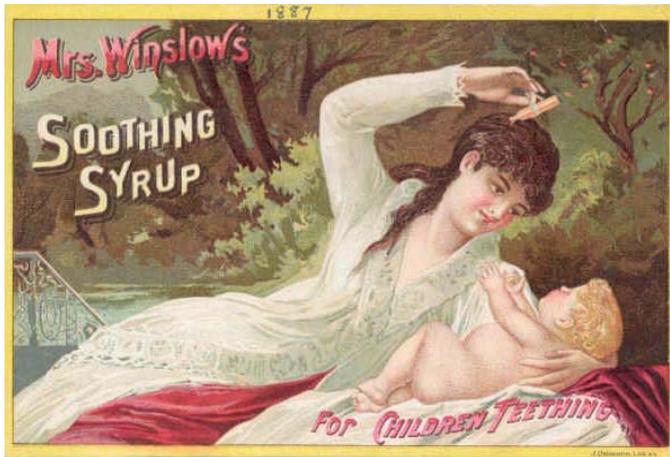
HISTORICAL OPIATE PRODUCTS



This bottle of Stickney and Poor's [paregoric](#) was distributed much like the spices for which the company is better known. McCormick also manufactured and sold paregoric, which is a mixture of opium and alcohol. Doses for infants, children, and adults are given on the bottle. At 46% alcohol, this product is 92 proof which is pretty potent in itself.



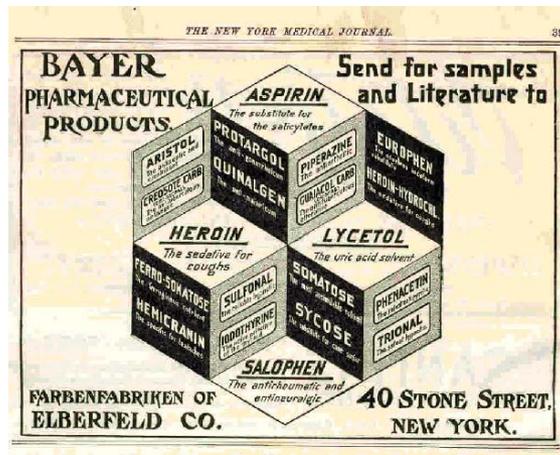
HISTORICAL OPIATE PRODUCTS



Many products, marketed for adults and children, were sold for pain and cough relief. They all contained opium.



HISTORICAL OPIATE PRODUCTS



There were ads in papers and journals for Bayer's many products, including aspirin and heroin.

BAYER
PHARMACEUTICAL PRODUCTS.

We are now sending to Physicians throughout the United States literature and samples of

ASPIRIN

The substitute for the Salicylates, agreeable of taste, free from unpleasant after-effects.

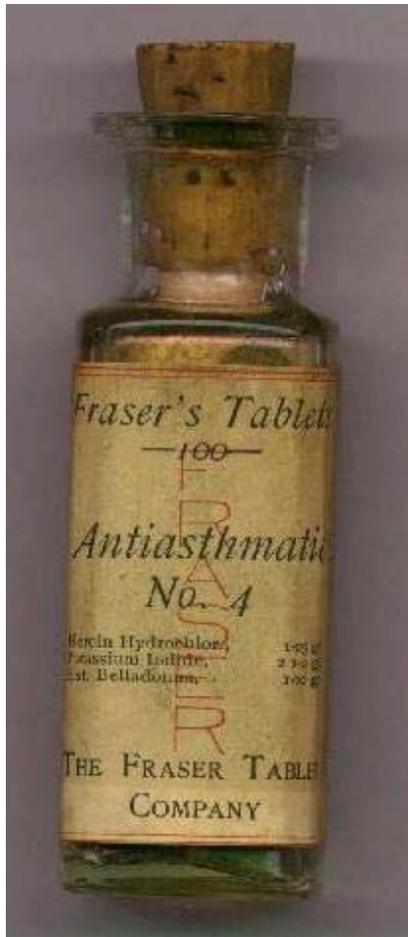
HEROIN

The Sedative for Coughs,
HEROIN HYDROCHLORIDE
Its water-soluble salt.
You will have call for them. Order a supply from your jobber.

Write for literature to
FARBENFABRIKEN OF ELBERFELD CO.
40 Stone Street, New York,
SELLING AGENTS



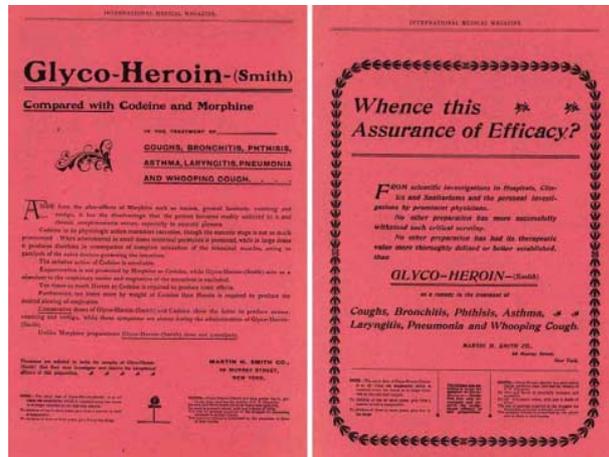
HISTORICAL OPIATE PRODUCTS



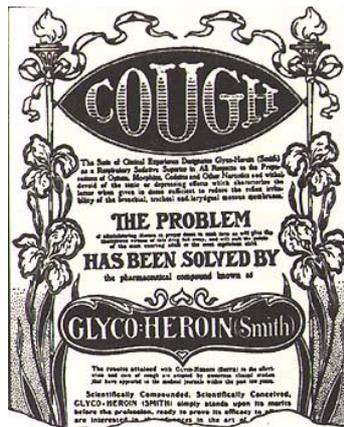
These heroin tablets, manufactured by the Fraser Tablet Company, were marketed for the relief of asthma.



1903 ADS



These magazine advertisements are for **Glyco-Heroin** manufactured by **Martin H. Smith Company** (New York). Heroin was widely used not only as an analgesic, but also as a remedy for asthma, coughs, and pneumonia. Mixing heroin with glycerin (and often adding sugar or spices) made the bitter-tasting opiate more palatable for oral consumption. (From *International Medical Magazine*, January, 1902.)



FEDERAL LAWS ASSOCIATED WITH THE CONTROL OF NARCOTICS

- **1914 – HARRISON ACT**
 - First federal legislation to regulate and control the production, importation, sale, purchase and free distribution of opium and drugs derived from opium
- **1922 – NARCOTIC DRUG IMPORT AND EXPORT ACT**
 - Intended to eliminate the use of narcotics, except for medical and other legitimate purposes
- **1924 – HEROIN ACT**
 - Made it illegal to manufacture heroin
- **1942 – OPIUM POPPY CONTROL ACT**
 - Prohibited growing opium poppies in the US, except under license



FEDERAL LAWS ASSOCIATED WITH THE CONTROL OF NARCOTICS

- 1956 – NARCOTIC CONTROL ACT
 - Intended to impose very severe penalties for those convicted of narcotics or marijuana charges
- 1966 – NARCOTIC ADDICT REHABILITATION ACT
 - Enhanced federal efforts to treat and rehabilitate narcotic addicts through three programs
 - These programs provided voluntary and pretrial civil commitment and sentencing to treatment of convicted addicts
- 1972 – DRUG ABUSE OFFICE AND TREATMENT ACT
 - Established NIDA
 - Established NIMH
- 1973 – METHADONE CONTROL ACT
 - Placed controls on methadone licensing
- 1973 – DRUG ENFORCEMENT ADMINISTRATION
 - BUREAU OF NARCOTICS AND DANGEROUS DRUGS was remodeled to become the DEA



FEDERAL LAWS ASSOCIATED WITH THE CONTROL OF NARCOTICS

- 1974 – NARCOTIC ADDICT TREATMENT ACT
 - Required separate DEA registrations for physicians who want to use approved narcotics
- 1986 – EXECUTIVE ORDER 12564
 - Mandated a drug-free workplace program
- 1988 – ANTI DRUG ABUSE ACT
 - Established the OFFICE OF NATIONAL DRUG CONTROL POLICY (ONDCP) in the executive office of the President of the United States to oversee all federal policies regarding research about control of drug abuse
- 2000 – CHILDREN’S HEALTH ACT
 - A section of this act dealt with drug addiction treatment (DATA)
 - Allowed qualified physicians to prescribe medications classified as schedule III, IV and V narcotics for treatment of addiction. This is the law that allows and regulates buprenorphine use in addiction treatment.



THE PRESENT

- 810,000 -1,000,000* heroin addicted individuals in the United States (2004)
 - 25% are involved in some type of treatment

*These are estimates; the incidence of heroin addiction may be under reported.



THE PRESENT

- Opiate-dependent patients are not just using heroin, but other narcotic drugs as well!
 - Data from the Drug Abuse Warning Network (DAWN*) revealed that narcotic mentions in ERs were higher than heroin mentions in the last several years. This highlights the fact that the opiate problem is not only related to heroin, but also to narcotic analgesics (pain medications) that are being diverted and abused.

*DAWN is a public-health surveillance system that monitors: drug-related visits to hospital emergency departments and drug-related deaths investigated by medical examiners and coroners.



HEROIN AND NARCOTIC (ANALGESIC) USE IN NYS - DAWN DATA

Heroin use in NYS is still high because the purity of heroin is extremely high (65%) and can be snorted instead of used intravenously.



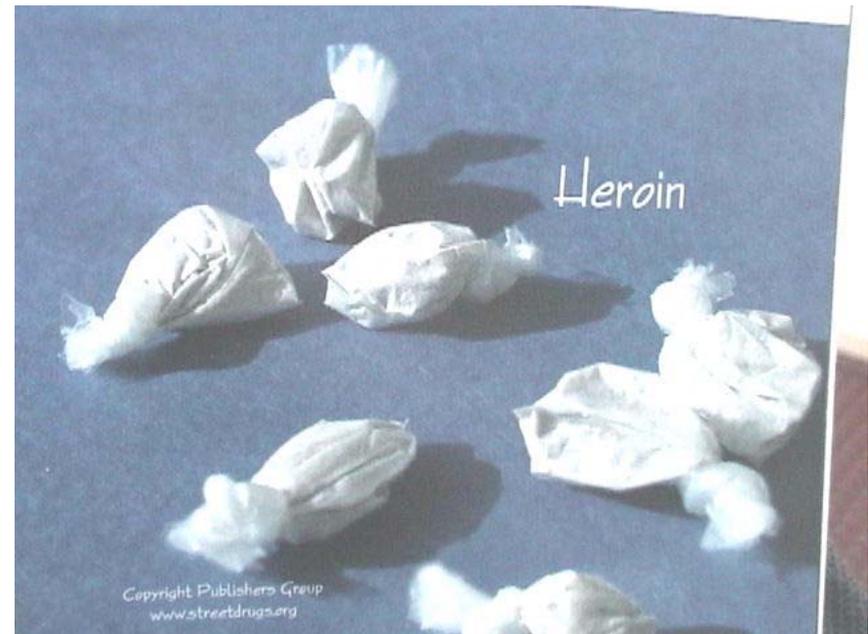
MARKETING AND DISTRIBUTION – THE PROCESS

- Growers
 - Southeast Asia
 - Middle East
 - Latin and South America
- Shippers
- Manufacturers
- Large wholesale buyers
 - Prices per kilo depend on the purchase amount
- Mid-range buyers
 - Dilute or “step on” the heroin using white substances that are not easily detected
 - These substances or “Cut” can be – lactose, mannitol, talc
- Continuous dilution can occur all the way down to the point of sale
 - Bag = 1/10 to 1/15 gram
 - 10 bags = bundle



MARKETING AND DISTRIBUTION

- Street retail
 - Bag in NYS may be a “cap” or “1/4 spoon” in other parts of US
 - “Dope” in NYS may be “smack” or “junk”

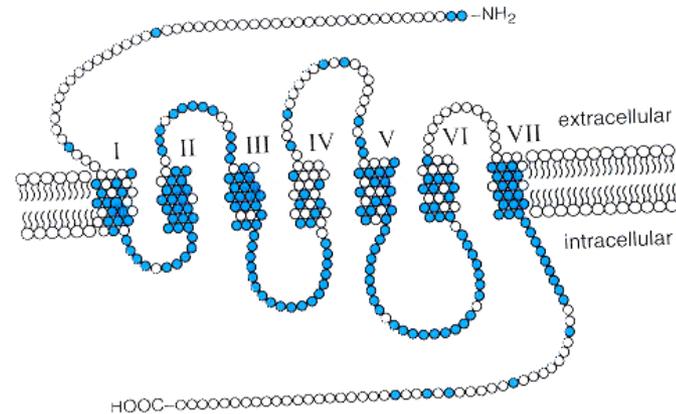


OPIATE PHARMACOLOGY



OPIATE PHARMACOLOGY

- Opiates work in the brain at specific “opiate receptors”
 - There are several types of opiate receptors but the main receptor is called “Mu”
 - Binding can cause full stimulation or effect at the receptor (agonist), or a partial effect (partial agonist) or block the effect of the receptor (antagonist)



Schematic of Mu Opiate Receptor

Source: Goodman and Gillman 9th ed, p. 526



OPIATE RECEPTORS AND ACTIVATION EFFECT

Mu₁ (μ₁)

analgesia, euphoria

Mu₂ (μ₂)

constipation, respiratory depression

Kappa

spinal analgesia, dysphoria

Delta

analgesia thru the endorphin, enkephalin and dynorphin system



RECEPTOR BINDING AT MU RECEPTOR

Agonist Morphine-like effect (e.g. heroin, weak binding except for Fentanyl)

Partial Agonist Weak morphine-like effects with strong receptor affinity (e.g. buprenorphine)

Antagonists No effect in absence of an opiate or opiate dependence (e.g. naltrexone)



EFFECT OF COMMON OPIATES AT MU RECEPTOR

Heroin, morphine, methadone

Agonist

Buprenorphine

Partial Agonist

Naltrexone, Nalmefene

Antagonists



MORPHINE

- Low oral bioavailability (25%)
- Crosses into the brain slower than heroin; addicted person would always choose heroin over morphine
- Active metabolite, or breakdown product, is morphine-6-glucuronide
 - Gets into the brain quicker than morphine
 - 10X more potent than morphine



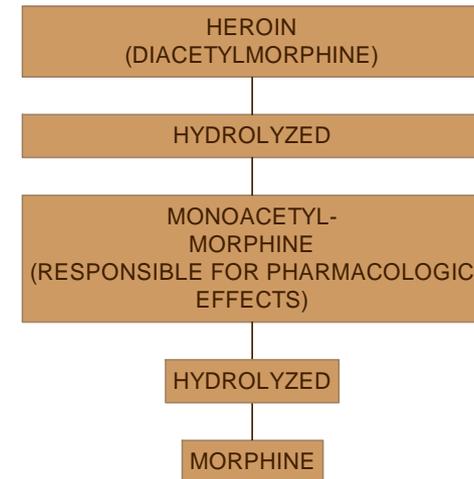
CODEINE

- Chemically known as: 3 – O – methyl morphine
- 10% metabolized into morphine
- Weaker Mu (main opiate receptor in the brain) agonist
- Was a cough medication ingredient until dextromethorphan was introduced
 - Cough suppression is not an opiate-receptor effect; we do not know how cough suppression works.



HEROIN

- Heroin is chemically known as diacetylmorphine
- Heroin is considered a prodrug because it is broken down into an active drug



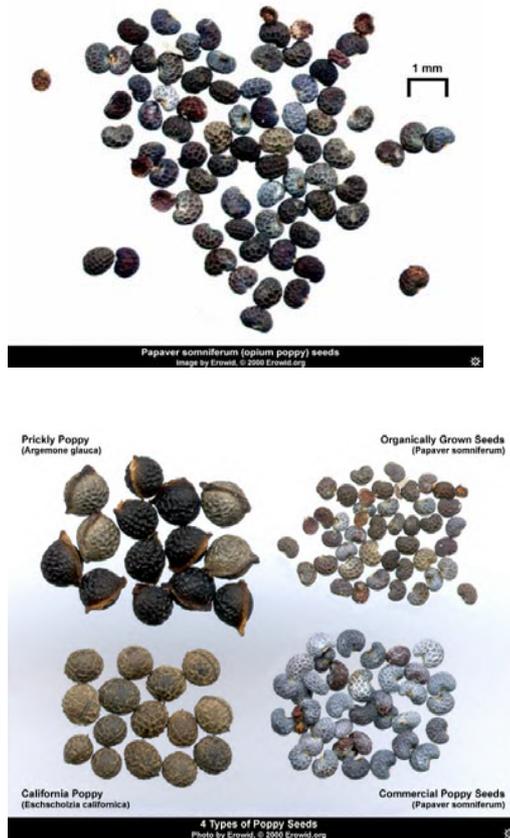
HEROIN

- HEROIN USE - URINE TOXICOLOGY CAN SHOW:
 - Free morphine
 - Morphine Glucuronide
 - Free codeine
 - 6 – Monoacetylmorphine (6 – MAM)
 - This metabolite, or breakdown product, is only seen with heroin use and no other opiate. It has a very short half – life* and is difficult to detect after heroin use.

*Half – life is the time it takes to break down 50% of the amount of the consumed substance by the body's metabolic processes.



OPIATES



- Poppy seeds, if eaten, can show up as a positive urine drug screen for morphine and codeine
- Depends on the amount of poppy seeds consumed and the content of morphine and codeine in that particular type of seed



OPIATES

- Morphine and/or codeine use may be found on evaluation of a urine specimen if the patient:
 - Used heroin
 - Ingested poppy seeds
 - In some studies, only 2 - 3 poppy-seed bagels or poppy-seed bread need to be eaten. It depends on the amount of poppy seeds in the cooked item.
 - Used a codeine containing product such as Tylenol #3
 - Used a morphine- containing product



MORPHINE AND CODEINE URINE TOXICOLOGY GUIDELINES

- High levels of total morphine in urine (>5000 ng/ml) are indicative of abuse of opiate product (heroin, morphine, codeine).
- High levels of codeine (>300 ng/ml) with a morphine-to-codeine ratio <2 is indicative of codeine use, not poppy-seed ingestion
- Presence of 6 – Monoacetylmorphine in urine is a positive indication of heroin use.
- When diagnosing a positive drug screen for opiates as a result of heroin use, clinical evidence of heroin use is necessary, unless 6-MAM is present.



MORPHINE AND CODEINE URINE TOXICOLOGY GUIDELINES

- Not all opiates contain or metabolize into morphine and/or codeine, a fact that is occasionally not known by a patient when he/she is trying to explain a positive drug test result.
 - Drugs/medications that do not metabolize to morphine and codeine include:
 - Hydrocodone (Lortab, Vicodin)
 - Hydromorphone (Dilaudid)
 - Methadone
 - Oxycodone (Oxycontin, Percodan*)

*Oxycodone in combination with aspirin



OPIATES

- What are the opiate user's desired effects?
 - Sedation
 - Euphoria
 - Analgesia



OPIATE EFFECTS

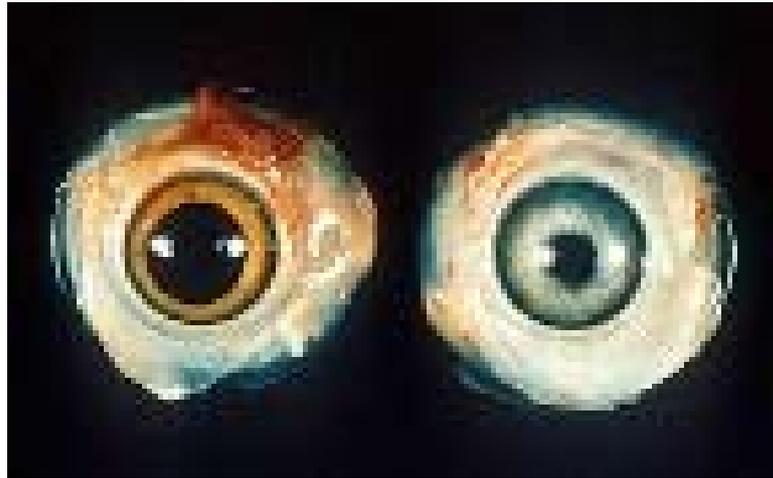
- **AFTER IV INJECTION**
 - Warm skin rush
 - Pruritis (severe itchiness), especially with morphine use which releases histamines
 - Pleasure, relaxation and satisfaction in 45 seconds



OPIATE INTOXICATION, OVERDOSE AND WITHDRAWAL



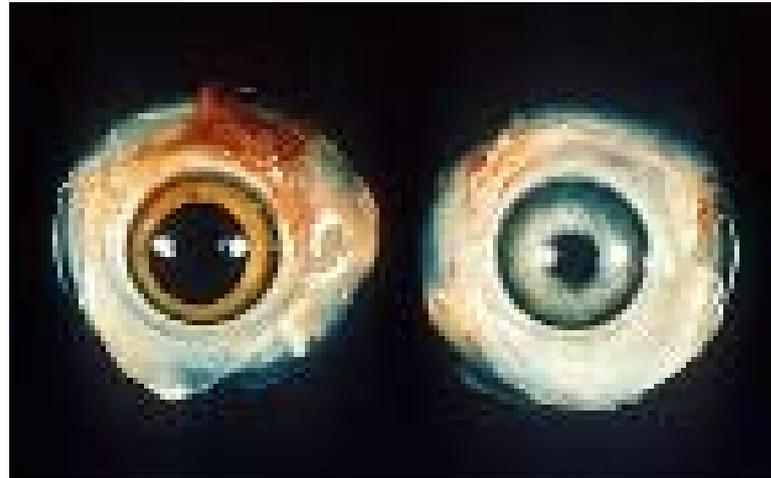
INTOXICATION OR WITHDRAWAL?



Always look at the pupils; the pupil size can give very good clinical information.



INTOXICATION OR WITHDRAWAL?



Withdrawal

Intoxication



OPIATE INTOXICATION

- **MOST COMMON**
 - Miosis (small pupils; except with Demerol use which causes paralysis of the ciliary body and pupils dilate)
 - Nodding
 - Hypotension
 - Depressed respiration
 - Bradycardia (slow heart rhythm)
 - Euphoria
 - Floating feeling



OPIATE OVERDOSE

- CLASSIC TRIAD SEEN IN OVERDOSE
 - Miosis
 - Coma
 - Respiratory depression
- Pulmonary edema
- Seizures
 - Demerol, Darvon, Talwin use



OPIATE OVERDOSE TREATMENT

- NARCAN
 - 0.4 mg IV push, if no response, then 2 mg IV push every 2 - 3 minutes until a total dose of 10 mg is given or a response.



3 OUT OF 10 UNTREATED HEROIN USERS DIE OF:

- Overdose
- Murder
- Suicide
- Street crime



OPIATE WITHDRAWAL

- In general, opiate withdrawal signs and symptoms are the same for all opiates; what differs is the time of onset and the length and intensity of withdrawal.
- The withdrawal is divided into early, middle and late phases to show the progression of symptoms when the patient is not treated.



OPIATE WITHDRAWAL - EARLY

- Lacrimation (eyes water)
- Yawning
- Rhino rhea (runny nose)
- Sweating

Sense Of Anxiety And Doom, Though Not Life Threatening



OPIATE WITHDRAWAL - MIDDLE PHASE

- Restless sleep
- Dilated pupils (mydriasis)
- Anorexia
- Gooseflesh
- Irritability
- Tremor



OPIATE WITHDRAWAL - LATE PHASE

- Increase in all previous signs and symptoms
- Increase in heart rate
- Increase in blood pressure
- Nausea and vomiting
- Diarrhea
- Abdominal cramps
- Labile mood
- Depression
- Muscle spasm
- Weakness
- Bone pain



HEROIN WITHDRAWAL TIME FRAME

- 1/2 life is 2 - 3 hours
- Onset after last dose is 8 - 12 hours
- Peak is 48 hours
- Duration is 5 - 10 days

*Longer-acting opiates have more prolonged $\frac{1}{2}$ lives and the onset of withdrawal is delayed as compared to heroin.



PROTRACTED OPIATE WITHDRAWAL

- CAN LAST UP TO 9 MONTHS WITH SOME OR ALL OF THE FOLLOWING:
 - Weight gain
 - Increased basal metabolic rate
 - Decreased temperature
 - Increased respiratory rate
 - Increased blood pressure
 - Menstrual irregularities (secondary to increased prolactin hormone levels)



OPIATE WITHDRAWAL TREATMENT

- CAN BE INPATIENT OR AMBULATORY DETOX
 - Involves the use of medication to dampen the increased signs of opiate withdrawal
 - Clonidine, an antihypertensive medication, has been used in many older protocols
 - Buprenorphine has recently been approved for use by authorized physicians
 - Methadone can be used if a detoxification program has the proper approvals



OPIATE WITHDRAWAL TREATMENT

- When treating withdrawal, prn (as needed) medications should always be considered an important component of the treatment
 - Examples include:
 - Vistaril for mild to moderate anxiety
 - Oxazepam (15-30 mg q 6 hours) or other benzodiazepine if severe anxiety
 - Motrin for muscle and joint aches
 - Tigan for nausea
 - Kaopectate for diarrhea
 - Bentyl for abdominal cramps



OPIATE COMPLICATIONS OF USE

- Many of the complications of opiate use are due to the route of use and the lifestyle of the user, not the drug
 - **NEUROLOGIC**
 - Toxic amblyopia (optic nerve pathology)
 - Mononeurpathy (dysfunction of a single nerve)
 - Polyneuropathy (dysfunction of several nerves)
 - Meningitis
 - Brain abscess
 - **DERMATOLOGIC**
 - Abscess
 - Tracks
 - Lymphangitis (swelling and dysfunction of the lymph system)
 - **PULMONARY**
 - Aspiration
 - Pneumonia
 - Lung abscess
 - Pulmonary emboli (clots going to the lung)
 - Pulmonary fibrosis (scarring of the lung)
 - Noncardiogenic pulmonary edema (lung fills with fluid not as a result of heart dysfunction)
 - **HEPATIC**
 - Hepatitis B,C,D,G
 - **INFECTIONS**
 - Endocarditis
 - Tetanus in immigrants in California



OPIATE MEDICATIONS

- OPIATE COMPARISONS (a helpful table to compare doses with equal potency)
 - 10 mg IM Morphine =
 - Codeine: 130mg IM; 200mg PO
 - Oxycodone: 15-30mg PO
 - Hydromorphone (Dilaudid): 1.5mg IM
 - Methadone: 10mg IM; 20mg PO
 - Demerol: 75mg IM; 300mg PO
 - Fentanyl: .1mg IM



OPIATE MEDICATIONS



- Hydromorphone
 - Formulations
 - Dilaudid®
 - 2, 4, 8 mg tablets, rectal suppositories, oral solution and injectables
 - Palladone®
 - 12, 16, 24, 32 mg extended release tablets
 - Schedule II
 - 2 to 8 times the analgesic potency of morphine but shorter acting and more sedating



OPIATE MEDICATIONS



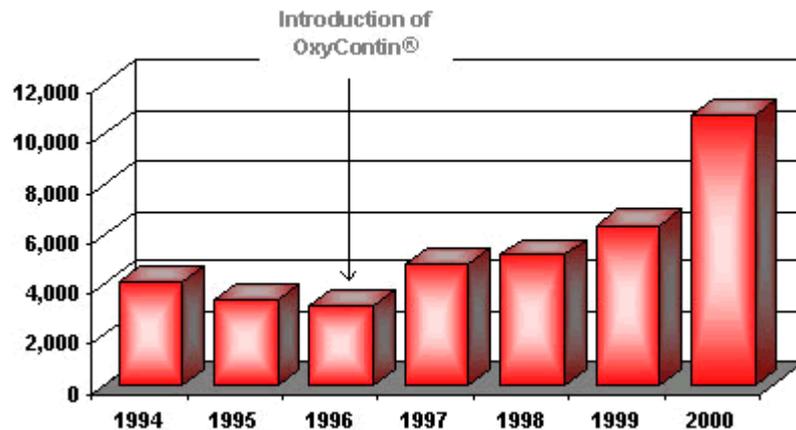
Oxycodone

- Formulations
 - Oxycontin®
 - 10, 20, 40, 80, 160 mg controlled release
 - Oxyir®
 - 5 mg immediate release
 - Percodan®
 - Combined with aspirin
 - Percocet®
 - Combined with acetaminophen
- Schedule II
- Oral, crushed and sniffed or dissolved in water and injected
 - Bypasses the slow release quality



THE OXYCONTIN PROBLEM

Table 1: Oxycodone DAWN ED Episodes



- Pain Therapeutics Inc. has reformulated oxycodone (Remoxy® - 3 substances were added to make a viscous fluid) so as to impair attempts at liberating the active ingredient from the sustained release formula.
- Other ideas
 - Add naloxone
 - Add capsaicin (from chili peppers) so that snorting, chewing or injecting would be unpleasant



OPIATE MEDICATIONS



Hydrocodone

- Formulations
 - Hycodan ®
 - Lorcet ®
 - Lortab ®
 - Tussionex ®
 - Vicodan ®
- Used as a Schedule II analgesic and antitussive
- Potency equals morphine



OPIATE MEDICATIONS



- Dextropropoxyphene
 - Formulations
 - Darvon®
 - Schedule IV
 - 1/2 to 1/3 the potency of codeine
 - Cannot be used in withdrawal protocols for opiate-dependent patients to replace the opiate, according to federal law



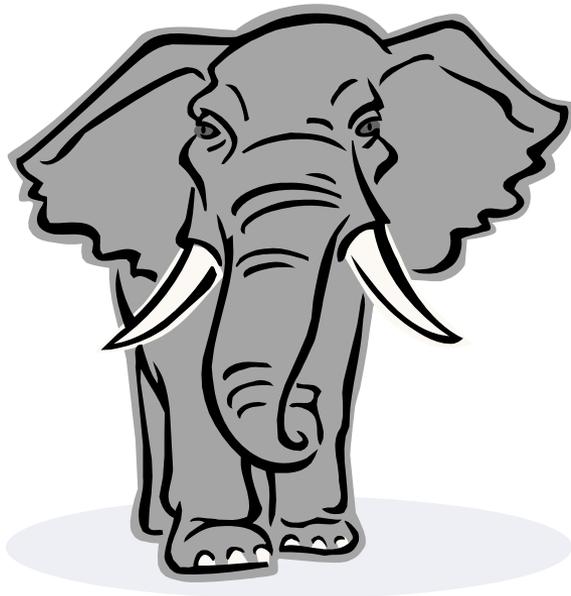
OPIATE MEDICATIONS

Fentanyl

- Formulations
 - Sublimaze ®
 - IV anesthetic
 - Duragesic ®
 - Transdermal patch
 - Actiq ®
 - “lollipop”
- All of the above have about 80 times the analgesic potency of morphine
- Routes of use include IV, smoked, snorted, oral or transdermal



OPIATE MEDICATIONS



- Fentanyl Analogs
 - Carfentanil
 - Wildnil® is an analog of Fentanyl and is used in Veterinary Medicine to immobilize large animals
 - At least 12 different Fentanyl analogs



OPIATE MEDICATIONS



- Pentazocine
 - Formulations
 - Talwin ®
 - Talwin NX ®
 - A formulation combining naloxone and Talwin to limit IV use
 - A partial agonist
- Butorphanol
 - Formulations
 - Stadol ® injectable
 - Stadol NS ® nasal spray



OPIATES

- **SPECIAL CASE**

- Clandestine labs making a Meperidine analog (MPPP) synthesized it incorrectly into MPTP which when used can lead to an irreversible Parkinson - like syndrome
- Meperidine metabolite, normeperidine, is toxic especially if given with an MAO inhibitor. Toxicity has been seen in post – operative patients given meperidine as an analgesic. Normeperidine can cause:
 - Seizures, tremor, confusion, increased reflexes, startle



CURRENT STATE OF TREATMENT: PROGRAMS



CURRENT STATE OF TREATMENT: PROGRAMS

- PROGRAMS*
 - METHADONE TREATMENT
 - PART 816 CRISIS SERVICES
 - OUTPATIENT TREATMENT
 - INPATIENT/RESIDENTIAL TREATMENT

*Opiate-dependent patients are treated in all OASAS levels of care.



METHADONE MAINTENANCE

- Methadone was first used in the 1960's by Drs. Dole and Nyswander. They believe that heroin addiction is a medical disease and, as such, can be treated with medications.
- Methadone maintenance for patients who are opiate-dependent was the impetus for the development of OASAS Methadone Treatment Programs.
- Federal and state regulations must be followed
- Rules of admission
 - 1 year addiction unless pregnant
 - 18 or older unless 2 prior treatment programs
- Other medications, as appropriate for the patient, can be offered.



METHADONE MAINTENANCE

- Oversight and Accreditation
 - Methadone treatment programs (MTP) must be approved by, and comply with, regulations from the US Center for Substance Abuse Treatment (CSAT), US Drug Enforcement Administration (DEA) and the NYS Office of Alcoholism and Substance Abuse Services (NYS OASAS)



METHADONE MAINTENANCE

- Oversight and Accreditation
 - As part of the CSAT certification process, all opioid treatment programs (OTP) must be accredited by an approved accreditation body:
 - Commission on Accreditation of Rehabilitation Facilities (CARF)
 - Council on Accreditation (COA)
 - Joint Commission on Accreditation of Healthcare Organizations (JCAHO)
 - Division of Alcohol and Substance Abuse Washington Department of Social and Health Services
 - Division of Alcohol and Substance Abuse State of Missouri Department of Mental Health
 - National Commission on Correctional Healthcare



METHADONE MAINTENANCE

- PHASE I
 - MEDICATION STABILIZATION
 - 3 to 9 months
 - Programs closely monitor and frequently counsel patients to help reach an effective methadone dose level and cease opioid use.
 - During this phase, programs inform patients about methadone and available services. Programs focus on medical issues and stable living arrangements.



METHADONE MAINTENANCE

- PHASE I
 - METHADONE INDUCTION
 - Safe induction and prevention of overdose is based on:
 - Careful diagnosis of current opioid physical dependence
 - Assessing the extent of opioid tolerance
 - Daily assessment during induction
 - Dose adjustments, with an understanding of the build up of methadone until a steady – state is reached (Payte 2003 Heroin Add & Rel Clin Probl)



METHADONE MAINTENANCE

- PHASE I (*Payte 2003 Heroin Add & Rel Clin Probl*)
 - 30 mg is a fairly typical initial dose for those with known tolerance
 - Increases in dose can be given to give opiate withdrawal relief in the peak hours (3 – 8 hours after initial dose)
 - In early induction, the relief will not likely last past 10 – 12 hours, but the levels will rise until steady state is reached (5 – 8 days at the same dose)
 - If during the first few days, the patient is not experiencing withdrawal symptoms after 24 hours, the dose might be too high and needs to be reconsidered. (steady state is not taught.)

Methadone Maintenance Treatment, Initial Dose	
Degree of Tolerance	Dose Range
Non - tolerant	10 mg +/- 5 mg
Unknown tolerance	20 mg +/- 5 mg
Known tolerance	20 – 40 mg



METHADONE MAINTENANCE

- PHASE II
 - SOCIAL INTEGRATION
 - 9 to 24 months
 - Programs help patients alter pre-treatment behavior and adopt positive habits and lifestyles, while stabilized on methadone.
 - During this phase, programs continue to deliver frequent counseling, if needed.
 - Programs focus on vocational training, educational assistance, or other productive activities that help patients become self-sufficient.



METHADONE MAINTENANCE

- PHASE III
 - MAINTENANCE/ONGOING SUPPORT
 - 24 to 48 months or longer
 - Patients may receive counseling services less frequently, if appropriate, while stabilized on methadone, as needed.
 - During this phase, programs focus on late-stage treatment needs, including continued maintenance, or tapering, or other personal issues presented by the patient.



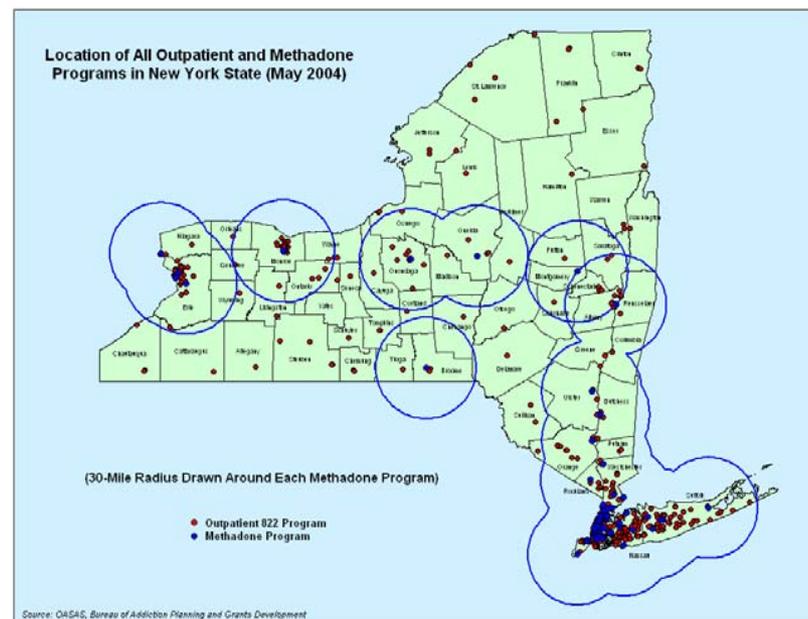
METHADONE MAINTENANCE

- **CONCURRENT TREATMENT ON SITE**
 - Individual treatment planning, behavioral individual, group and family counseling, vocational/educational programming, 12-Step meetings and medical care are offered
- **OFFSHOOT IS MEDICAL MAINTENANCE**
 - At a physician's office
 - 28-day take-home of medication
 - Medical problems addressed



WHERE ARE METHADONE TREATMENT PROGRAMS LOCATED IN NYS?

- In NYS, there are 122 approved Methadone Treatment Programs providing treatment for approximately 46,000 patients
 - 91 programs are located in NYC with available treatment for almost 38,000 patients
 - The remaining programs are in major metropolitan areas on Long Island, in Westchester County and in several cities in upstate NY
 - There are few programs in the rural areas of the state



2003 Admissions into MTP's in NYS

Admissions: 13,340	
Age Range	No. & %
56/+	576 (4%)
36-55	8909 (67%)
26-35	2964 (22)%
21-25	768 (6%)
19-20	97 (1%)
17-18	23 (<1%)
15-16	1 (<1%)



2003 Admissions into MTP's in NYS

Age of First Use:	
Age Range	%
<15	12%
15-19	35%
20-29	34%
30<	19%



2003 Admissions into MTP's in NYS

Admission Demographics:

Male	70%
Female	30%
Latino	47%
White	27%
African-American	24%
Other	2%



2003 Admissions into MTP's in NYS

Educational Data:

Non H.S. Graduate	44%
H.S. Graduate/GED	37%
More than H.S./GED	18%



PHYSICIAN OFFICE-BASED TREATMENT

- Methadone medical maintenance can be provided, under specific guidelines, in physician offices.
- Buprenorphine, according to DATA 2000 and NYS regulation, can also be provided by physicians.



CURRENT STATE OF TREATMENT: ADDICTION MEDICATIONS



CURRENT STATE OF TREATMENT: ADDICTION MEDICATIONS

What do we know about opiate-dependence treatment using addiction medications?



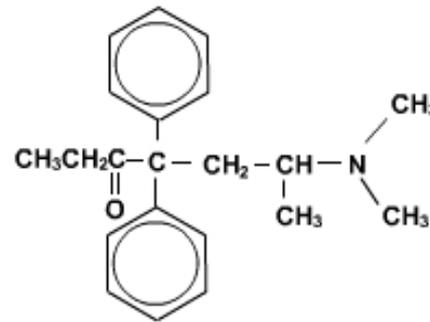
CURRENT STATE OF TREATMENT: ADDICTION MEDICATIONS

- We know that addiction/dependence is a brain disease that is Manifested by:
 - Loss of control over the use of a substance
 - Time spent in trying to obtain the substance
 - Biopsychosocial dysfunction
 - Continued use despite problems
 - Associated denial and dishonesty
 - Progressive and potentially fatal
- This medical model allows one to treat the disease with medications, realizing that addiction is a complex disease where interdependent roles are played by the host, the addictive agent and the environment.



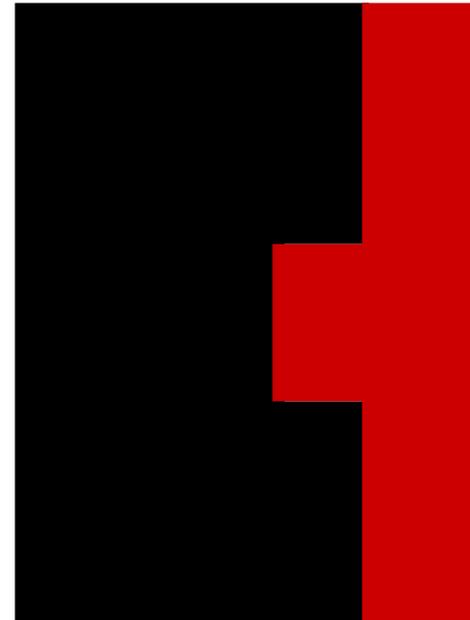
CURRENT STATE OF TREATMENT: ADDICTION MEDICATIONS

- Methadone, a synthetic opiate, was invented in Germany around the WWII era. It was first used in addiction treatment in the 1960's by Drs. Dole and Nyswander. It was their belief that treatment of the cravings and withdrawal in the heroin-addicted person was a very important factor in the successful outcome of the opiate dependent patient.
- Since that point in time, methadone and methadone treatment has been stigmatized as substituting one drug for another, despite the fact that it is an extremely successful treatment modality.



CURRENT STATE OF TREATMENT: ADDICTION MEDICATIONS

- Pharmacotherapy using methadone is based on agonist maintenance. LAAM was another agonist that was previously used, though pharmaceutical production has ceased.



AGONIST – FULL MU EFFECT
(Agonist in red fits perfectly into the receptor)



THEORIES OF NARCOTIC ADDICTION IMPLICATIONS OF METHADONE MAINTENANCE

Prevents the “**off and on**” switch of fluctuating opioid blood levels that lead to euphoria alternating with cravings...

Continuous occupation of the endogenous ligand-opioid receptor system allow interacting physiological and behavior systems to become normal.

The patient is functionally normal.

Dole, Vincent P.
JAMA,
Nov 25, 1988
Vol. 260, No. 20



RATIONALE FOR OPIOID AGONIST MEDICATIONS

- OPIOID AGONIST TREATMENT
 - Most effective treatment for opioid dependence
 - Controlled studies have shown significant
 - Decreases in illicit opioid use
 - Decreases in other drug use
 - Decreases in criminal activity
 - Decreases in needle sharing
 - Improvements in prosocial activities
 - Improvements in mental health



METHADONE

- Methadone blood levels are available to see if the patient has a therapeutic level. P= peak level where blood is drawn 2 hours after the methadone is given. T = trough where the blood is drawn immediately before the methadone is given (both on the same day).
 - Increase methadone dose if P/T ratio < 2.5 and trough less than 200
 - Maintain dose of methadone if trough 200- 480 with P/T < 2.5
 - Decrease dose of methadone if trough > 480 and P/T < 2.5
 - Split dose of methadone if P/T > 2.5
 - Split and increase dose of methadone if trough < 200 and P/T > 2.5
 - Split and decrease dose of methadone if peak > 960 and P/T > 2.5
 - (If split give 100% in am and 50% pm first day, then 50% twice a day for the next days)

* Use the above as a guide, but always listen to the patient and evaluate what is happening with him/her.



METHADONE

- Methadone levels go down with the concurrent use of:
 - Carbamazepine
 - Alcohol
 - Pentazocine
 - Phenobarbital
 - Dilantin
 - Rifampin
 - Rifabutin
- Methadone levels go up with the concurrent use of:
 - Tagamet
 - Ketoconazole
 - Erthyromycin



METHADONE

If a patient is unable to eat, such as after surgery, and he or she is maintained on methadone, give 80% of the total dose (40% in the morning and 40% in the evening by intramuscular injection).



METHADONE

- Methadone is also an excellent analgesic for those patients who suffer from chronic pain.
- Care must be used when dosing methadone and especially when converting a patient from another analgesic to methadone (as the long half-life can cause accumulation of the medication and an overdose possibility)

* See the Pain and the Substance Abuser OASAS CD for more information on pain management



LAAM

- 1 - alpha - acetylmethadol acetate
- Long-acting, orally active analog of methadone, originally approved for use by the FDA in 1993 but is **not being manufactured at present** by Roxanne Laboratories, Inc.
- LAAM dose is 1.2 – 1.3 the dose of methadone



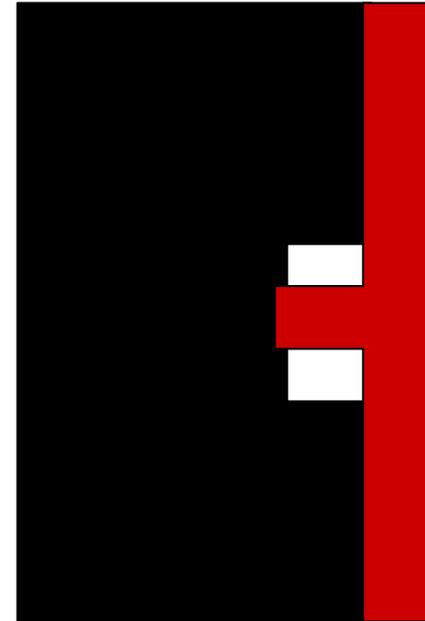
LAAM

- Advantages over methadone
 - Slower onset
 - Longer duration of action
 - Administer 3 times /week so less diversion
 - 1.2 - 1.3 times the patient's usual methadone dose
- Disadvantages
 - ROXANNE/FDA ISSUED BLACK BOX WARNING AS THERE IS THE POTENTIAL FOR CARDIAC ARRHYTHMIAS (TORSADES de POINTES)



CURRENT STATE OF TREATMENT: ADDICTION MEDICATIONS

- Pharmacotherapy using partial agonists, such as buprenorphine, offer another alternative to the treatment of the opiate-dependent patient.
- Partial opioid agonist
 - At low dose, acts as an agonist
 - At high doses, acts as either an agonist or antagonist
 - Partial agonist at the Mu receptor
 - Very high affinity for Mu receptor
 - Will displace morphine, methadone



**Partial - Agonist – partially blocks Mu effect
(Partial agonist in red blocks/activates the receptor only partially)**

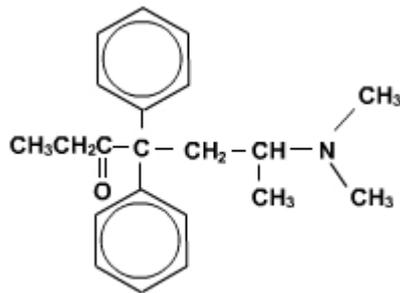


BUPRENORPHINE

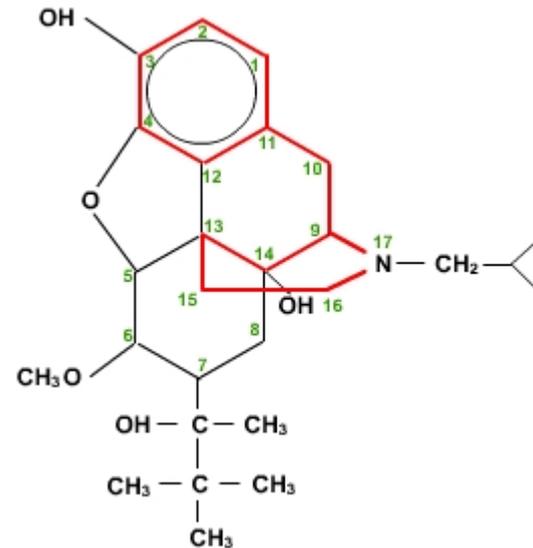
- Thebaine derivative, therefore, buprenorphine is legally classified as an opiate.
- Partial opioid agonist
- Will not and should not take the place of methadone
 - Special populations
 - Consider use in the adolescent, the patient with multiple medications where drug - drug interactions have been a problem and the incarcerated patient.
 - Underserved areas where methadone treatment programs are not available for the opioid dependent patient



METHADONE & BUPRENORPHINE



METHADONE



BUPRENORPHINE



BUPRENORPHINE

- Partial opioid agonist
 - Desirable properties
 - Low abuse potential
 - Lower level of physical dependence
 - Safety if ingested in overdose quantities
 - Weak opioid effect as compared to methadone
 - Poor oral bioavailability
 - Sublingual (under the tongue) with absorption through the oral mucosa
 - Slow dissociation rate
 - Prolonged therapeutic effect - so can be given every other or every third day



BUPRENORPHINE

- Pharmacologic uses
 - Potent analgesic
 - Available in many countries as a sublingual tablet (0.3 - 0.4 mg) called Temgesic®
 - Available in the U.S. as a parenteral (intravenous, intramuscular) form called Buprenex ®

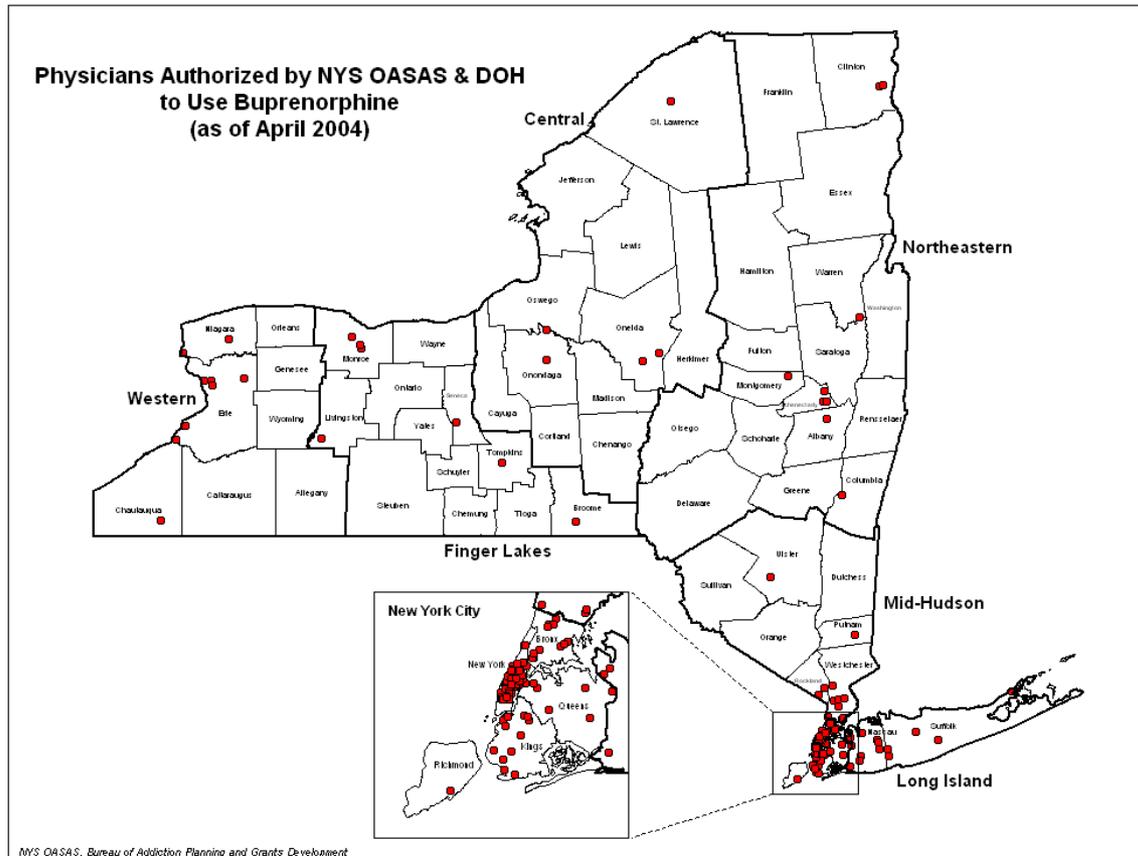


BUPRENORPHINE

- Pharmacologic uses
 - Treatment of addictions
 - In the U.S. distributed by Reckitt Benckiser
 - Subutex®
 - 2 & 8 mg sublingual white tablets
 - Schedule III under the controlled substance act
 - Suboxone®
 - Hexagonal orange sublingual tablets in 2 strengths
 - 2 mg buprenorphine with 0.5 mg naloxone
 - 8 mg buprenorphine with 2 mg naloxone
 - Schedule III

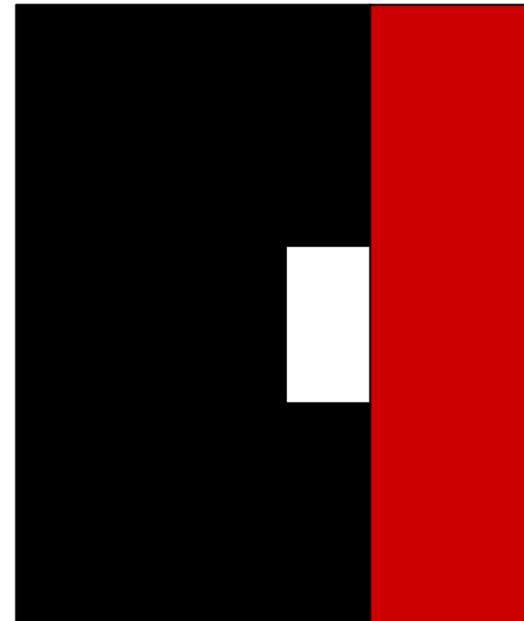


BUPRENORPHINE



CURRENT STATE OF TREATMENT: ADDICTION MEDICATIONS

- Pharmacotherapy using an antagonist such as naltrexone for the treatment of opiate-dependent patients should always be in conjunction with a behavioral counseling program
 - Marketed as Trexan®
 - Designated an orphan drug by the US FDA
 - Opiate receptor blocker or antagonist
 - Blocks the euphoric reinforcement produced by self administration of opiates
 - Reportedly decreases opiate craving within 3 – 5 weeks of starting naltrexone
 - Long-lasting effect after oral dosing (1- 3 days)



**Antagonist – blocks Mu effect
(Antagonist in red blocks the
receptor so it cannot be activated)**



NALTREXONE

- Who might benefit from naltrexone ?
 - Highly motivated individuals
 - Former opiate-dependent individuals who are employed and socially functioning
 - Those recently detoxed from methadone/buprenorphine maintenance
 - Those who are leaving prison
 - Those who are leaving residential treatment settings
 - Those who sporadically use opiates but are not on methadone/buprenorphine maintenance
 - Those not eligible for methadone/buprenorphine maintenance
 - Those in a long waiting period for methadone/buprenorphine maintenance
 - Those wishing to prevent relapse
 - Adolescents not wishing to go on methadone/buprenorphine maintenance
 - Healthcare professionals not wishing to go on methadone/buprenorphine maintenance



NALTREXONE

- For opiate-dependent patients
 - Dosing
 - Must wait 5 – 7 days after last use of a short-acting opiate (heroin) or 7 – 10 days after a long-acting opiate to prevent withdrawal.
 - Can perform a narcan challenge test* to see if withdrawal can be induced, thus not safe to start naltrexone yet
 - Should always have a negative urine drug screen for opiates before starting
 - Start with 25 mg first day, then 50 mg per day thereafter.
 - Can dose for 3 times a week (100mg – 100mg – 150 mg on Monday, Wednesday and Friday)

*See next page for Narcan Challenge Test



NALTREXONE

- Narcan Challenge Test
 - Do not do test if patient is showing symptoms of opiate withdrawal
 - Do not do test if patient is suspected of recent opiate use
 - Do not do test if urine drug screen is still positive for opiates
- Why? Will precipitate withdrawal



NALTREXONE

- **Narcan Challenge Test**
 - IV or subcutaneous injection of narcan
 - IV
 - 0.2mg iv and observe for 20 minutes for signs of opiate withdrawal. If no withdrawal, inject the remaining 0.6 mg and watch for withdrawal for an additional 20 minutes
 - Subcutaneous
 - Inject entire 0.8 mg and observe for 20 minutes for withdrawal
 - **IF A POSITIVE NARCAN CHALLENGE (OPIATE WITHDRAWAL IS OBSERVED), DO NOT START NALTREXONE. NARCAN CHALLENGE TEST CAN BE REPEATED IN 24 HOURS TO EVALUATE USE OF NALTREXONE**



NALTREXONE

- For opiate-dependent patients
 - Side effects
 - Nausea in 10% of the patients
 - Other side effects include
 - Anxiety
 - Headache
 - Sleeping trouble
 - Weakness
 - Skin rash



NALTREXONE

- For opiate-dependent patients
 - Poor compliance appears to be a major limiting factor
 - Use of this medication is not addictive; by itself, it will not cause opiate withdrawal
 - New research being conducted on implantable slow release formulas that last 6 - 8 weeks and will improve compliance and treatment outcomes



REFERENCES

1. Principles of Addiction Medicine – 3rd Edition edited by Graham et al
2. “Practical Considerations for the Clinical Use of Buprenorphine”, H. E Jones Science and Practice Perspectives – August 2004
3. TIP 28 – Naltrexone and Alcohol Treatment
4. TIP 40 – Clinical Guidelines for the use of Buprenorphine in the Treatment of Opiate Addiction

