

# Stimulants: Cocaine and Methamphetamine

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# Learning objectives

At the end of this session, participants will be able to:

1. Understand how and why people use stimulants
2. Know the characteristics of stimulant intoxication and withdrawal syndromes
3. Understand the consequences of these drugs
4. Know the current options for treatment of stimulant dependence

# Roadmap

1. History
2. Epidemiology
3. Dopamine and the reward pathway
4. Acute and chronic effects
5. Treatment

# History

# History: Methamphetamine

- 1893 methamphetamine first synthesized in Japan as decongestant.
- Used by German, English, American, and Japanese military in WWII for performance enhancement.
- First epidemic occurred in Japan when the military dumped large quantities into the civilian market
- Popular among truckers and west coast bikers in 1970s
- DESOXYN to treat ADHD and obesity
- *Speed, Crystal, Crank, Ice, Meth, Tina*



# History: Cocaine

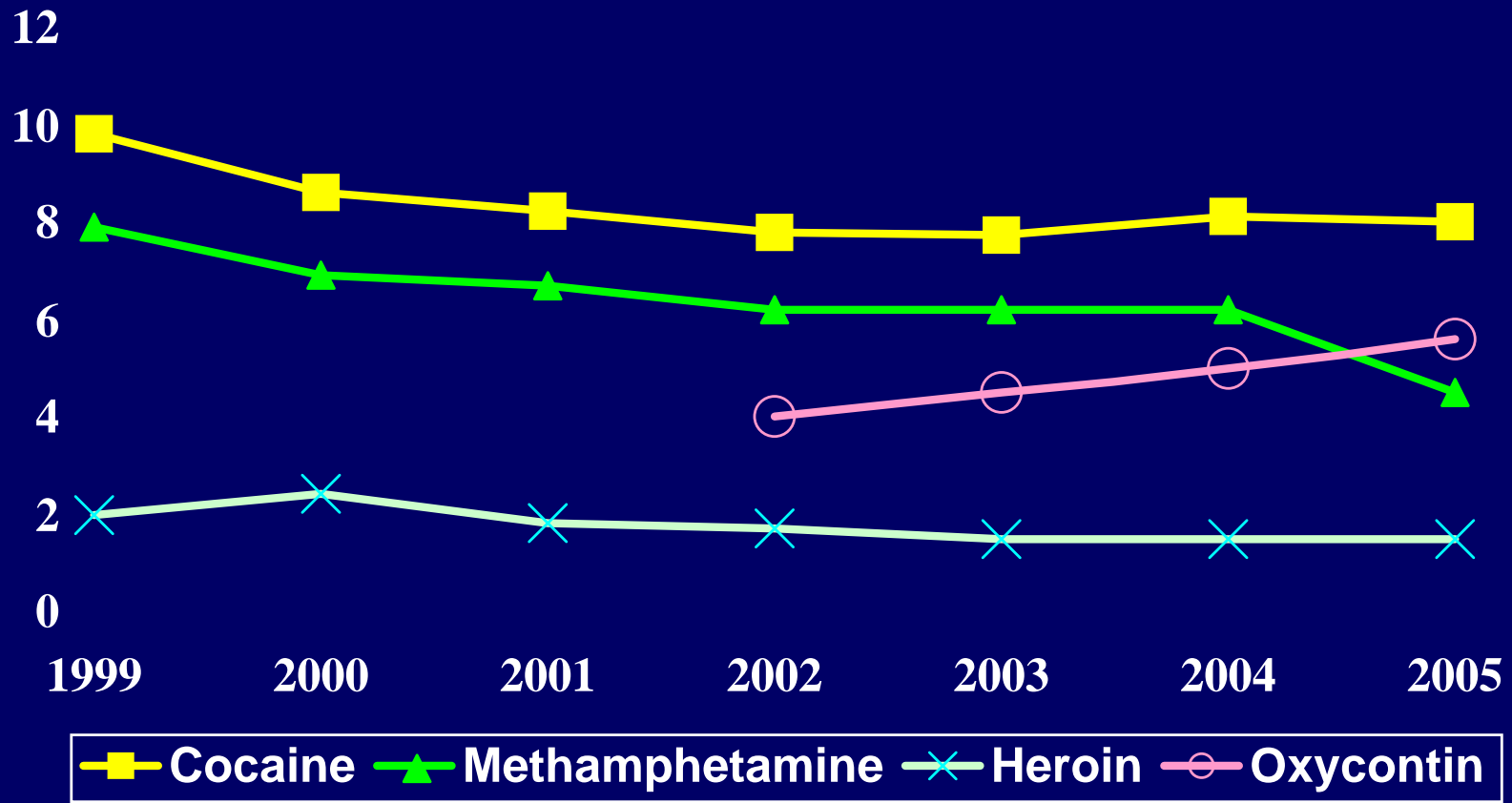


- From erythroxyton coca leaves in Andes
- Leaves chewed for thousands of years as stimulant
- 1885 Halsted published study about anesthetic uses
- 1886 Halsted raided ship medicine cabinet for fix
- Used in medicines and beverages until early 1900s
- Street preparations 10-50% cocaine
  - Hydrochloride powder is snorted or injected
  - Alkaline rocks (aka crack) are smoked
  - *Crack, Rock, Base*



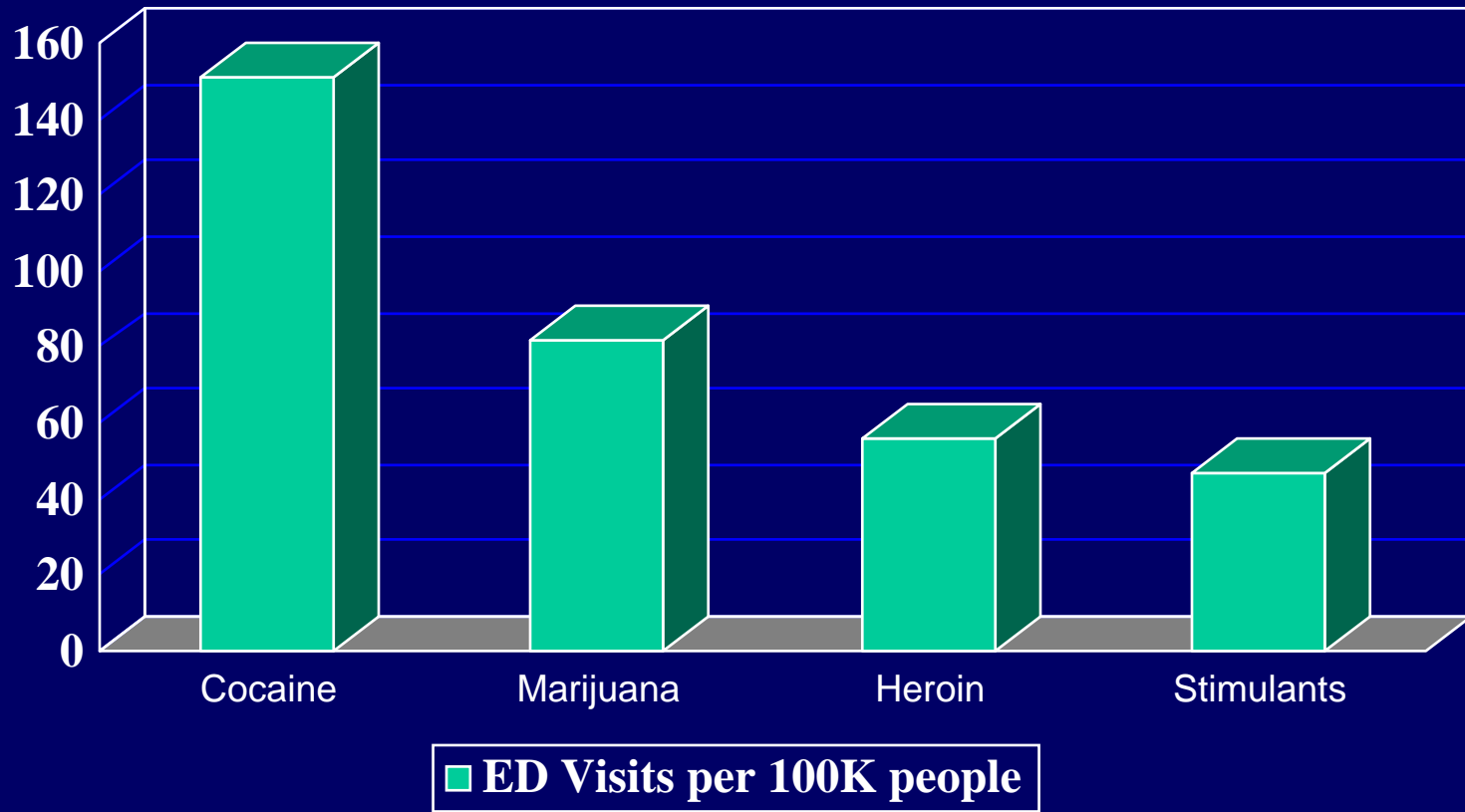
# Epidemiology

# % lifetime use by 12th graders

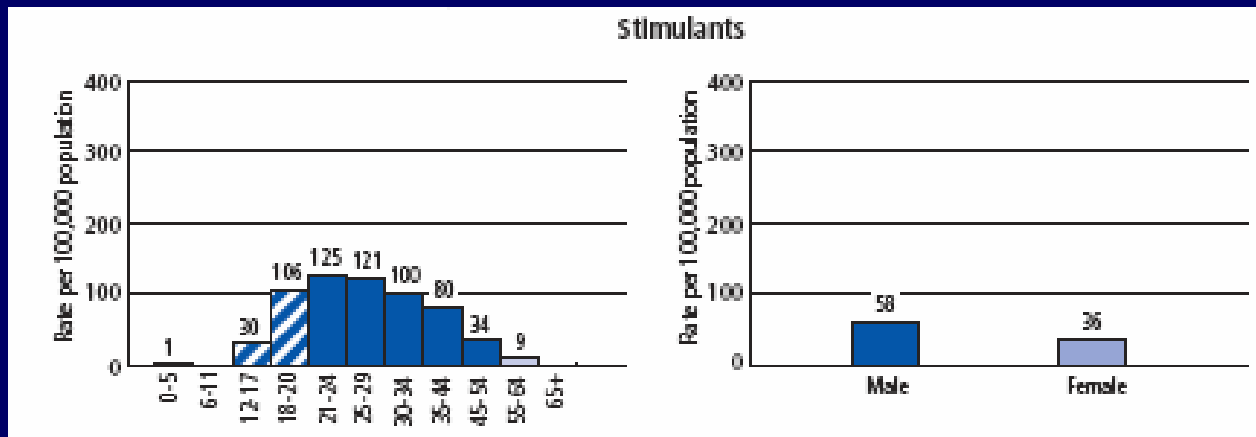
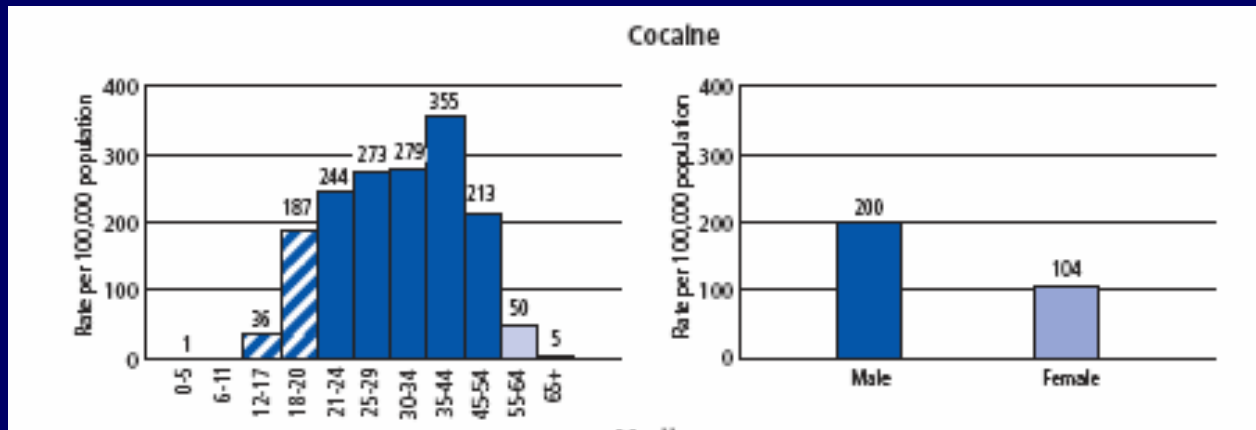




# 2005 drug-related ED visits



# 2005 drug-related ED visits



# From where do these drugs come?

- Methamphetamine
  - Super labs – Primarily Mexico and California
  - Local clandestine labs
    - Production of 1 pound of MA creates 6 pounds of toxic waste
- Cocaine -
  - 75% grown in Columbia with 75% via Mexico/ Central America

# Cocaine processing



<http://www.colombiajournal.org/cocainephotos.htm>  
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“No lies here folks this recipe will manufacture methamphetamine this will get you into trouble if you do this BE CAREFUL!”

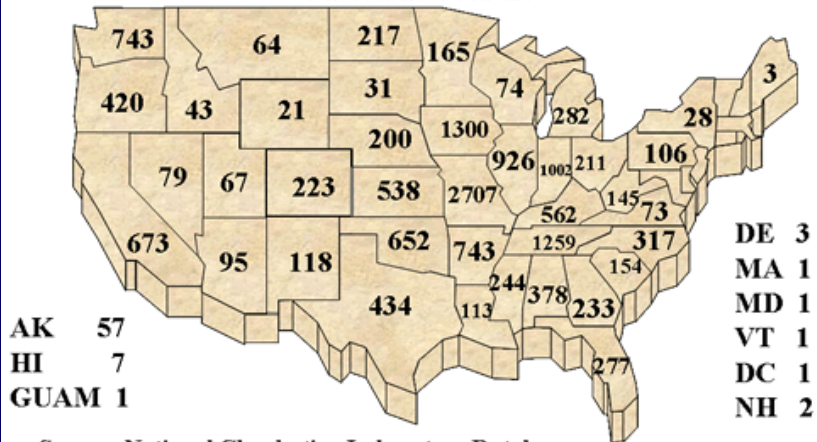
First of all let's talk about supplies:

- 1 Case Regular Pint size Mason Jars ( Used for canning)
- 2 Boxes Contact 12 hour time released tablets.
- 3 Bottles of Heet.
- 4 feet of surgical tubing.
- 1 Bottle of Rubbing Alcohol.
- 1 Gallon Muriatic Acid ( Used for cleaning concrete)
- 1 Gallon of Coleman's Fuel
- 1 Gallon of Aceton
- 1 Pack of Coffee Filters
- 1 Electric Skillet
- 4 Bottles Iodine Tincture 2%
- 2 Bottles of Hydrogen peroxide
- 3 20 Oz Coke Bottles (Plastic type)(with Lids/caps)
- 1 Can Red Devils Lye
- 1 Pair of sharp scissors
- 4 Boxes Book Matches (try to get the ones with brown/red striker pads)
- 1 pyrodex baking dish
- 1 Box execto razor blades single sided
- 1 digital scale that reads grams
- 2 gallons distilled water
- 1 Roll Aluminum foil tape

“That's what you would have to go buy if you wanted to make meth.”

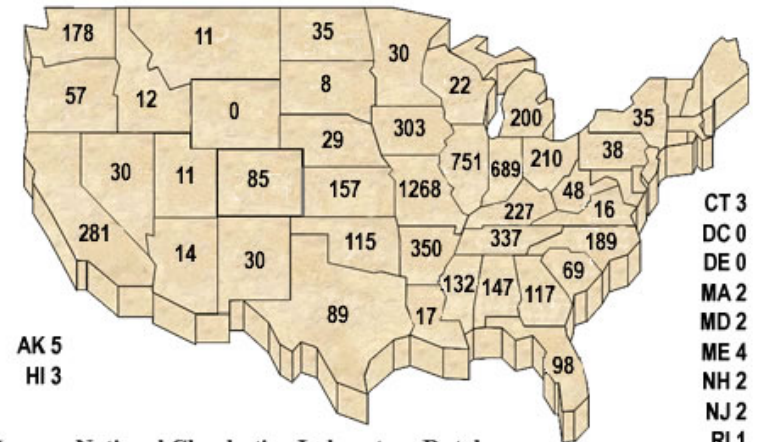
# Clandestine lab incidents

Total of All Meth Clandestine Laboratory Incidents Including Labs, Dumpsites, Chem/Glass/Equipment  
Calendar Year 2004



Source: National Clandestine Laboratory Database  
Total: 15,994 / 49 States Reporting  
Dates: 01/01/04 to 12/31/04

Total of All Meth Clandestine Laboratory Incidents Including Labs, Dumpsites, Chem/Glass/Equipment  
Calendar Year 2006



Source: National Clandestine Laboratory Database  
Total: 6,435  
Dates: 01/01/2006 - 12/31/2006

Map last updated February 2007

# Stimulant Effects

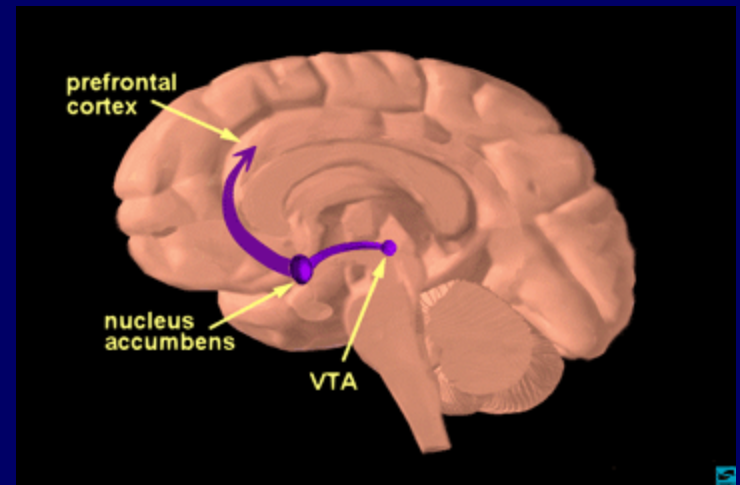
# Why do people use drugs?

1. To feel good
2. To feel better

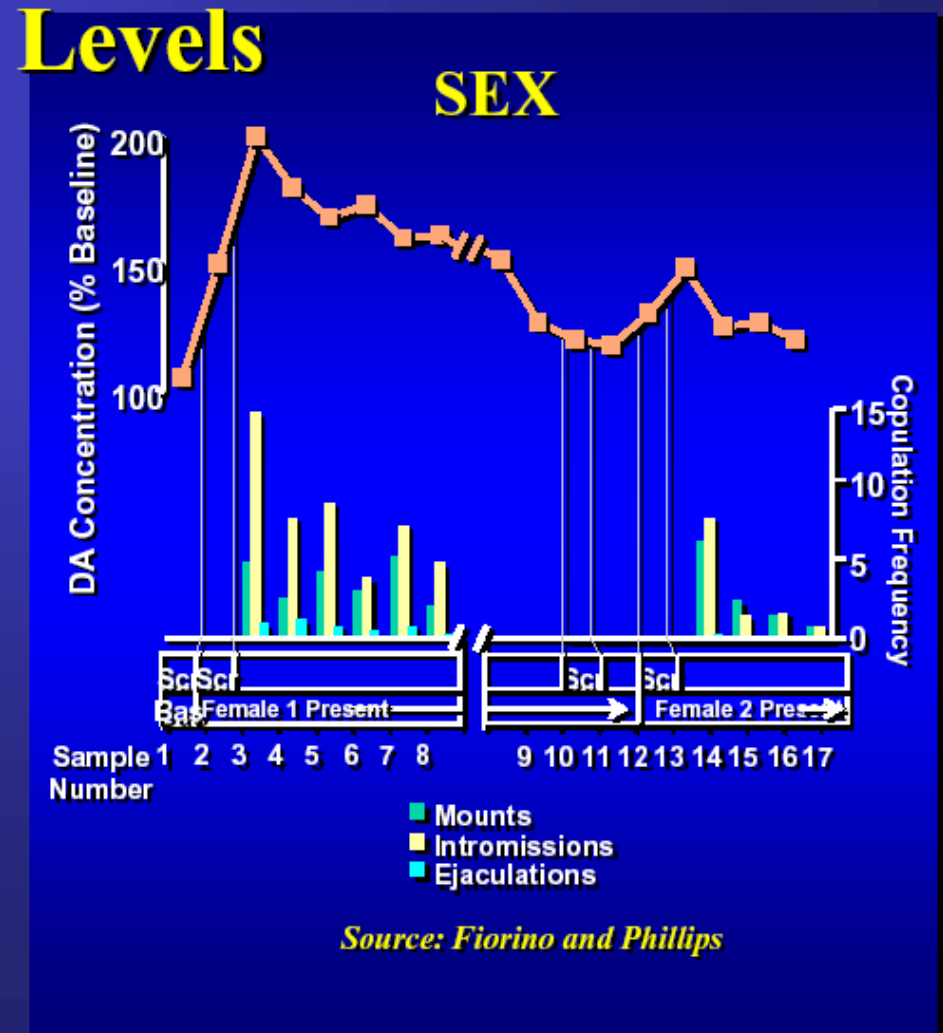
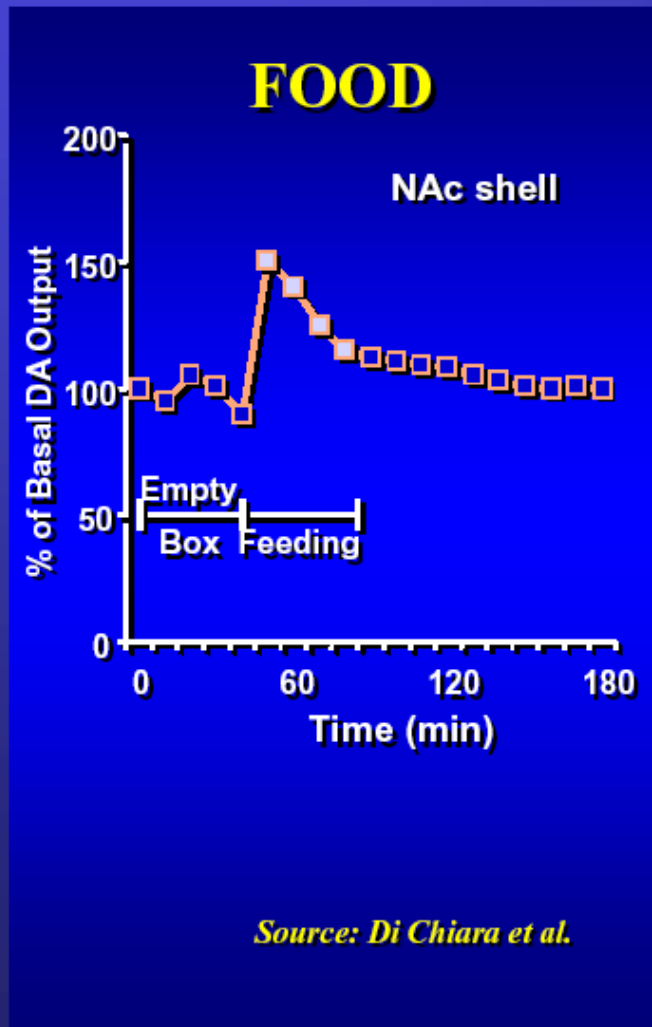


# Why do people use stimulants?

- Euphoria - Rush
  - Onset and intensity depends on delivery method
- Increased energy, alertness, libido
- Diminished social inhibition
- Decreased appetite

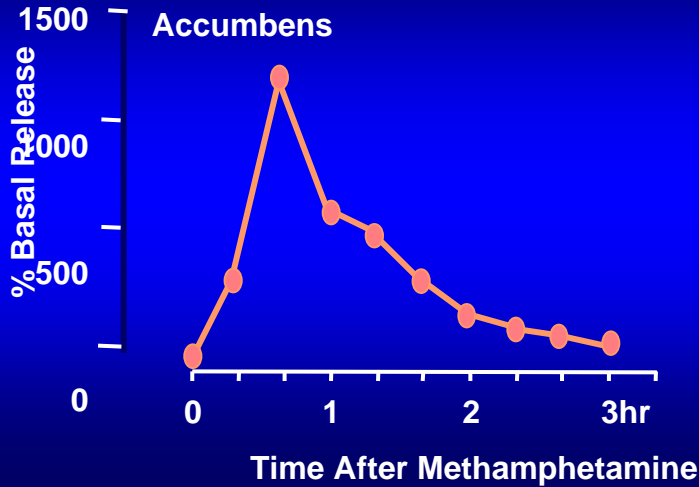


# Natural Rewards Elevate Dopamine

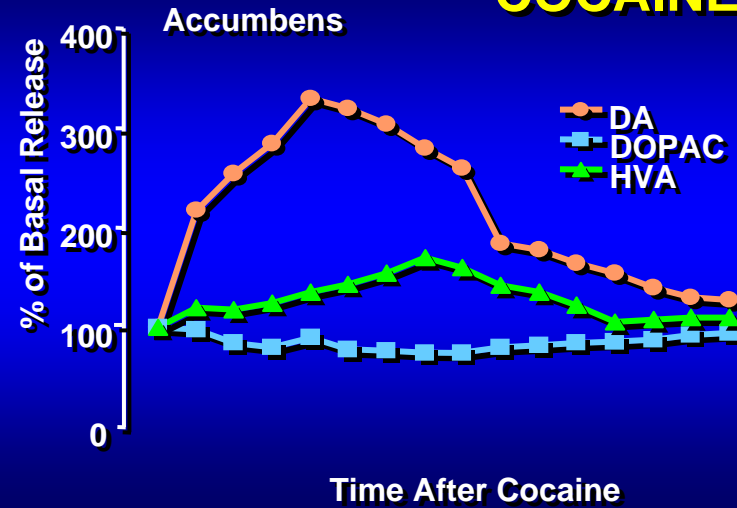


# Effects of Drugs on Dopamine Release

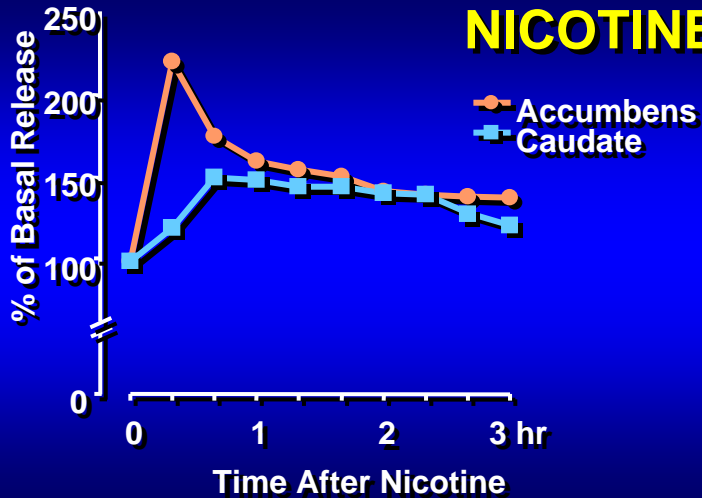
## METHAMPHETAMINE



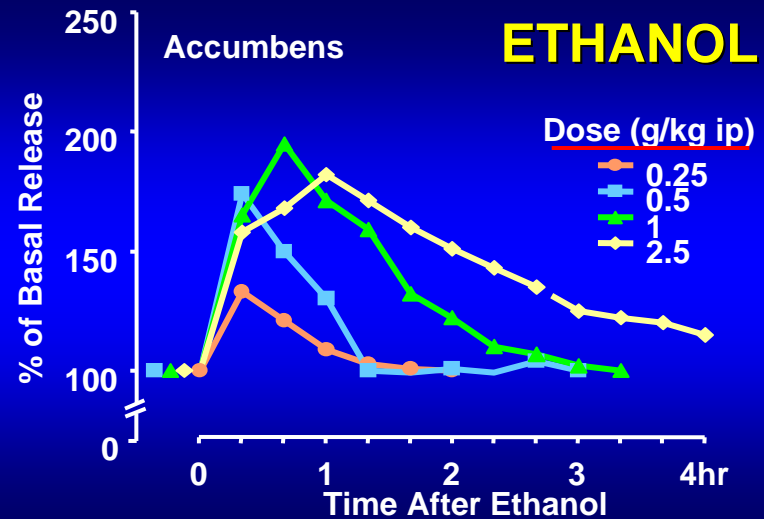
## COCAINE



## NICOTINE



## ETHANOL



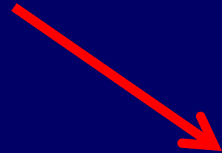
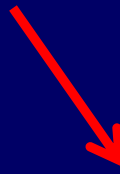
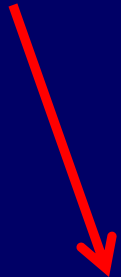
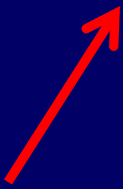
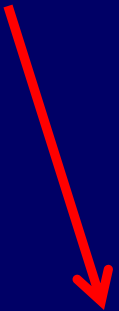
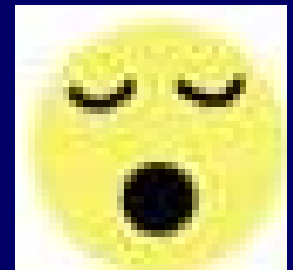
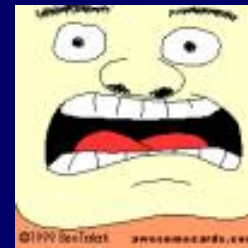
# PK: Cocaine

	IV	Smoked	Snorted
Time to effect	10-60sec	3-5sec	1-5min
Peak concent.	3-5min	1-3min	15-20min
Half-life	20-60min	5-15min	60-90min

Lange, R. A. and L. D. Hillis (2001). "Cardiovascular complications of cocaine use." *N Engl J Med* 345(5): 351-8.

# PK: Methamphetamine

	IV	Smoked	Snorted	Ingested
Time to effect	15-30 sec	Immediate	3-5 min	15-20 min
Peak concent.	2-4 h	2-4 h	2-4 h	2-4 h
Half-life	10-12 h	10-12 h	10-12 h	10-12 h





# Binges

- 2-3 day binges are typical, called runs
- Regular redosing to maintain rush or high in setting of acute tolerance
- Ends when drug or money runs out, or paranoia/ disorganized thinking sets in

# Acute Toxicity

- Elevated BP and HR
- Arrhythmia
- Vasoconstriction
- Hyperthermia
- Acute psychosis → prolonged psychosis
  - Paranoid delusions
  - Visual, sensory, and auditory hallucinations (ie formications)
- Agitation
- Rhabdomyolysis
- Seizure

# Withdrawal dopamine depletion

- Intense craving
- Depression
- Fatigue
- Unpleasant dreams
- Hypersomnia, then insomnia
- Increased appetite
- Agitation/ anxiety/ paranoia
- Limited ability to experience pleasure



# Health Consequences

## Dental

- Darkened teeth
- Caries
- Periodontal disease

## Pulmonary

- Acute pulmonary edema
- Pulmonary HTN
- Inhalation injury

## Cardiovascular

- Hypertension
- DCM
- Arrhythmia/ Tachycardia
- Acute Coronary Syndrome
- Aneurysm/ dissection
- Erectile dysfunction

## Infectious

- HIV risk
- HCV/ HBV
- STDs



## Neuro-psychiatric

- Stroke
- Seizure
- Depression
- Anxiety
- Mania
- Impulsivity
- Paranoia
- Auditory/ visual hallucinations + formications
- Violence

## Renal/Metabolic

- Rhabdomyolysis
- Dehydration
- Acute Renal Failure
- Acidosis
- Hyperthermia

## Skin

- Cellulitis/ abscess
- Excoriations
- Chemical burns

# Cocaine and HIV

- Crack cocaine use is associated with increased number of sex partners, sex work, and HIV infection, independent of IVD use.
- IV cocaine leads to HIV through frequent injection Chaisson. JAMA. 1989 Jan 27;261(4):561-5.



# MA and HIV

- Increased libido, social disinhibition, increased energy lead to prolonged unsafe sexual encounters and increased rates of HIV transmission
- PDE5 inhibitors are used to mitigate MA-induced erectile dysfunction



# Cocaethylene

- Psychoactive substrate from EtOH+cocaine
- ETOH commonly used to “come down” from a cocaine binge
- EtOH before cocaine inhibits cocaine metabolism, producing cocaethylene
- 60-90% of cocaine abusers abuse ETOH
- Greater cardiac toxicity
- Greater rates of seizures, hepatic damage

# Cocaine and heroin

- 30-80% of heroin users use cocaine
- Cocaine use results in more injections
- Cocaine worsens opiate treatment success
- For 50% of co-users, MMT reduces cocaine

# Cardiomyopathy and Methamphetamine

- In a case-control study, researchers examined the association between methamphetamine use and cardiomyopathy (CM).
- Subjects included patients aged 45 years or younger discharged from a tertiary care medical center in Honolulu.
- Through medical record review, researchers identified...
  - 107 cases (had a discharge diagnosis of CM or congestive heart failure) and
  - 114 controls (ejection fraction  $\geq 55\%$  and no wall motion abnormalities).

# Cardiomyopathy and Methamphetamine

- 42% of cases and 20% of controls had ever used methamphetamine.
- Methamphetamine use was significantly more common in cases than in controls.
- OR in analyses adjusted for age, body mass index, and renal failure, 3.7



# Methamphetamine and Trauma

- To assess the prevalence and impact of methamphetamine use (MU) in trauma patients, researchers surveyed the records of...
  - 4932 (76%) patients who were seen in a Level I trauma center in San Diego between 2003–2005 and
  - underwent a urine toxicology screening during their visit.

Swanson SM, et al. *J Trauma*. 2007;63(3):531

# Results

- The rate of MU (defined as a positive urine screen), but not other illicit drug use, increased from 2003 to 2005 (from 9% to 15%).
- In adjusted analyses, patients with MU were more likely to have...
  - been injured in a violent way (OR, 2.0),
  - attempted suicide (OR, 1.7),
  - been a victim of domestic violence (OR, 2.5),
  - required more medical care (e.g.,  $\geq 1$  operations [OR, 1.5], mechanical ventilation [OR, 1.6]), and
  - died from their injuries (OR, 2.3).

Swanson SM, et al. *J Trauma*. 2007;63(3):531

# Treatment



# Pharmacologic Treatment

- Pharmacologic treatments studied
  - Dopamine agonists
  - Antidepressants
  - Opioid partial agonists and antagonist
  - Carbamazepine, phenytoin, lithium
- None proven effective

De Lima MS. Addiction. 2001; 97, 931-949.

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# Pharmacologic Treatment

- Dopaminergic
  - Disulfiram – Carroll. Arch Gen Psychiatry. 2004;61:264-272
- GABA modulators
  - Tiagabine – Gonzalez. Drug Alcohol Depend. 2007; 87: 1-9.
  - Topiramate
  - Baclofen – Heinzerling. Drug Alcohol Depend. 2006 Dec 1;85(3):177-84.
- Stimulant replacement
  - Modafinil – Dackis. Neuropsychopharmacology. 2005 Jan;30(1):205-11.
  - Methylphenidate
  - Bupropion
- Vaccine

Sofuoglu & Kosten. Expert Opin Emerg Drugs. 2006; 1: 91-8.

Gorelick & Gardner. Drugs. 2004; 64: 1547-73.



# Non-drug Treatment

- Cognitive behavioral therapy
- Self-help/ 12 step groups
- Therapeutic communities
- Recovery houses
- Contingency management

# Contingency Management

- Intermittent, escalating re-enforcement
  - 1000 chips
    - 500 “Good job”
    - 250 “Small” - \$1 value – i.e. toiletries
    - 209 “Large” - \$20 value – i.e. kitchenware
    - 1 “Jumbo” – \$80-100 value – tv, stereo
  - # of draws = # of weeks with clean urine

# Contingency Management

Participants With Specified Weeks of Continuous Stimulant/Alcohol-Negative Samples (n=388)



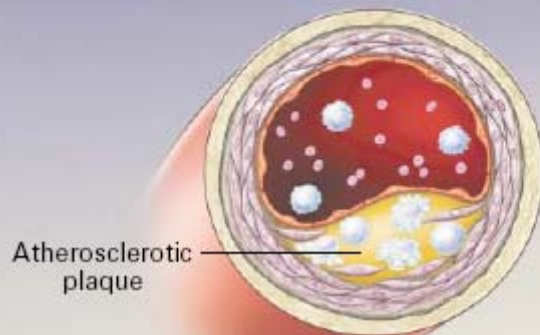


# Thanks!

Alex Walley, MD  
awalley@bu.edu

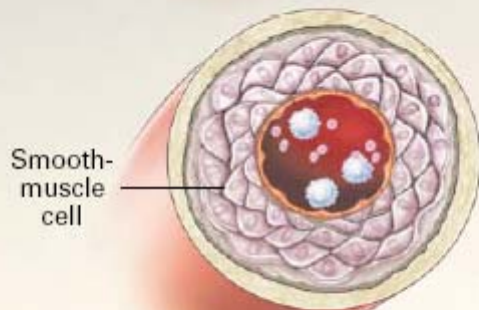
# Cocaine chest pain

- First-line
  - Oxygen
  - Nitrates
  - Benzos
- Second line
  - CCB, like verapamil
  - Non-selective beta-blocker, like labetolol
- Use lytics only if PTCA not available and MI is evolving despite medical therapy



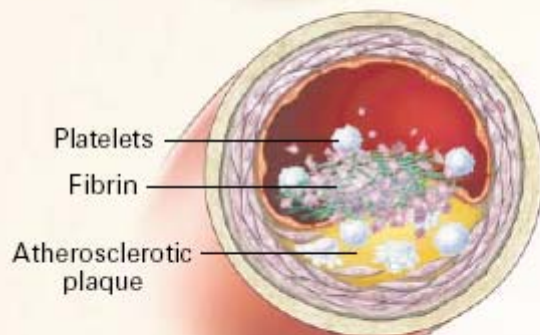
**Increased myocardial oxygen demand with limited oxygen supply**

- Increased heart rate
- Increased blood pressure
- Increased myocardial contractility



**Vasoconstriction**

- Increased  $\alpha$ -adrenergic stimulation
- Increased endothelin production
- Decreased nitric oxide production



**Accelerated atherosclerosis and thrombosis**

- Increased plasminogen-activator inhibitor
- Increased platelet activation and aggregability
- Increased endothelial permeability

# MA and HIV

- Feb 11, 2005 - NYC announces infection of man with rapidly progressive, multi-drug resistant strain of HIV
- Late 40s
- 5 negative HIV tests from 9/2000 to 5/2003
- History of multiple anonymous sex partners in setting of MA use

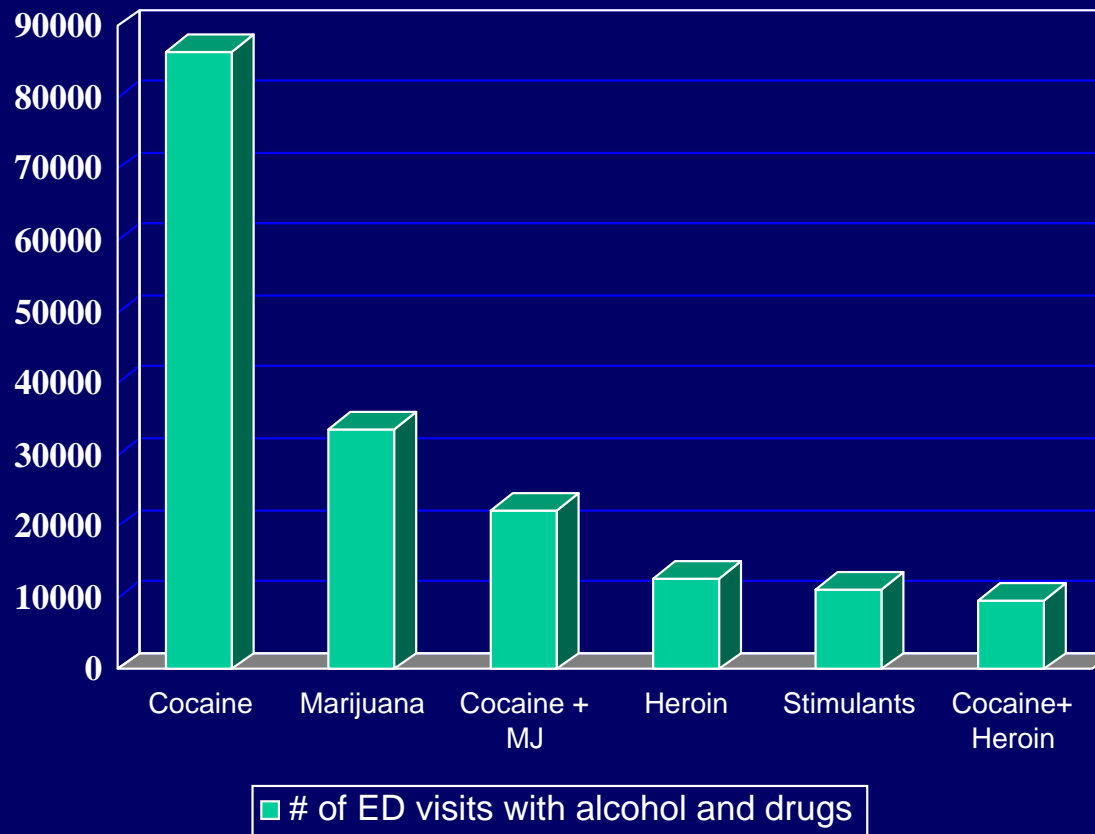


# Intoxication Treatment

- Minimize sensory stimulation
- Neuroleptics (ie haldol) for agitation
- Benzos to control seizures
- Treat hyperthermia (external cooling)
- For increased BP+HR, use vasodilators and CCB or non-selective beta-blockers



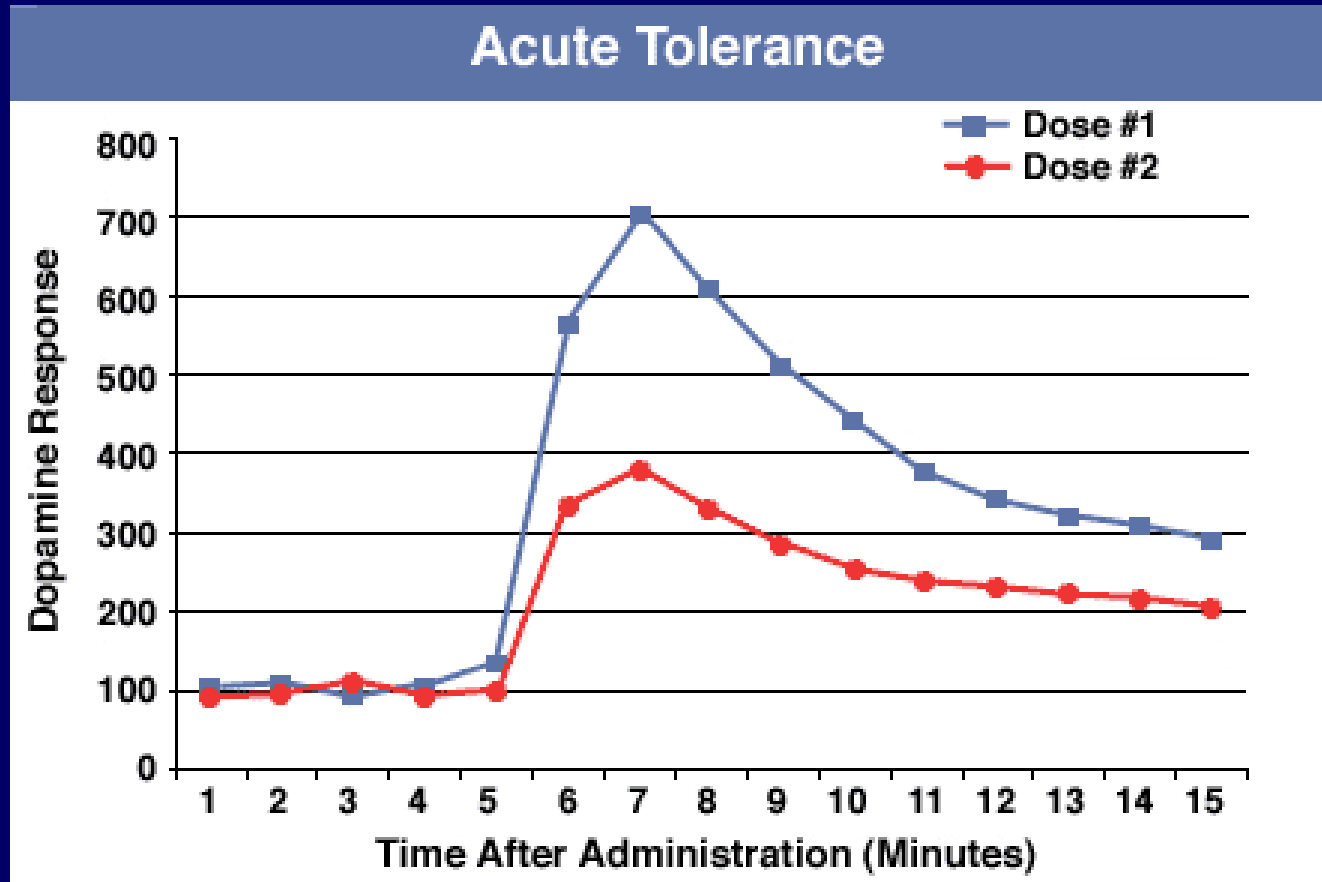
# 2005 alcohol-related ED visits



# Prevalence and Price

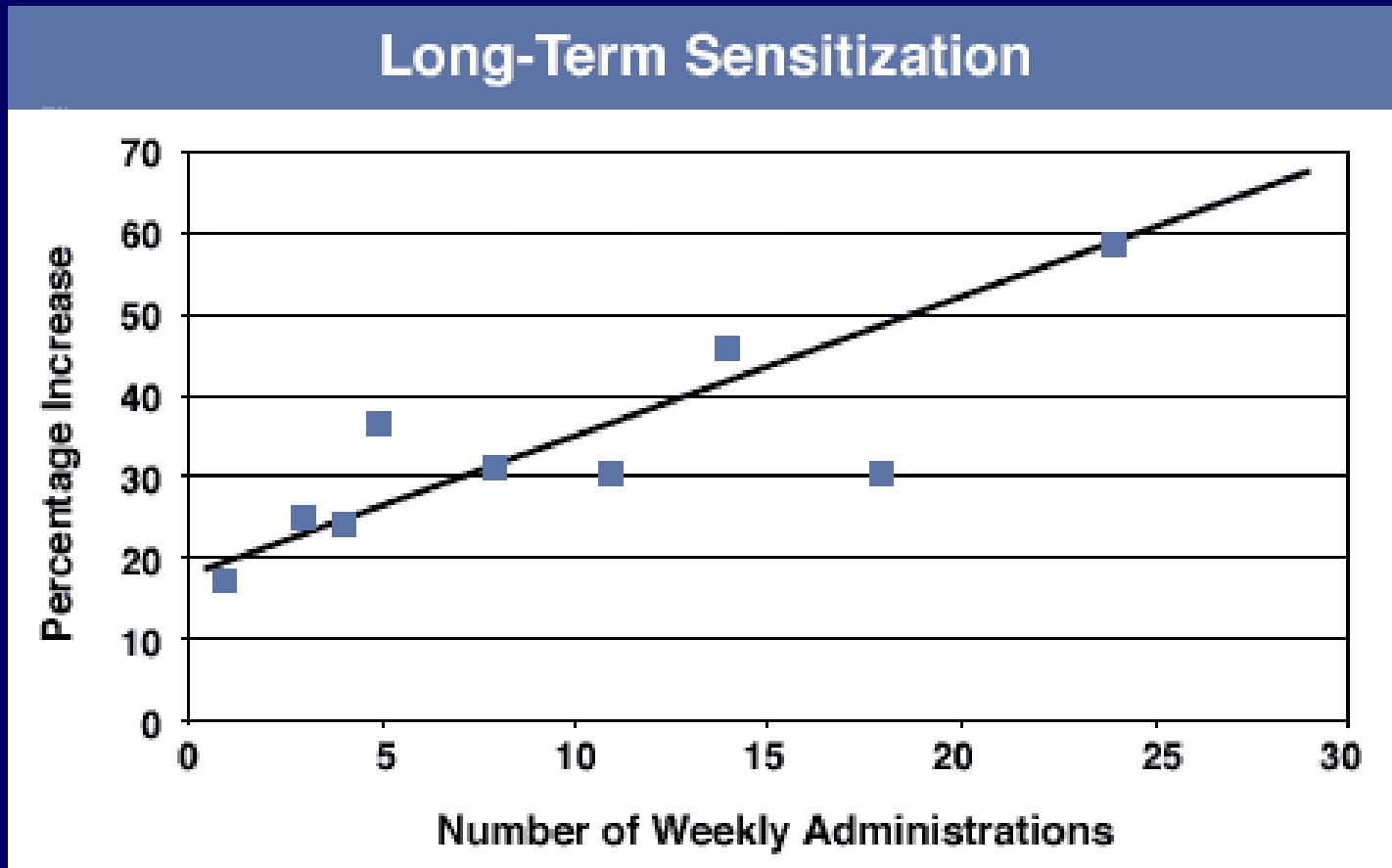
- Cocaine
  - 33M lifetime users
  - 8M for crack
  - 1.5-3.7M chronic users
  - Up to 1/2 of arrestees are positive
  - 37% of all Federal arrests
  - \$20-100 per gram
  - \$3-50 per rock of crack
- Methamphetamine
  - 12M lifetime users
  - 600k monthly users
  - >1/3 of arrestees are positive in the West
  - Moving east with no decreases in 2002
  - \$20-300 per gram

# Mesolimbic dopamine response to cocaine





# Dopamine levels with chronic cocaine use



NIDA Notes Volume 16, Number 3 (August, 2001)

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MA causes long-term neurotoxicity to striatal neurons and short-term toxicity to thalamic neurons that is reversible

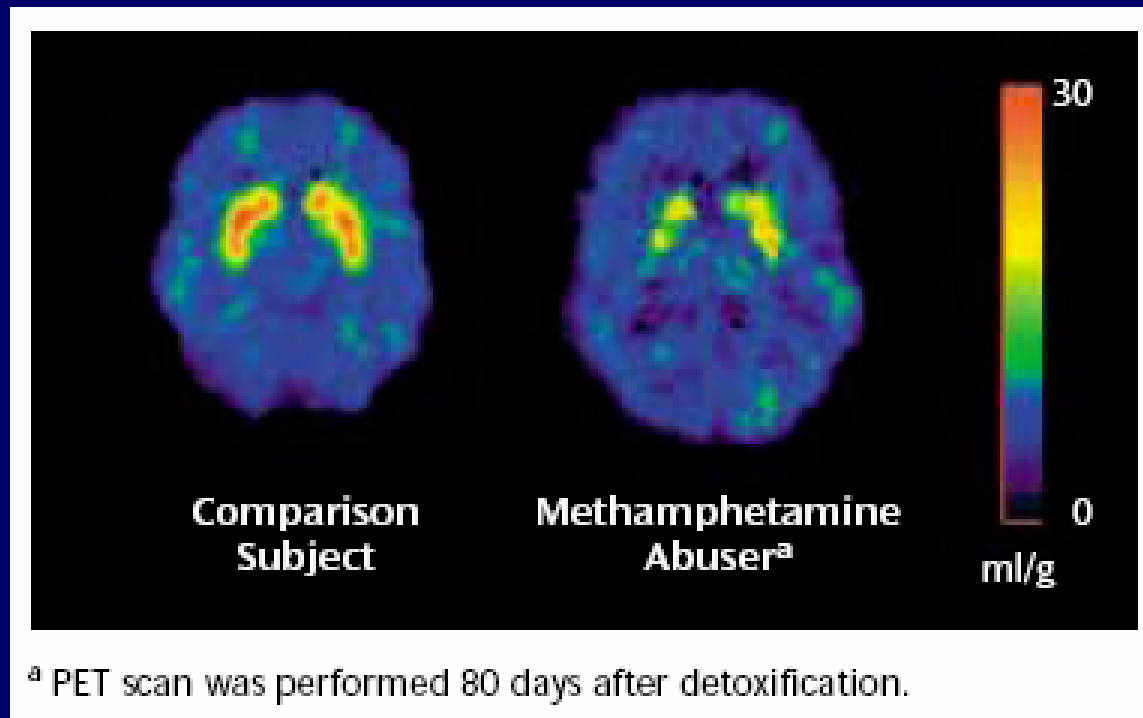
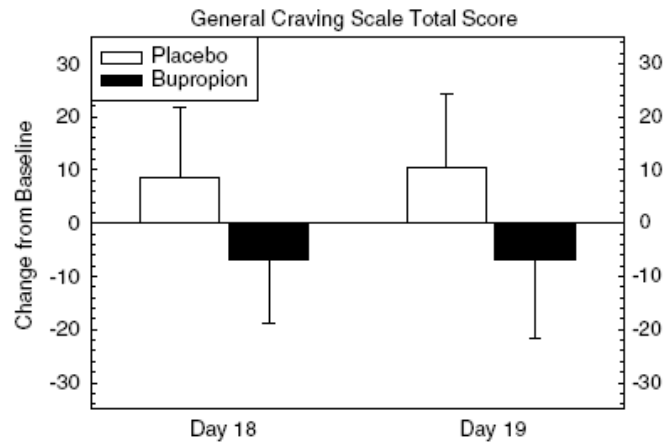
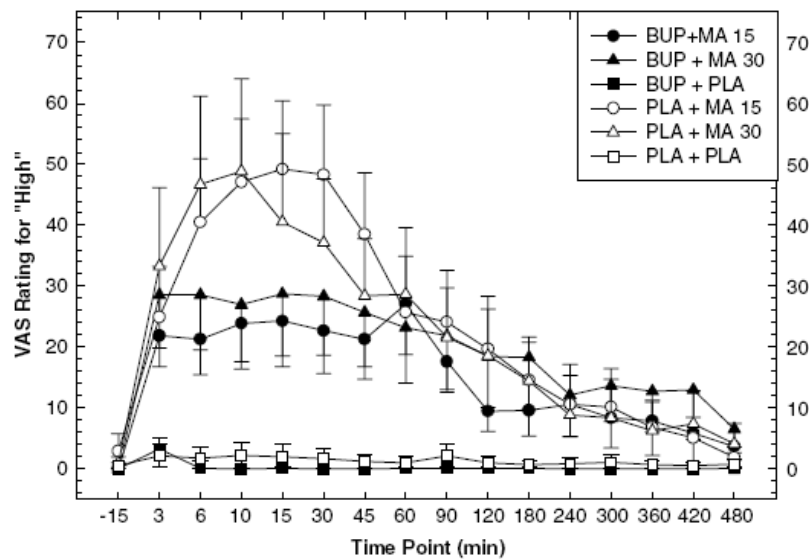


FIGURE 1. Striatal Distribution Volume of the Dopamine Transporter Ligand [<sup>11</sup>C]*d-threo*-Methylphenidate in a 33-Year-Old Male Comparison Subject and a 33-Year-Old Male Methamphetamine Abuser

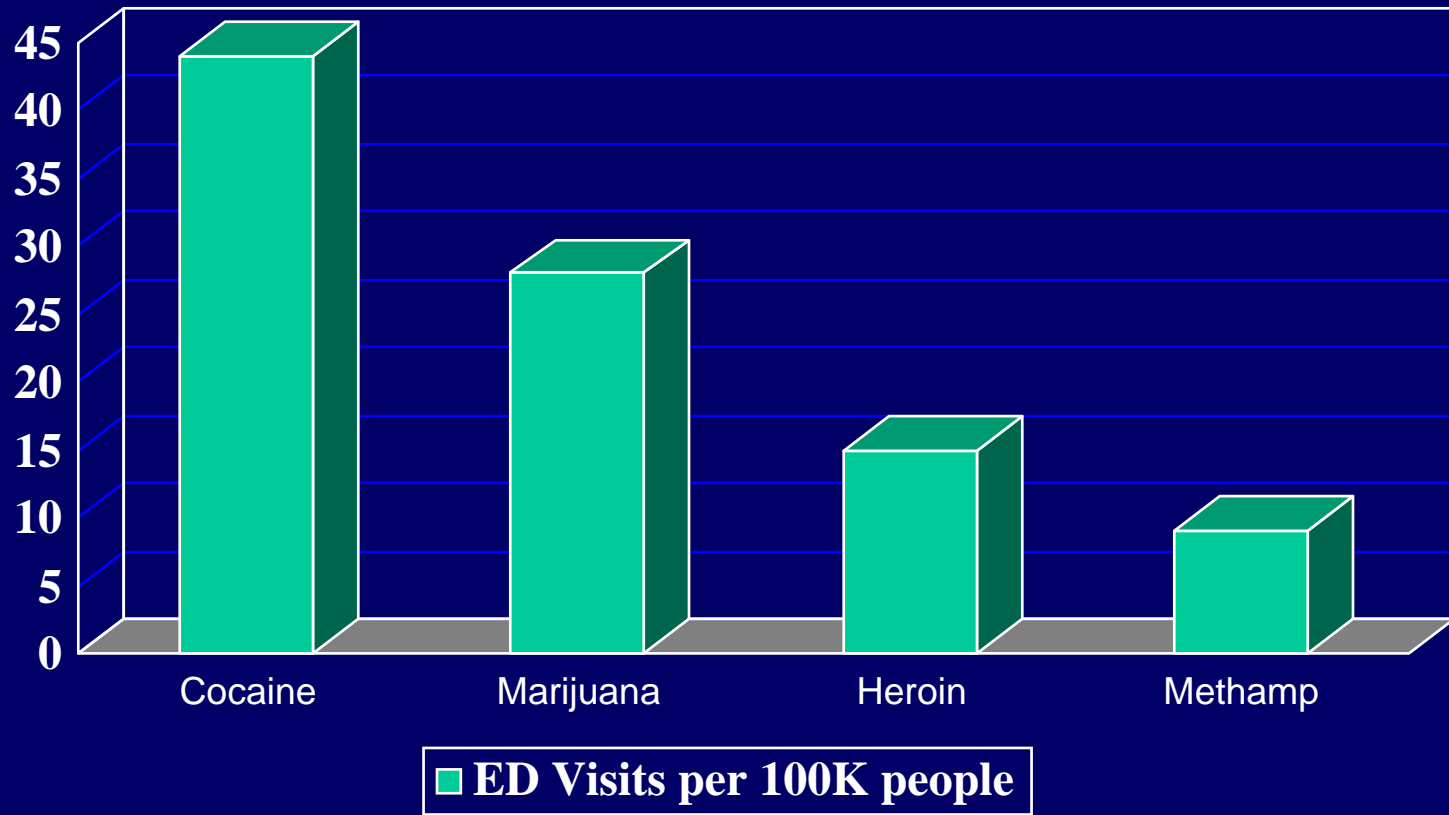


**Figure 4** Effects of cue exposure on craving (mean  $\pm$  SEM). Bupropion treatment (filled bars) significantly reduced cue-induced changes in craving as compared to effects observed in patients treated with placebo (open bars).

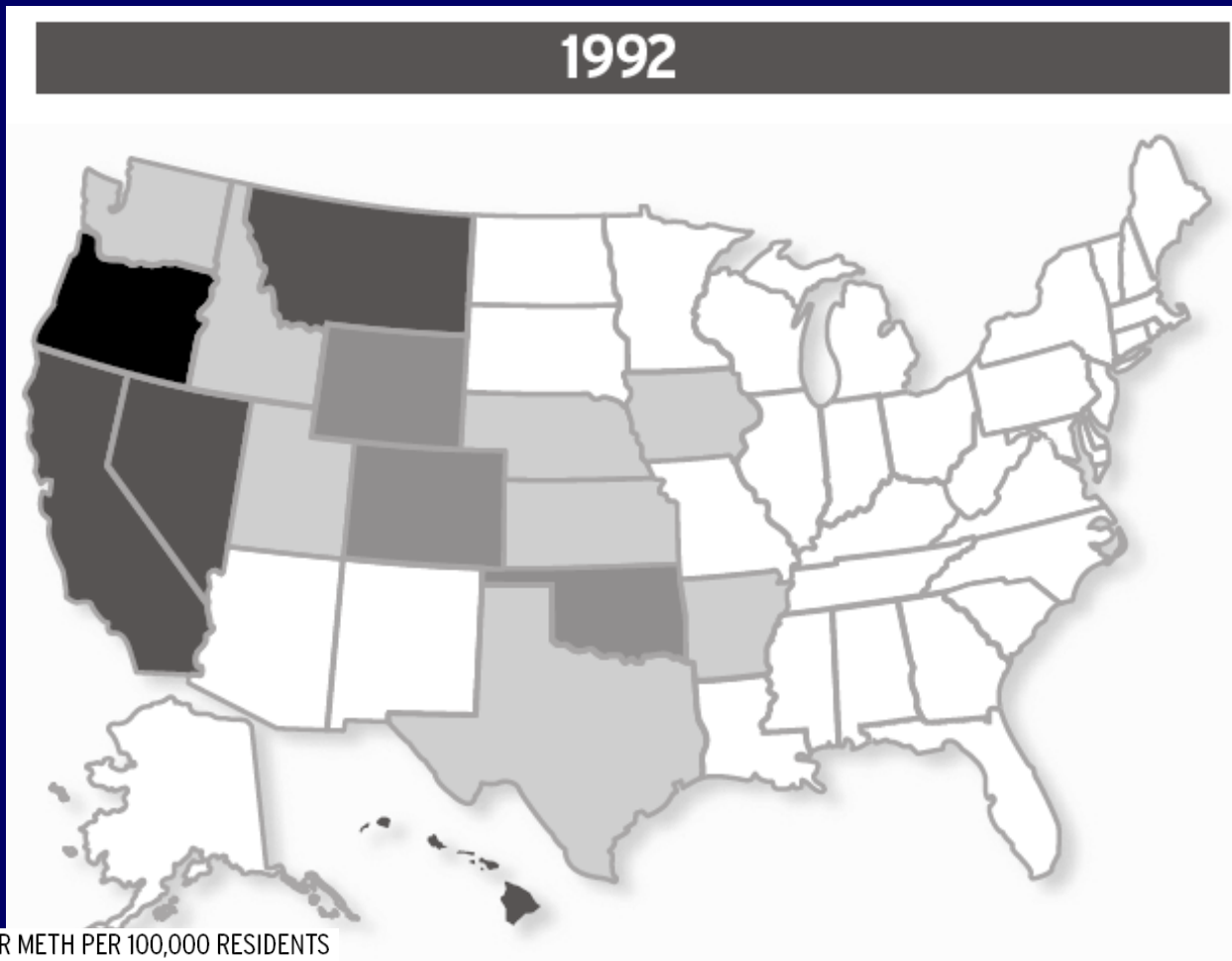


**Figure 2** Ratings for 'high' (mean  $\pm$  SEM). The full time-course is shown following acute administration of placebo (squares), 15 mg (circles), and 30 mg (triangles) methamphetamine 6 days after initiation of twice-daily oral placebo (open symbols) or bupropion (filled symbols).

# 2003 drug-related ED visits



# MA rehab admits per 100,000



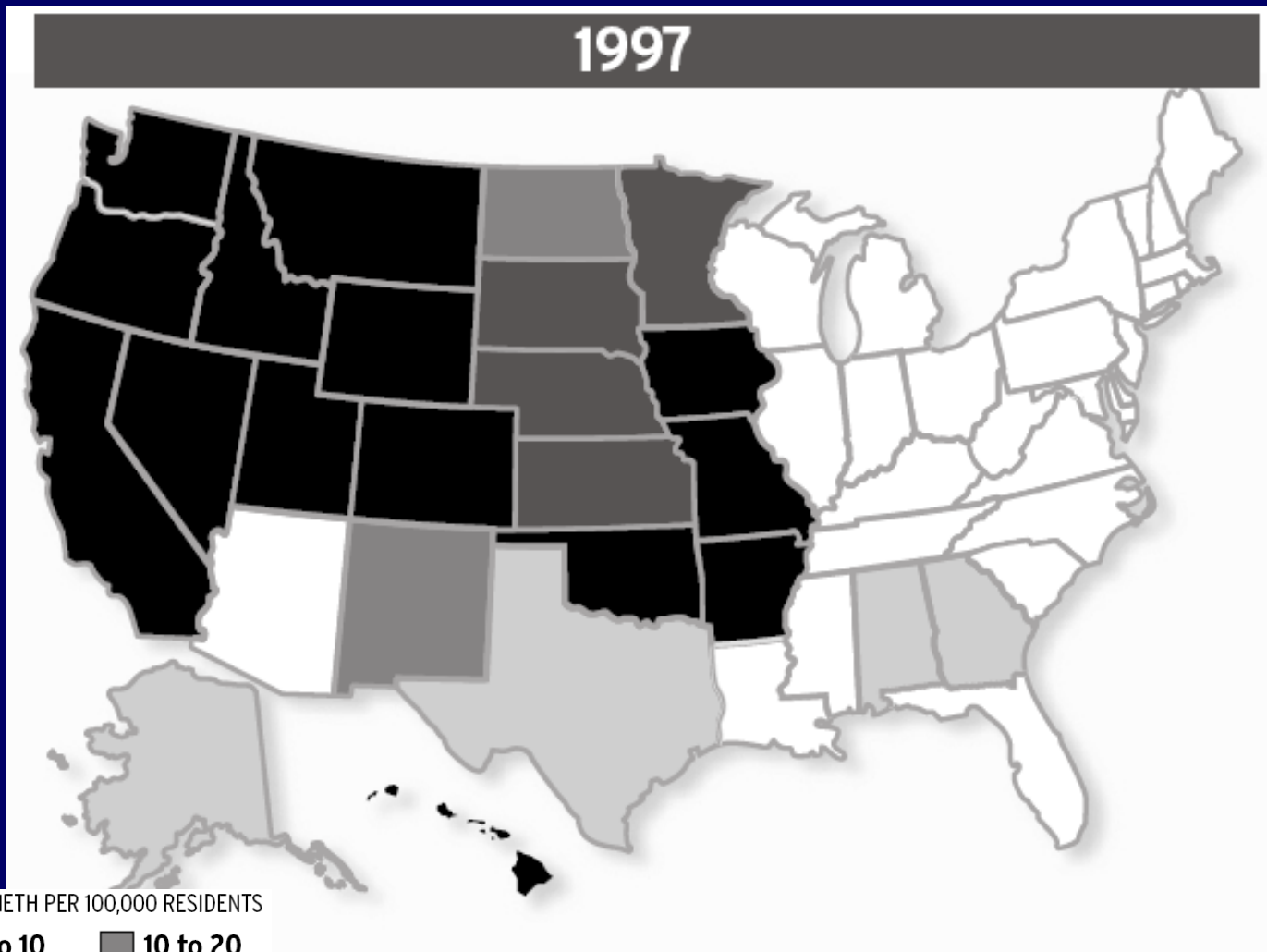
REHAB ADMISSIONS FOR METH PER 100,000 RESIDENTS

- 0 to 5
- 5 to 10
- 10 to 20
- 20 to 40
- 40 or more

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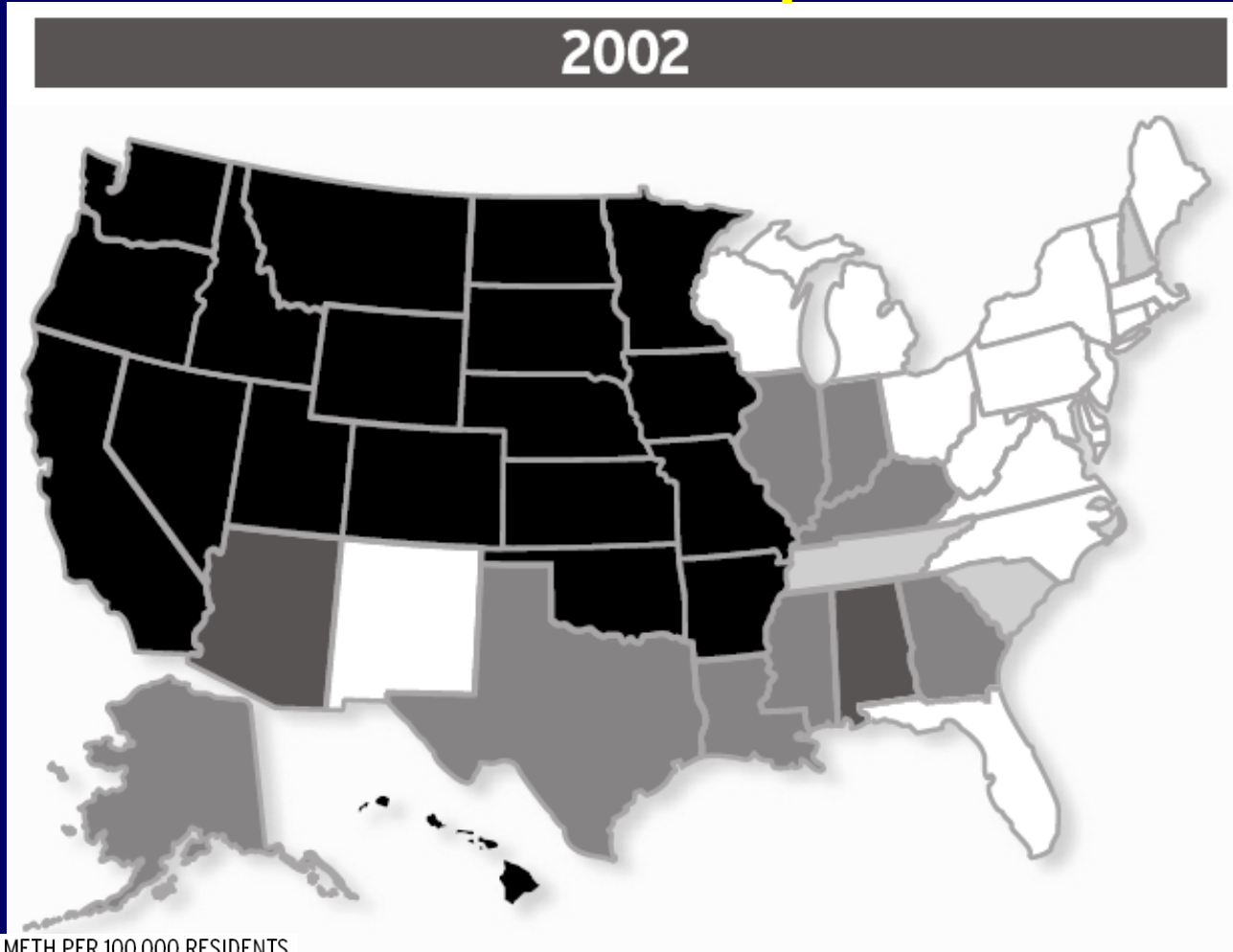
# MA rehab admits per 100,000



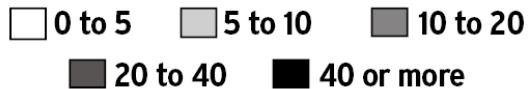
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# MA rehab admits per 100,000



REHAB ADMISSIONS FOR METH PER 100,000 RESIDENTS



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