Objective

Participants will be able to:

- Discuss the role of opioid maintenance in reducing morbidity and mortality
- List the regulations for prescribing buprenorphine
- Describe the basic components of buprenorphine induction and maintenance
Injection Drug and Heroin Use: 2006

Estimates

- 108,500 injection drug users in New York
- 150-200,000 heroin users, at least 50% of whom inject regularly
- Unknown number of prescription opioid users

Frank MSJM 2000, Friedman J Urban Health 2005, Des Jarlais – personal communication
Age-adjusted Rates of Drug-Related Hospitalizations, by UHF Neighborhood in New York City
Adults ages 18 years or older, 2005

Age Adjusted Rate (any diagnosis)
- 0.0 - 575.5
- 575.6 - 1159.2
- 1159.3 - 2201.1
- 2201.2 - 5992.8

Source: Statewide Planning and Research Cooperative (SPARCS), NYSDOH, 2005 (updated July 2006).
Data prepared by NYC Dept of Health & Mental Hygiene, Bureau of Epidemiology Services, April 2008.
Opioids: Heroin

- **Use**: nasal, injected, smoked and oral
- **Why**: Euphoria, sedation, reduce pain
- **Negative**: Dependence, overdose, injection related illnesses
- **Withdrawal**: severe, not life threatening
- **Pregnancy**: Withdrawal dangerous to fetus, initiate and maintain on methadone
Comments: Heroin

- **Overdose**: most common when mixing drugs or after period of abstinence

- **Interactions with HAART**
  - In theory ritonavir may increase potency
  - Analgesics are mixed with HAART

*Sporer BMJ 2003, Faragon AIDS Inst, NYSDOH, HIVGuidelines.org 2005*
History of Maintenance Therapy

- Prior to 1914 opiates freely available
- 1914 Harrison Act: led to the end of physician ability to maintain an addiction
- 1960s: redevelopment of maintenance model
- 1972: FDA approval and strict regulation of methadone

Joseph Mt Sinai J 2000
2000: Drug Addiction Treatment Act

- Allows for office based maintenance with schedule III, IV or V medications
- Buprenorphine is the *only* approved medication
What Gaps Does The Law Fill?

- Methadone maintenance has been shown to be highly effective in reducing heroin use and the incidence of co-morbidities such as HIV
- Access to methadone is limited by regulation and stigma
Opioid Maintenance and HIV Prevention

- Patient on buprenorphine and methadone reduce risky behaviors: sharing injection equipment
- Methadone patients are 3-6 times less likely to become HIV infected

HIV Risk Reduction

137 Patients from previous study
Buprenorphine:47
Methadone:51
LAAM:39
Result: all groups had major reductions in injection related risk behaviors

Lott, JSAT2006
Maintenance and the HIV+ Heroin User

- Among HIV+ patients maintenance is associated
  - more consistent use of antiretrovirals
  - higher rates of adherence
  - less hospitalizations

Further Benefits

- Reductions in lethal overdose due to decreased use of heroin and maintaining tolerance
- Reductions in crime and incarceration
- Reductions in sex work

Buprenorphine prevents overdose

1996 Subutex and methadone

French population in 1999 = 60,000,000

Patients receiving buprenorphine (1998): N= 55,000

Patients receiving methadone (1998): N= 5,360

Auriacombe et al., 2001
Goals of Maintenance Therapy

- Prevent drug withdrawal
- Block the effects of heroin if taken
- Prevent the powerful craving that continues for some people long after detoxification

Joseph, MSJM 2000
Underpinnings of Addiction

- Genetic predisposition possibly based on variations in opiate receptors
- Environmental factors may bring it out: use of the drug, perhaps stress or other influences
- Physiological changes possibly in the receptors for endogenous opiates which are long term and probably permanent

Nestler Trends Pharmac Scit 2004, Kreek Pharmacol Rev 2005
Maintenance Therapy

Hypothesis: opioid addiction is a metabolic illness

Opioid maintenance may be compared to the treatment of diabetes with insulin
Length of treatment

- Data from MMTP (generally patients with well established dependence) finds that 80-90% of those ending maintenance will return to heroin use - a treatment, not a cure

- Success in long term abstinence not predictable by life stability

- No data on buprenorphine patients

Magura MSJM 2000
Buprenorphine

- Is available by prescription from qualified physician offices
- Suboxone: Buprenorphine: naloxone 4:1, 2mg/0.5mg and 8mg/2mg
- Subutex: Buprenorphine alone, 2mg and 8mg
Higher safety profile

Difficult to overdose on buprenorphine alone

- “Partial agonist”- a ceiling effect above which higher doses do not increase activity- respiratory depression leading to fatal overdose unlikely

- Sublingual medication- low activity if swallowed, therefore safer around children

Ling JSAT 2002
Lower anticipated street value

Effects on a person who is:

- Dependent on opioid: “high” or “straight” - severe withdrawal whether taken under tongue or injected
- Dependent on opioid: in withdrawal - relief
- An occasional user - gets high especially if injecting but mixed with naloxone (full antagonist) which is activated if injected so reduced high

*Ling JSAT 2002*
Prescribing regulations

- Be a qualified physician: complete an 8 hour training
- Physician Assistants and Nurse Practitioners can manage patients with supervision/collaboration of on-site physician
Other physician regulations

- Register with the DEA
- Required to have access to appropriate psychosocial services: 1-800-Lifenet
- Limited to 30 patients per doctor for the first year then 100 patients per doctor
Primary Care Protocol

- Initial history and physical
  - 40 minutes
- Follow-up phone call in 24 hours
- Follow-up visit in one week
  - Usually 20 minutes
- Monthly evaluation for refill/follow-up and preventive health care
  - 15 minutes

M. Campopiano 16th Int. AIDS conf
Induction

- Patient must be moderate withdrawal (get patient to describe first 3 symptoms)
- Test dose (2-4mg)
- Titrate up to comfort level over 1+ days
- In-person is recommended by guidelines but many do it by phone, e-mail etc

Alford JGIM 2007
Maintenance

- Most patients can be stabilized on 12-24mg. Because of a ceiling effect few will be on >32mg.
- Some patients can dose q 2-3 days
- Frequency of visits determined by MD/patient
- Training encourages urine testing but it is not required by law
Managing continued illicit drug use

- Psychosocial services may be helpful: counseling, day treatment, self-help groups
- More frequent visits for prescribing if concerned about diversion
- Consider transfer to a higher level of care however discharge is not necessary
Use in detoxification

- 4 days to 6 months
- Stabilize on comfortable dose, then taper eg 16-16- 12-12- 8-8-4-4-2-2
- Additional medications are usually not necessary
- No particular detoxification regime has been shown to be more likely to lead to long term abstinence
Side effects

- Similar to other opioids: constipation, nausea, vomiting
- Precipitated withdrawal in agonist dependent patient
- Pregnancy category C- studies are in progress

*Johnson Drug Alc Dep 2003*
Severe Adverse Reactions to BUP Treatment Relatively Rare

Physicians Report .5% of Patients Experienced Severe Adverse Rx

- Specific reactions reported (unweighted):
  - Withdrawal: 103
  - Allergic reactions: 12
  - Respiratory depression: 9
  - Drug interactions: 9
  - Liver problems: 2
  - Renal insufficiency (or aggravation of it): 2
  - Unspecified: 80

Physicians reported 217 patients with adverse reactions, out of a total 47,664 patients induced (unweighted).

Stanton, 2006  http://buprenorphine.samhsa.gov/ASAM_06_Final_Results.pdf
Drug Interactions

Chronic pain management
- Chronic opiate agonists contraindicated
- Buprenorphine can relieve moderate pain—studies in progress
- Methadone may be better choice for some

Benzodiazepines
- Increased potential for fatal overdose
- Combination of buprenorphine and benzodiazepines less sedating than with methadone

Lintzeris, Drug Alc Dep 2007
Medical Co-morbidities

Screen for:

- Hepatitis B- and vaccinate
- HIV
- Hepatitis C
- STDs
Psychiatric co-morbidities

Common among opiate misusers

- Mood disorders and personality disorders most common
- Not a contraindication to buprenorphine but some patients may do best co-managed with psychiatry
Homeless vs Housed Patients

- Retrospective study of 44 homeless and 41 housed opioid addicted people

- Homeless:
  - Heroin use- 84%
  - Self-reported psychiatric illness- 94%

- Housed
  - Heroin use-63%
  - Self-reported psychiatric illness- 54%

Alford JGIM 2007
Protocol

Induction
- Homeless patients had on-site induction and frequent visits early in care
- Housed patients had home induction and less frequent visits

Maintenance
- 1-4 week refills based on treatment response ability to secure medications

Alford JGIM 2007
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Homeless</th>
<th>Housed</th>
</tr>
</thead>
<tbody>
<tr>
<td>In care at 12 months</td>
<td>55</td>
<td>63</td>
</tr>
<tr>
<td>Treatment failure</td>
<td>21</td>
<td>22</td>
</tr>
</tbody>
</table>

At 12 months no significant difference in opioid use or counseling. Initially the homeless required more counseling. At 12 months 36% of homeless were housed.

*Alford JGIM 2007*
Which Patients?

- Consider anyone using illicit opioids
- Those in areas with limited or no access to methadone
- Contraindications: heavy use of benzodiazepines, need for opioid based pain management, pregnancy
Methadone Patients?

- Very appropriate for some patients
- Transition easier from 30-50mg
- Tapering may put patient at risk of relapse
- Multiple needs sometimes more easily addressed by methadone program
Methadone vs. Buprenorphine

Methadone:
- Advantages: may have higher retention, associated with multiple services
- Disadvantages: access is limited, highly regulated and greater potential for overdose.

Buprenorphine:
- Advantages: office based access.
- Disadvantages: pain management interaction.
Summary

Buprenorphine

- Moves addiction treatment into primary care
- May bring patients into care before various co-morbidities have an impact
- May increase use of and response to HIV treatment
On-line resource

http://buprenorphine.samhsa.gov/

- Listing of trainings
- Guidelines
- Updates
- Evaluation