

# Clinical Management of Drug Abuse and Co-occurring Infections

Jag H. Khalsa, PhD, MS  
Chief

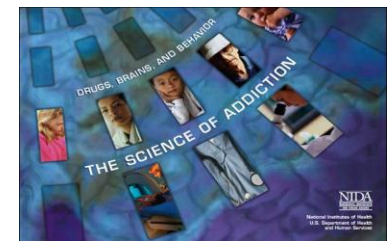
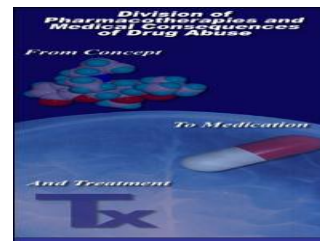
Medical Consequences Branch  
Division of Pharmacotherapies and  
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NIH Institutes

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ON DRUG ABUSE





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## Epidemiology

### Substance Abuse:

200-500 million-110 million life-time users, 19 million current

### Cost to the US society:

\$561 billion/year

(Illicit drugs,181; Tobacco, 195; Alcohol, 185);

(Diabetes: \$160 b/yr; Cancer: \$210 b/yr)

### Infections:

Approximately 2.5 billion worldwide

300 Hepatitis B, 170 Hepatitis C, 33 million HIV

### Other bacterial infections

# Substance Abuse Co-morbidity

- **CNS and Other Physiological Systems**
- Depression, Anxiety disorder, Conduct disorder, PTSD, Neuropathy
- Cardiovascular, Hepatic, Metabolic, Drug-interactions
- Infections

# Pharmacological Interventions

## Medical detoxification and treatment

- Opiates (Methadone, LAAM, buprenorphine)
- Nicotine (the “patch”)
- Sedative/Hypnotics
- Alcohol
- Cocaine
- Hallucinogens and Club Drugs

## Treatment of HIV

### HIV

Treatment saves lives  
Extends life for 15 years (UK study)

Guidelines: CD4 counts, <350  
Anti-retroviral medications: 24 in 5 classes

Next slide

# Antiretroviral Medications

PIs	NRTIs	NNRTIs	Fusion inhibitors	Integrase Inhibitors
Amprenavir	Abacavir	Delavirdine	Enfiurvirtide,T20	Raltegravir
Atazanavir	Didanosine (ddl)	Efavirenz	Maraviroc	
Daranuvir	Emtricitabine	Nevirapine		
Fosamprenavir	Lamivudine			
Indinavir	Stavudine			
Lopinavir	Tinofovir			
Nelfinavir	Zalcitabine			
Ritonavir	Zidovudine (AZT)			
Saquinavir				
Tipranavir				

**PIs**=Protease inhibitors; **NRTIs**=Nucleoside or nucleotide reverse transcriptase inhibitors; **NNRTIs**=Non-Nucleoside reverse transcriptase inhibitors ; **IIs**=Integrase inhibitors

## Treatment of Infected Drug Abusers

### HIV

Substance abusers have poor HIV-related health outcomes

Less access to health care

Less access to ARTs

Worse adherence to ART

Slower decline in morbidity and mortality

Cunningham 2004

## Treatment of Infected Drug Abusers

### HIV

#### CASE Management:

Unmet needs; Income assistance, Health insurance, Home health care, Emotional counseling, and Increased HAART

#### Integration of Primary Care and DA Treatment

##### **METHADONE**

Feasible and safe

Increased utilization of HIV Primary care services

Decreased high risk behavior

Decreased opioid use

Improvement in education and employment

Cunningham 2004

## Treatment of Infected Drug Abusers

### HIV

### Integration of Primary Care and DA Treatment

### **BUPRENORPHINE**

Approved to treat opioid dependence in the primary care setting

Can be prescribed by physicians who qualify for a waiver: 8-hr training session or other mechanisms

<http://buprenorphine.samhsa.gov/>

Cunningham 2004

## Treatment of Infected Drug Abusers

### HIV

#### AWARENESS OF POTENTIAL PROBLEMS RELATED TO HIV AND SUBSTANCE ABUSE

Illicit drugs and HIV

Methadone/Buprenorphine and ART

Mental Illness

Pain

Hepatitis C virus and liver disease

TB

Cunningham 2004

## Treatment of Infected Drug Abusers

### HIV

#### ILLICIT DRUG INTERACTIONS WITH ART

DRUG	EFFECT
Amphetamine	May inc. levels 2-3x w <b>Ritonavir</b>
Meth	Inc. HIV replication, fatal OD w Ritonavir/ saquinavir
Cocaine	HIV replication, dec. immune func
MDMA	Overdose or death w Ritonavir
Heroin	Levels dec. or inc. w Ritonavir

#### METHADONE INTERACTIONS WITH PIs, NRTIs, NNRTIs

Cunningham 2004

## Treatment of Infected Drug Abusers

### HIV

#### ILLICIT DRUG INTERACTIONS WITH ART

#### BUPRENORPHINE INTERACTIONS WITH ART

DRUG	EFFECT
NRTIs	No change in AZT
NNRTIs	Likely decrease in Bup levels
PIs	Increased Bup with Ritonovir> indinavir>saquinavir
Fusion inhibitor	No data

McCance Katz, 2001 and others

# Antiretroviral Medications

PIs	NRTIs	NNRTIs	Fusion inhibitors	Integrase Inhibitors
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Atazanavir	Didanosine (ddl)	Efavirenz	Maraviroc	
Daranuvir	Emtricitabine	Nevirapine		
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Saquinavir				
Tipranavir				

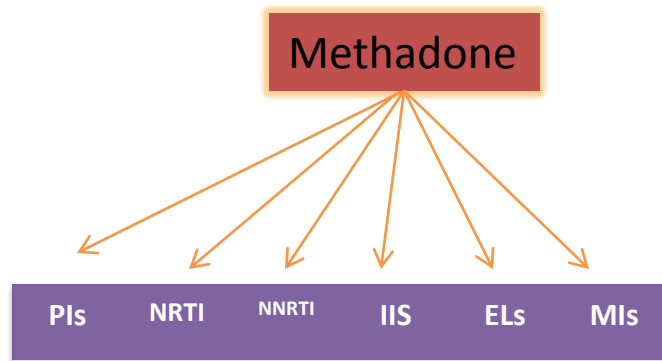
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# Summary

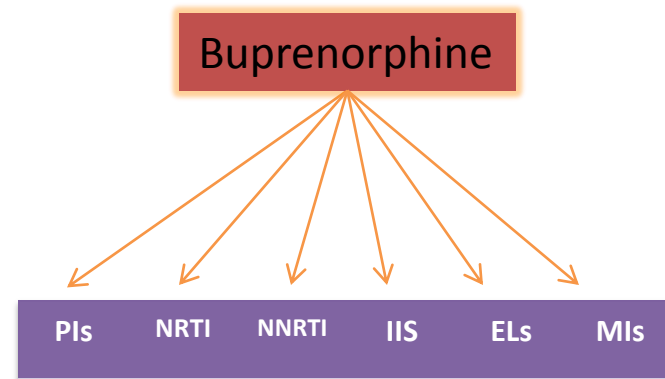
**Treatment of Opioid dependence:**  
**Antiretroviral medications (ARVs):**

4 drugs approved by FDA  
24 drugs approved by FDA

- Protease inhibitors (PIs),
- Nucleoside and nucleotide reverse transcriptase inhibitors (NRTI),
- Non-nucleoside reverse transcriptase inhibitors (NNRTI),
- Integrase inhibitors (IIs),
- Entry inhibitors (or fusion inhibitors) (EIs),
- Maturation inhibitors (MIs)



Meth ↓ AZT ↑ Efvirenz  
ddl ↓ Nevirenz  
Meth ↑ Meth (E,M) ↓  
(D) Meth (D) ↑



+ (AT) Bup ↑  
None None Nevirapine  
(F, T, R) (ddl, L, T) (no Withdraw)

## Treatment of Infected Drug Abusers

### HCV

Highest prevalence (50-90%)  
Highest incidence (10-40%/year)

~ 1 million IDUs with HCV in the US

**Barriers to Care:** poverty, homelessness, drug abuse, mental health, negative health experiences

**Lack of available services;** health, social support etc.;  
lack of comp primary care

**Physician concerns:** poor adherence, neuropsych side effects; re-infection

Few people who inject drugs are in care; even fewer receive treatment

## Treatment of Infected Drug Abusers

### HCV

#### TREATMENT MODELS

**Collaborative:** Community-based Needle exchange prog and tertiary

**Multidisciplinary:** Primary care, mental health care, substance abuse tx and intensive care tx.

**Integrated:** Staff cross institutional boundaries, tertiary care provided in community-based settings

**Intensive case management:** Effective Edlin (an example of 69% SVR, 6% drop-out)

## Treatment of Infected Drug Abusers

### HCV

#### TREATMENT:

#### Pharmacologic treatment:

Ribavirin (Ribapak, Rebeton [Schering])

peg-Interferon alfa 2b (Pegintron, Merck)

Telaprevir (Incivek, Vertex)

Bociprevir (Victrelis-Meck)

Combinations

Caution: Severe ADRs with the first two.

## Medical Consequences (Infections)

**Staph aureus, Pseudomonas, Streptococcal strains A, B, & viridans**

Endocarditis (infection of the heart valves):

Tx: Penicillin/streptomycin, gentamycin, nafcillin etc.,  
cephalosporins-ciprofloxacin, rifampin

**Streptococcal infections, E.coli, Klebsille, Clostridia, fungal pathogens e.g., Candida species**

Skin and soft tissue infections:

Tx: antifungal and antibiotics

**Pseudomonas aeruginosa, and fungal infections**

Bone joint infections-osteomyelitis:

Tx: antibiotics

## ***Medical Consequences: Infections (contd.)***

**Viral Hepatitis-B, C, D, from parenteral drug use**

*Hepatitis/hepatic fibrosis, liver cancer:*

*Tx: vaccines for A and B; interferons, ribavirin, boceprevir, telaprevir*

***HTLV-I and II: Human T-cell Leukemia/lymphoma virus: types I and II  
more severe consequences if co-infected with HIV-1: Cancers, immune  
dysfunction, neurological disorders:***

*Tx: ARTs, interferons*

**Cytomegalovirus (CMV), Epstein Barr virus (EBV)**

*Pathogens found when immune system is severely impaired (e.g., with HIV):*

Neurological, ocular and GI disorders; Tx: acyclovir, foscarnet, gancyclovir.

## ***Medical Consequences: Infections (contd.)***

### **Human immunodeficiency Virus (HIV):**

#### **AIDS:**

**Tx: ARVs (PIs, NRTIs, NNRTIs, Fusion, and CCR5 blocker (Selzentry)**

#### **HIV:**

**Pneumocystis carinii pneumonia: affects the respiratory tract-immunodeficiency, AIDS-defining condition:**

**Tx: Dapsone, pentamidine, atovaquone**

#### **Mycobacterium tuberculosis:**

**Tuberculosis (TB) of the lung, and other organs:**

**Tx: isoniazid+pyridoxine; isoniazid+rifampin, pyrazinamide, ethambutal, streptomycin, Cipro.**

## ***Medical Consequences: Infections (contd.)***

### **Toxoplasmosis gondii: protozoal parasite**

leading to toxoplasmic encephalitis with clear neurologic signs:

Tx: TMP-SMX (Bactrim); dapsons+pyrimethamine+folic acid

### **Fungal infections: Candida, Histoplasmosis, cryptococcoses, coccidiomycosis**

Vaginitis, meningitis:

Tx: fluconazole, ketoconazole, itraconazole.

### **Opportunistic Viral Infections: Herpes simplex virus (HSV)**

Vaginitis and other mucocutaneous tract infections:

Tx: acyclovir

# Chemicals/Medications in Development for Substance Abuse Dependence

Alcoholism	Cocaine	Opiates	Tobacco
<b>ALKS 33</b> Rensselaer Polytechnic Institute (O)	<b>Cocaine abuse vaccine TA-CD</b> ImmuLogic Pharmaceutical (O)	<b>Buprenorphine implant Titan</b> Pharmaceuticals (O)	<b>GSK 598809 GW 468816</b> GlaxoSmithKline (O)
<b>Baclofen/ALKS 33</b> Alkermes (O)	<b>EMB 001</b> Embera Neuro -Therapeutics (O)	<b>Buprenorphine/naloxone</b> Nanotherapeutics (O)	<b>Nalmefene</b> UMiami, Rockefeller, & Biotie Therapies Corp. (O); Somaxon Pharm (Licensee)
<b>DOV 102677</b> DOV Pharmaceutical (O)	<b>Neboglamine</b> Rottapharm (O)	<b>Ibudilast - Avigen</b> Kyorin Pharmaceutical (O)	<b>Nicotine abuse vaccine</b> Nabi Biopharm (O)
<b>KRL 901</b> Krele Pharmaceuticals (O)	<b>Vigabatrin</b> - Brookhaven National Lab (O) Catalyst Pharm Partners (Licensee)	<b>Lofexidine</b> Britannia Pharm (O) US World Meds (Licensee)	<b>Nicotine inhalation</b> Aradigm Corp (O)
<b>LY 2196044</b> Eli Lilly (O)	<b>Vigabatrin</b> - sanofi-aventis (O)	<b>Naltrexone-CR</b> Alkermes (O)	
<b>Nalmefene</b> U. Miami, Rockefeller, & Biotie Therapies Corp. (Os); Somaxon Pharm (Licensee)			
<b>Olanzapine/ondansetron</b> TransOral Pharm (O)			
<b>OpRA II</b> Eli Lilly (O)			
<b>Quetiapine</b> AstraZeneca (O)			
<b>Topiramate</b> Johnson & Johnson Pharm R&D LLC (O), Janssen-Ortho (Licensee)			

## **Medical Consequences:** *New PA/PAS*

[Drug Abuse Aspects of HIV/AIDS \(R01\) PA-10-129](#)

[Drug Abuse Aspects of HIV/AIDS \(R01\) PA-10-130](#)

[Drug Abuse Aspects of HIV/AIDS \(R01\) PA-10-131](#)

[International Research Collaboration on Drug Abuse and Addiction Research \(R01\)PA-09-020](#)

[International Research Collaboration on Drug Abuse and Addiction Research \(R01\)PA-09-021](#)

[International Research Collaboration on Drug Abuse and Addiction Research \(R01\)PA-09-022](#)

<http://www.nida.nih.gov>

## ***Contact***

**Jag Khalsa, Ph.D.  
Chief**

**Medical Consequences Branch, DPMC  
National Institute on Drug Abuse  
6001 Executive Blvd., Room 4137, MSC 9551  
Bethesda, MD 20892-9551**

**Telephone: 301-443-2159**

**E-mail: [jag.khalsa@nih.gov](mailto:jag.khalsa@nih.gov)**

**[www.drugabuse.gov](http://www.drugabuse.gov)**

**Thank you !**