

2008 CSAM Addiction Medicine Review Course
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Stimulants: Cocaine and Methamphetamine

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Overview: Cocaine and Methamphetamine

- I. Background & History
- II. Epidemiology
- III. Diagnostic factors
- IV. Pharmacology
- V. Pathophysiology/Adverse effects of abuse
- VI. Treatment

Background & History

- Traditional use of cocaine
- Modern use

Coca

- *Erythroxylon coca*
- shrub grows in Andes
- used by indigenous people in South America for millenia
- contains 0.5% cocaine
(Gold & Miller 1997)



Traditional use of *coca*

- Leaves are harvested
- Chewed with cud inside cheek
- Lime used to change mucosal pH to help absorption
- Effects mild compared to pure cocaine



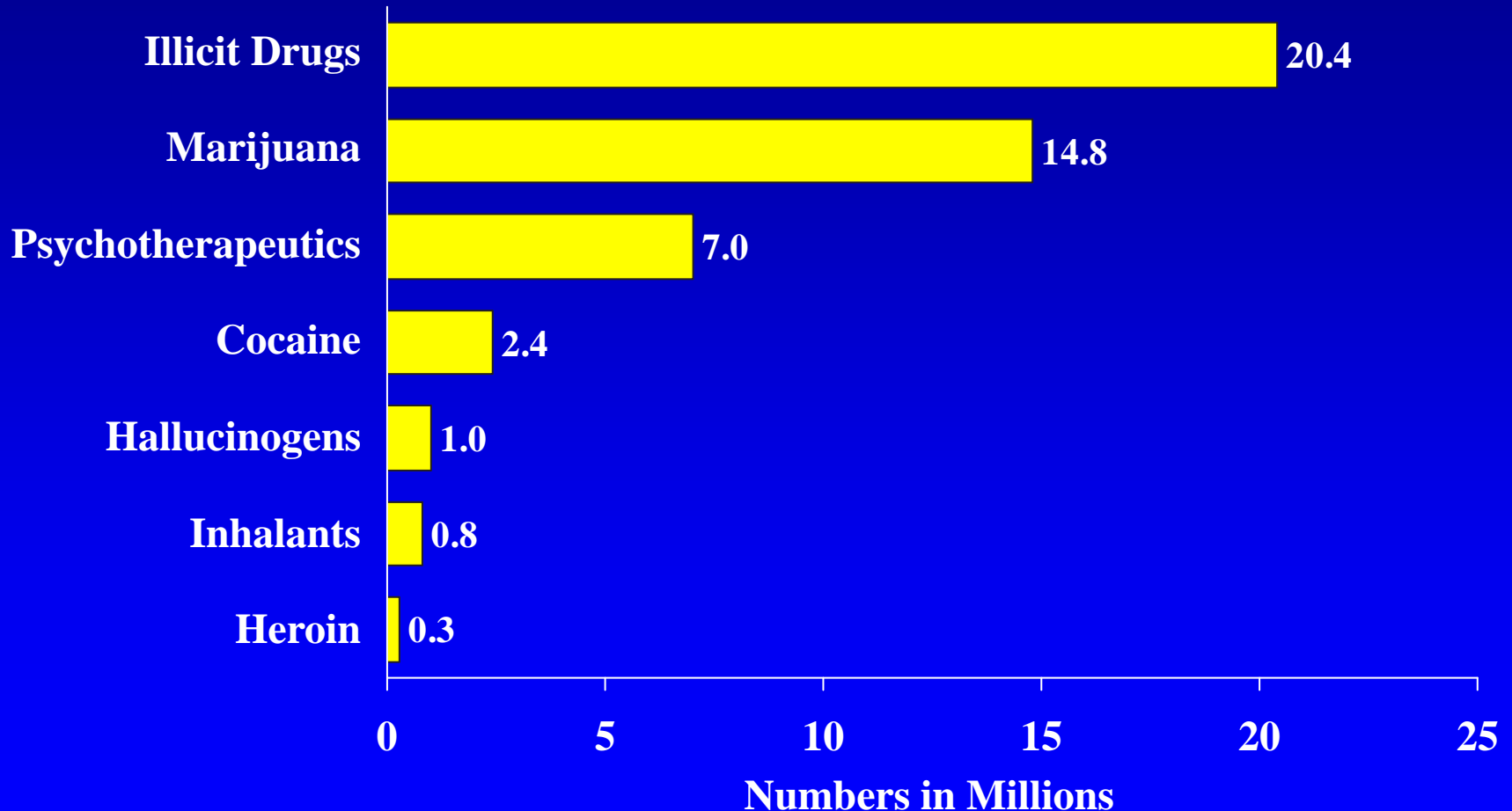
Modern History of Cocaine

- Cocaine isolated 1860
- Local anesthetic 1884
- Freud: *Über Coca* 1884
- Harrison Act: 1914
- Epidemics in 1920s, 1970s
- Crack in 1980s-now

Epidemiology

- Prevalence of cocaine use in the general population
- Prevalence of emergency department mentions for cocaine and other stimulants

Past Month Use of Specific Illicit Drugs among Persons Aged 12 or Older: 2006 (NSDUH 2006)

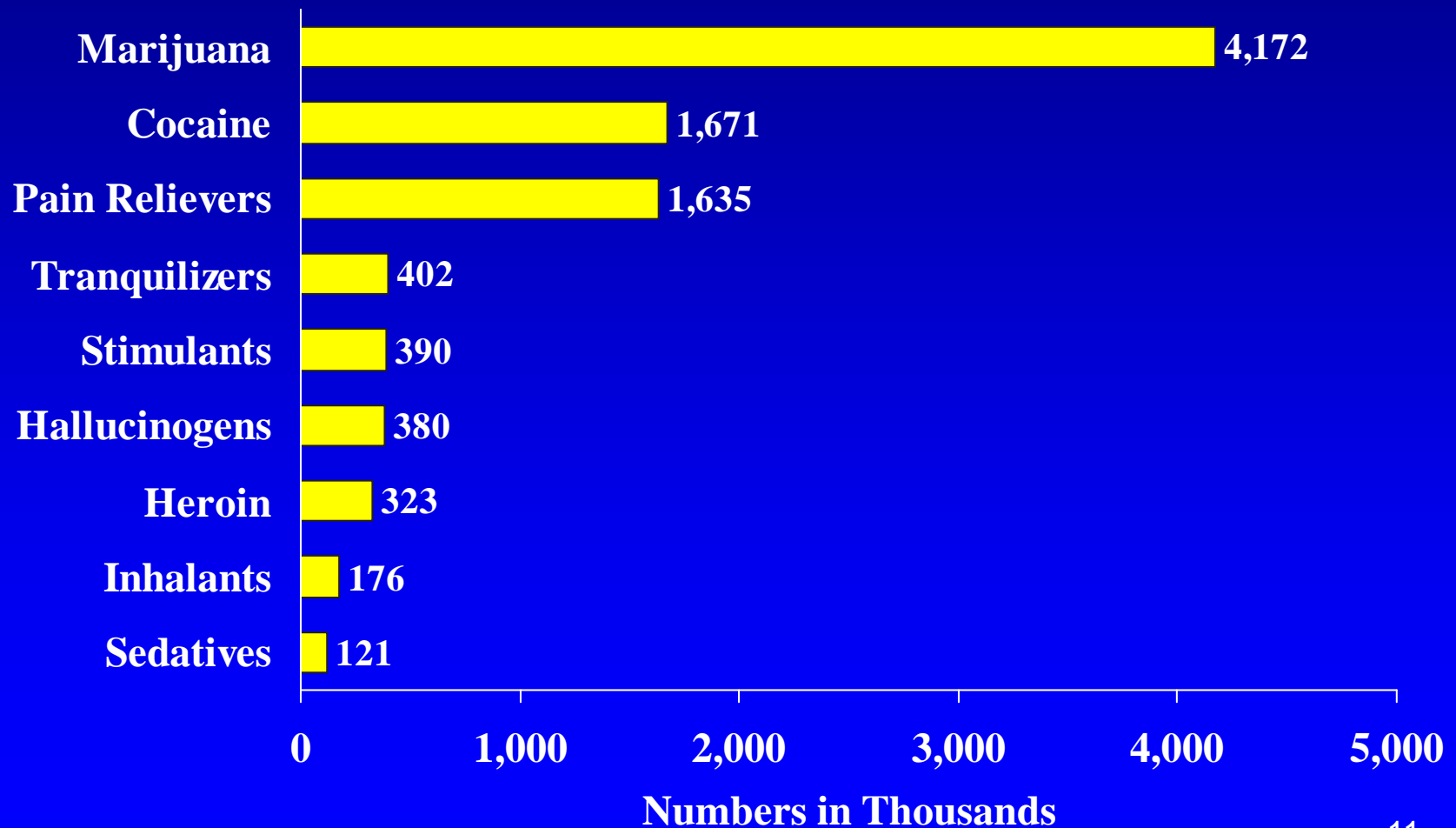


Prevalence of Cocaine Use (in >12 y.o.)

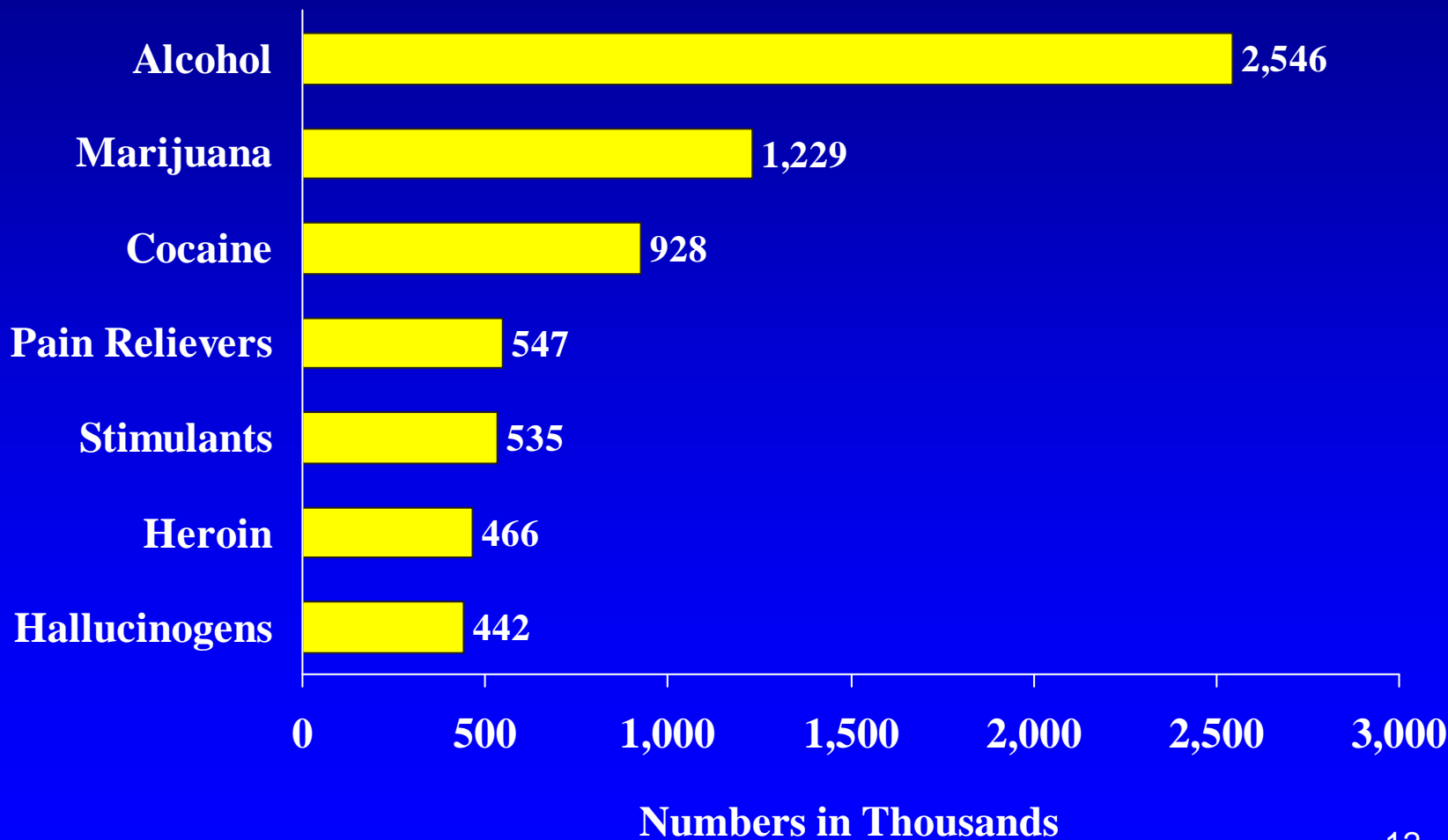
2000 National Household Survey on Drug Abuse

- 11.2% of U.S. population report ever using cocaine
- 1.5% report using cocaine within the past year
- 0.5% report using within the past month
- Most common in 18-25 age group
- 494,000 received treatment for cocaine in past year

Dependence on or Abuse of Specific Illicit Drugs in the Past Year among Persons Aged 12 or Older: 2006 (NSDUH 2006)



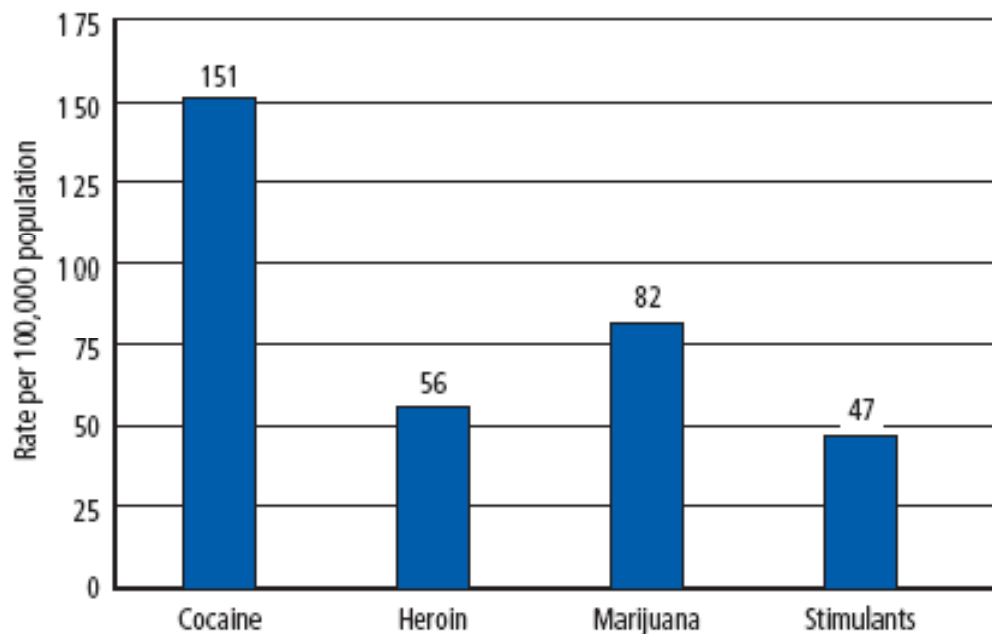
Substances for Which Most Recent Treatment Was Received in the Past Year among Persons Aged 12 or Older: 2006 (NSDUH 2006)



DAWN 2005 Rates of Cocaine and Stimulant ED Visits

Figure 1

Rates of ED visits involving selected illicit drugs: 2005



SOURCE: Office of Applied Studies, SAMHSA, Drug Abuse Warning Network, 2005 (04/2006 update).

Demographic Characteristics of DAWN 2000 ED Mentions: COCAINE (n=96,282)

GENDER

Male 64.5 %

RACE/ETHNICITY

White 38.8 %

Black 39.6 %

Hispanic 13.5 %

Unknown 8.1 %

AGE

12-17 years 1.8 %

18-25 years 15.4 %

26-34 years 27.1 %

35 years and older 55.4 %

Genetics of Cocaine Dependence

Saxon et al (2005) Genetic determinants of addiction to opioids and cocaine. Harv Rev Psychiatry. 2005 Jul-Aug;13(4):218-32.

- Genetic epidemiologic studies support a high degree of heritable vulnerability for both opioid and cocaine dependence.
- Polymorphisms in the genes coding for dopamine receptors and transporter, opioid receptors, endogenous opioid peptides, cannabinoid receptors, and serotonin receptors and transporter all appear to be associated with the phenotypic expression of this vulnerability once opioids or cocaine are consumed.
- **CONCLUSION:** Despite progress, identification of specific genes and quantification of risk remain to be elucidated.

Diagnostic Categories - DSM-IV

- abuse
- dependence
- withdrawal
- intoxication delirium
- cocaine-induced disorders:
 - mood disorder
 - anxiety disorder
 - sexual dysfunction
 - sleep disorder

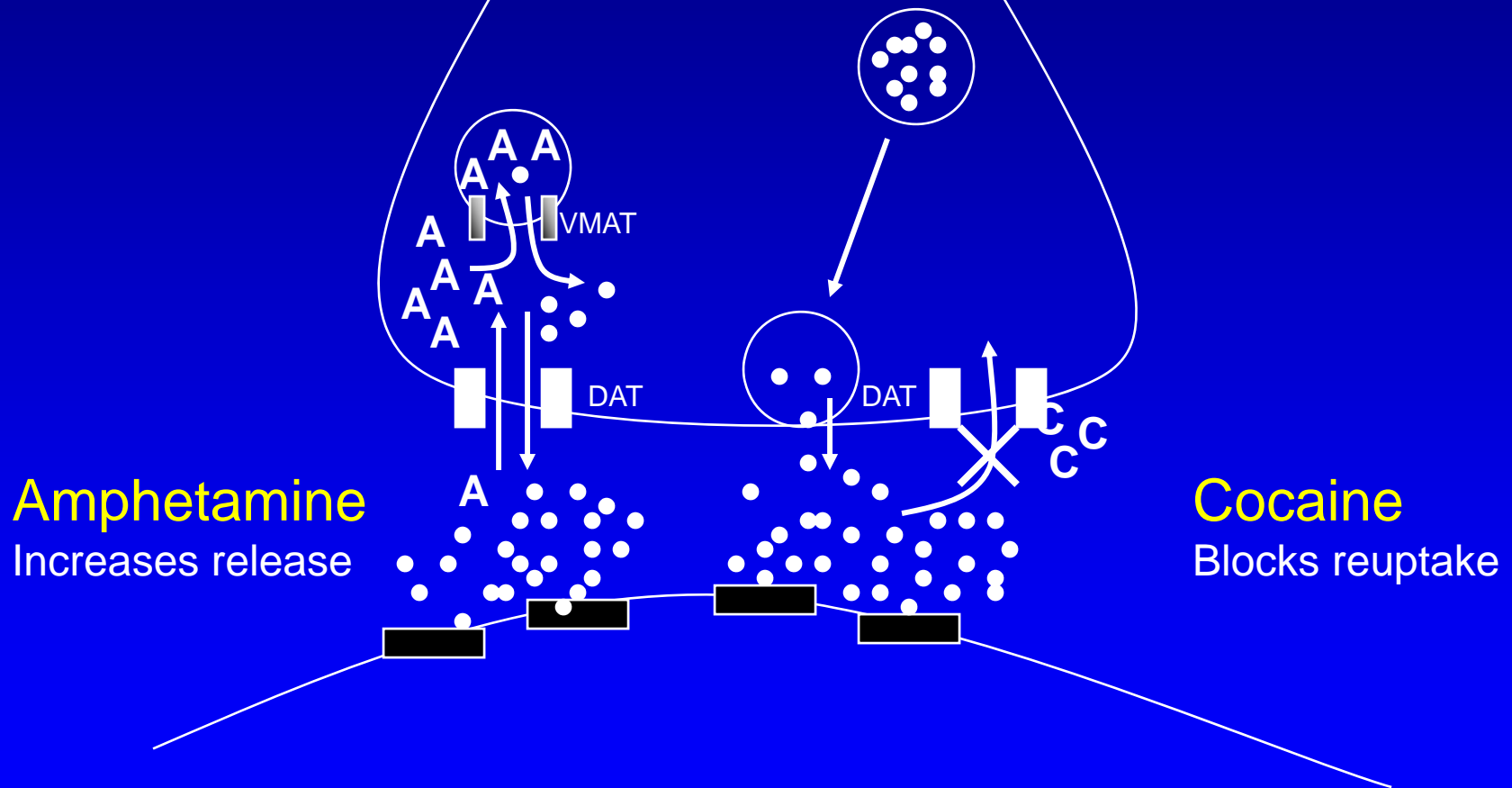
Pharmacology

- Pharmacological action of cocaine
- Pharmacokinetics
- Clinical effects

Major Acute Actions of Cocaine

- Local anesthetic
 - Blocks membrane sodium channels
- Stimulates CNS
 - Blocks presynaptic neurotransmitter reuptake pumps (transporters): dopamine, norepinephrine, serotonin
- Stimulates sympathetic nervous system
- Chronic effects unclear (neurotransmitter depletion? receptor upregulation?)

Cocaine vs Methamphetamine: Effects at the Synapse



Mechanism of Cocaine's Psychoactive Effects

- Binding to dopamine transporter correlates best with behavioral potency in animals → ↑ dopamine levels in nucleus accumbens
- Lesions of mesolimbic dopamine circuit (“reward” circuit) abolish cocaine self-administration
- However, “knockout” mice without dopamine transporter do not show motor stimulation or sleep suppression, but still get reinforcement from cocaine

Sensitization to Cocaine and other Stimulants

- Sensitization (reverse tolerance) = enhanced response to drug because of prior exposure
- Kindling = low intensity, intermittent brain stimulation (electrical, pharmacological) leads to enhanced response to later stimulation

Forms of Cocaine Use

Powdered Cocaine HCl
for Intranasal or Injection use



Making freebase cocaine



Crack cocaine



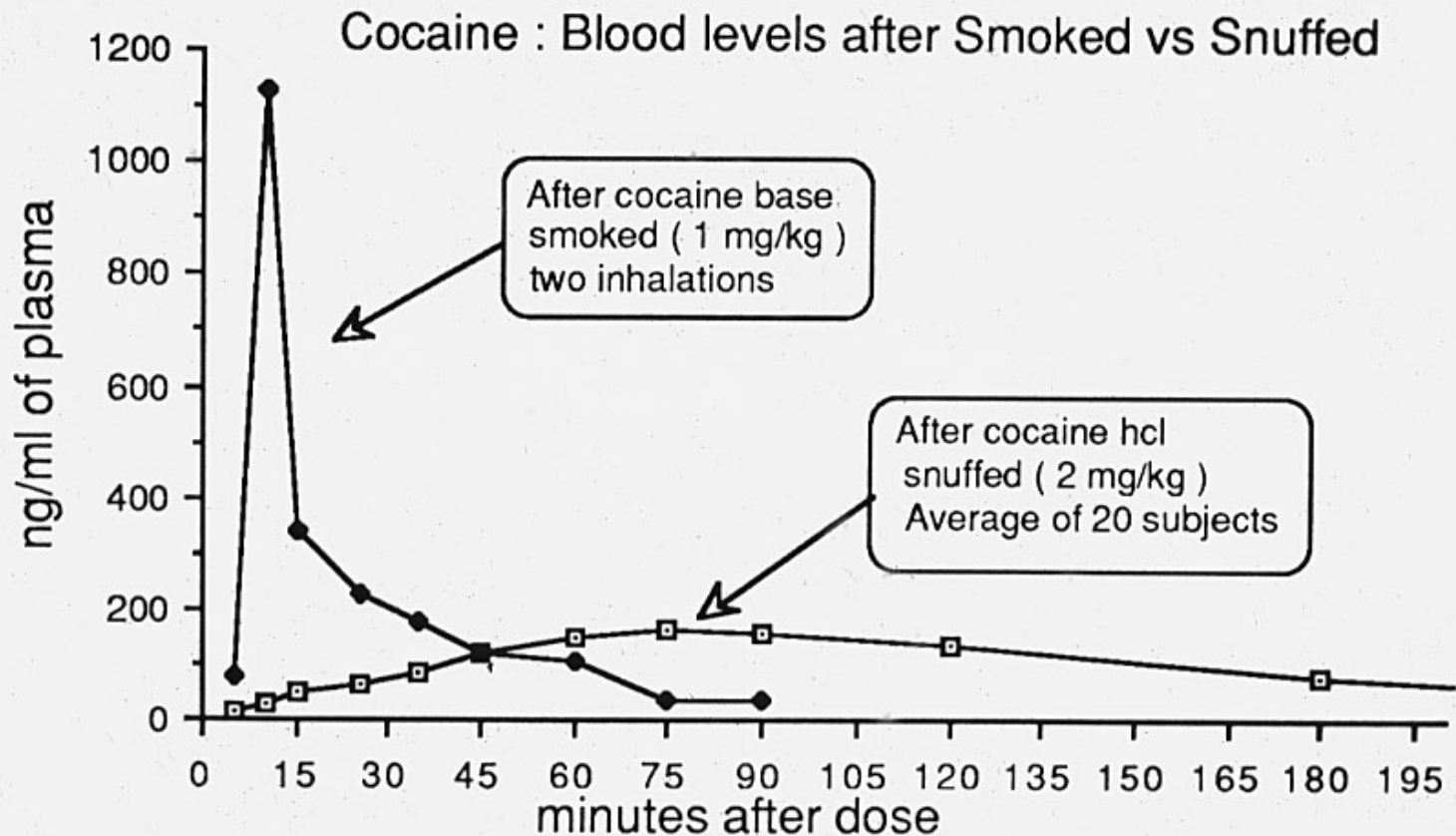
Routes of Administration and Forms of Cocaine

- Intranasal (nasal insufflation, snorting)
 - powder cocaine HCl, water soluble
- Injection
 - powder cocaine HCl
- Pulmonary (smoked)
 - crack = free base cocaine, alkaloidal cocaine, has lower melting point and can be smoked

Pharmacokinetics, 1: Routes of Administration and Absorption

- Pulmonary: quickest absorption, along with IV injection, in blood in 6-8 seconds
- Injection (intravenous and other), 6-8 seconds
- Intranasal: slower absorption
- Oral: slowest

Kinetics of Smoked Cocaine



Cocaine Pharmacokinetics, 2: Metabolism

- Metabolism
 - primarily (95%) by esterases
 - principal metabolite is benzoylecgonine (BE)
- Half-life of cocaine (plasma)
 - generally ranges from 40-90 min
 - acute ~40-60 min; chronic ~ 1.5 h or longer

Cocaine Pharmacokinetics, 3: Excretion

- Excretion
 - largely eliminated in urine
 - BE is metabolite in highest concentration
- Detection by urine drug tests
 - generally 24-72 hrs, may be as long as 96 hrs

Cocaine Pharmacokinetics, 4: Cocaine and Alcohol forms Cocaethylene

- alcohol-cocaine forms cocaethylene
- metabolite formed in presence of heavy alcohol intake together with cocaine
- formed by transesterification
- similar effects to cocaine, longer half-life, more severe toxicity when present along with cocaine
- greater than additive effects on heart rate and violence potential (Pennings et al. 2002 Addiction)

Cocaine Pharmacokinetics, 5

- Drug-drug interactions, Antidepressants:
 - monoamine oxidase inhibitors (MAOIs)
 - hypertensive crisis
 - other antidepressants
 - SSRIs
 - increased seizure risk of cocaine in combination with SSRIs in mouse model (O'Dell et al. 2000, Exp Clin Psychopharmacol)
 - human implications unclear--wide experience with SSRIs and cocaine in human research has appeared safe
 - TCAs
 - Theoretical potential for HTN due to TCA NE reuptake inhibition and cocaine

Medical Use of Cocaine

- Topical, local anesthetic

Cocaine - Subjective and Behavioral Effects

- Onset
 - Intranasal effects within minutes (5-15)
 - Smoked effects within seconds
- Effects
 - Euphoria, hyperactivity (motoric & verbal), hypersexuality initially
 - Insomnia, anorexia.
 - Persecutory delusions (paranoia) and hallucinosis (aud, vis, & tactile), agitation
 - Confusion rare except in very high doses when delirium can occur
 - Stereotyped movements may occur (teeth grinding, skin picking)
- Chronic use produces tolerance to euphoria, positive effects decrease, agitation & anxiety increase

Cocaine Effects: Physiological

- Sympathomimetic effects
 - Elevated
 - BP
 - HR
 - Temp
- At high doses:
 - Hyperthermia
 - Rigidity
 - Seizures

Cocaine: Characteristics of Withdrawal

- “Crash” after discontinuation of prolonged high dose use (Gawin & Ellinwood 1988)
 - Early outpatient study: depression, fatigue, may be accompanied by suicidal ideation
 - Later inpatient studies report mild depression, anxiety, anhedonia, insomnia or hypersomnia, increased appetite and psychomotor retardation that improves over several weeks (eg Weddington 1990)
 - Withdrawal symptoms not uniformly reported
 - Intense craving and anhedonia are common

Changes in Mood with Cocaine Abstinence

Weddington et al, Arch Gen Psych 1990

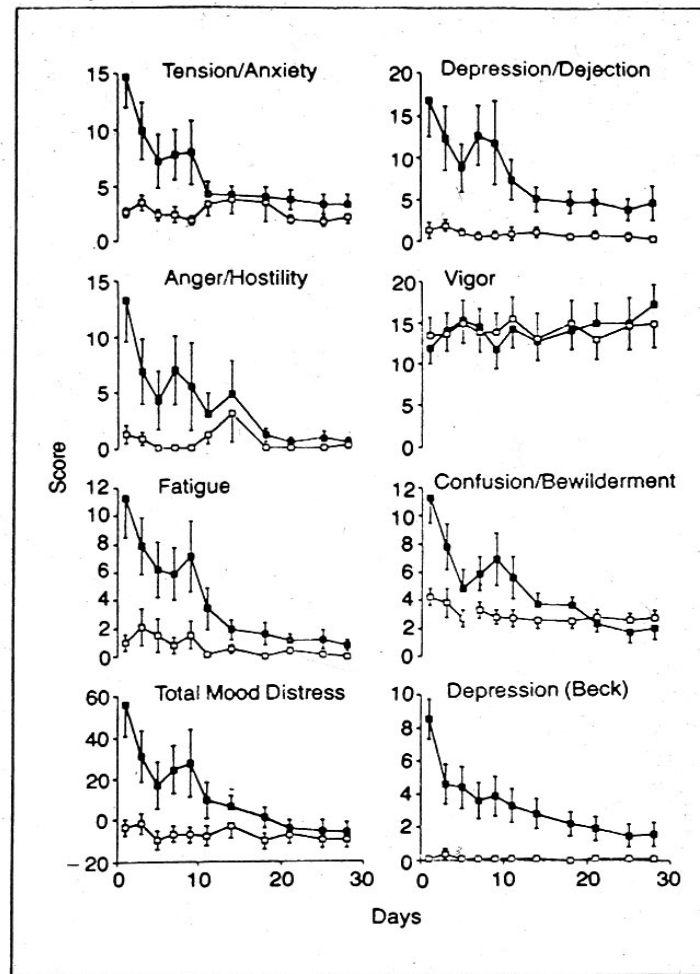


Fig 1.—Mean (\pm SEM) scores of mood over time using the Profile of Mood States and the Beck Depression Inventory. Day 1 is the day of admission. Solid squares represent cocaine-addicted subjects; open squares, control subjects. Addicted subjects demonstrated significantly elevated scores of mood disturbances and rates of mood change over time for all scores other than "Vigor" (see Table 2).

VI. Pathophysiology & Adverse Effects of Abuse - Overview

- Medical
- Psychiatric
- Psychosocial

Medical Complications of Cocaine

- Complications reflect primarily:
 - excessive CNS stimulation
 - vasoconstriction
- Cardiac
 - Myocardial ischemia/infarct
 - Arrhythmias
 - Myocarditis
- Central Nervous System
 - Hyperpyrexia
 - Seizures
 - Cerebral infarct
 - Cerebral hemorrhage

Medical Complications, 2: Pathophysiology

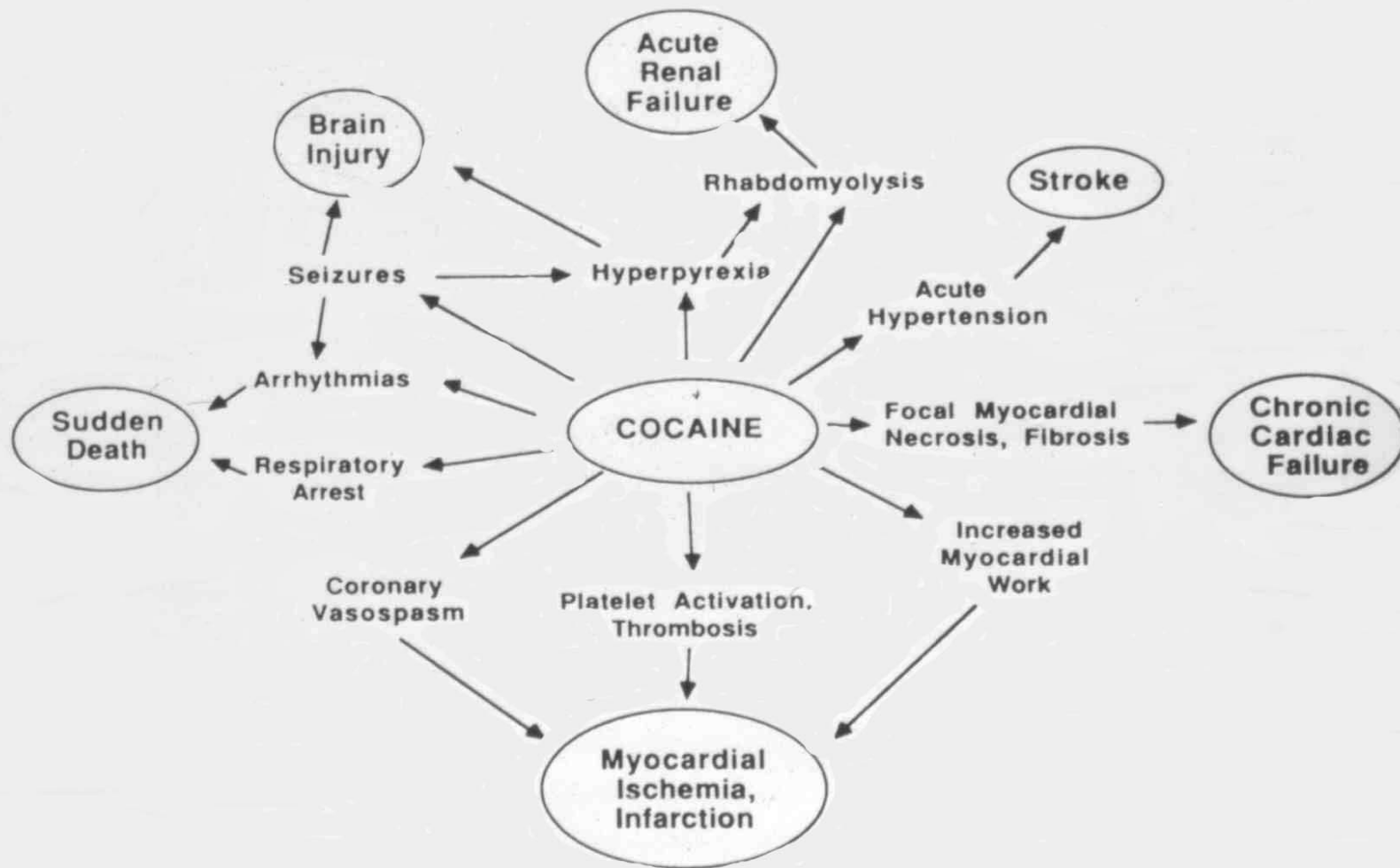


FIG. 3 Pathophysiology of medical complications of cocaine abuse (except for reproductive complications).

Medical Complications, 3: Association with Routes of Cocaine Administration

- Intranasal use
 - erosion of nasal mucosa & perforated septum
- Injection Use
 - HIV
 - hepatitis C and other hepatitis
 - endocarditis
 - soft tissue infections: abscesses & cellulitis
- Smoking
 - pulmonary edema, pneumonitis, pneumothorax

Cocaine and Pregnancy

- Irregular placental blood flow
- Placental abruption
- Premature rupture of membrane (PROM)
- Premature labor and delivery

- In a recent meta-analysis, the only adverse event significantly associated with cocaine was PROM (Addis et al. 2001 Reprod Toxicol)

Putative Effects of Cocaine on Birth and Fetal Development

- Frequently attributed effects:
 - Prematurity
 - Low birth weight
 - Decreased head circumference
 - Lower developmental test scores
 - Delayed language skills
- Less frequently attributed effects
 - Transient EEG abnormalities
 - Cerebral infarct
 - Seizures
 - Small brain hemorrhages

Meta-analysis of Effects of Cocaine on Early Childhood Development

- Conclusion of recent JAMA review:
 - among children aged 6 or younger
 - there is no convincing evidence that prenatal cocaine exposure is associated with developmental toxic effects
 - that are different in severity, scope, or kind from the sequelae of multiple other risk factors.
 - many findings once thought to be specific effects of in utero cocaine exposure are correlated with other factors,
 - including prenatal exposure to tobacco, marijuana, or alcohol,
 - and the quality of the child's environment.
 - “Further replication is needed of preliminary neurological findings.”

(Frank et al. 2001 JAMA)

Treatment

- Overview:
 - Pharmacologic
 - Non-pharmacologic

Cocaine Use Disorders: Information for Treatment Planning

- Key variables to help determine what level of care is needed
 - severity of cocaine use
 - stage of the cocaine use (intoxication vs. abstinence syndrome)
 - readiness for change (motivation)
 - level of social support
 - other psychiatric and medical comorbidity

Psychosocial Treatments

- Community Reinforcement
- Community Reinforcement plus Vouchers
- Contingency Management (Voucher based reinforcement)
- Cognitive/Behavioral Therapy (CBT)-Relapse Prevention, e.g. the Matrix Model
- 12-Step facilitation
- Acupuncture

(CSAT 1999; Knapp et al 2007)

Community Reinforcement Approach (CRA)

CRA is an individualized treatment designed to promote lifestyle change in key areas needed for recovery

1. Marital therapy if spouse is not a user
2. Vocational assistance
3. New social networks and recreational activities that promote recovery
4. Self-help participation
5. Relapse prevention skills training (refusal skills, mood regulation, time management, etc.)
6. Disulfiram and compliance support

(CSAT 1999)

Community Reinforcement Approach (CRA) Plus Voucher Incentives

- CRA superior to standard counseling
- Voucher-based incentives for cocaine-free urine tests added to CRA
- Use of Incentives improved CRA outcomes further
 - * 75% vs 40% completed 24 weeks of tx
 - * 12 vs 6 weeks continuous cocaine abstinence

Higgins et al, 1994

Recent Research on Psychosocial Treatments for Cocaine Dependence

- Method
 - Large (n=487), controlled study over a 6-month period:
 - Group Drug Counseling (GDC)
 - Individual Drug Counseling (IDC) (12-Step Facilitation) + GDC
 - Cognitive Behavioral psychotherapy (CBT) + GDC
 - Supportive Expressive psychotherapy (SET) + GDC
- Results
 - IDC + GDC provided greatest improvement on ASI and days of cocaine use over past month
 - Psychotherapy was not superior to GDC for those with severe psychiatric illness
 - CBT not superior for treatment of ASP

Review of Psychosocial Treatments for Cocaine and Amphetamine, 1.

- 27 randomized controlled studies; 3663 subjects
- Cocaine was the psychostimulant used by participants in all but one that studied amphetamine.
- Comparisons were made of psychosocial treatments but most of them did not show statistically significant differences between interventions,
- *Evidence currently available does not have data supporting a single psychosocial treatment approach.*

Review of Psychosocial Treatments for Cocaine and Amphetamine, 2.

- Overall, cognitive behavioral interventions reduced dropouts from treatment and use of cocaine when compared with drug counseling.
- Behavioral interventions also performed better than clinical management (psychotherapy sessions attended), usual care (lower rates of cocaine users at 1 and 3 months), information and referral (non-attendance).
- A multimodal intensive intervention was more effective than non-intensive delivery
- Cognitive behavioral treatments with contingency management (voucher-based incentives) also showed benefits.
- Many of the results come from single studies, which limits their generalizability.
- Simple reduction in the amount of drug used or retention in treatment is not a measure of meaningful changes in lifestyle

Acupuncture

- Multicenter trial (Margolin et al, JAMA 2001)
- Randomized, controlled with sham acupuncture
- n=620
- Results: no differences between treatment conditions

Treatment of Acute Cocaine Intoxication, 1

- **Psychosis**
 - Usually resolves spontaneously
 - First line-treatment should be a benzodiazepine, preferably lorazepam (CSAT 1999)
 - Antipsychotics are an effective backup if benzodiazepines alone are inadequate
 - Warning -- typical antipsychotics will lower seizure threshold and increase risks of rigidity/hyperthermia
 - inadequate data on use of atypicals in emergencies

Treatment of Acute Cocaine Intoxication, 2

- **Hypertension, tachycardia, hyperthermia, seizures**
 - Supportive treatment
 - Sedation with benzodiazepines
 - Lower body temp
 - Treat seizures with diazepam, phenobarbital or phenytoin (CSAT 1999)

Pharmacotherapy for Cocaine Withdrawal

- Numerous medications have been tried
- Dopaminergic agonists among most frequently tested
 - e.g. Amantadine (200-400 mg/day) and Bromocriptine (BCT) (dose range: 0.625-7.5 mg/day)
 - Results of clinical trials are inconsistent, perhaps a bit more evidence for amantadine
 - Some overdose lethality risk with amantadine
 - Adverse effects with BCT make use inadvisable
 - There may be a subset of patients who benefit; but characteristics of such patients not yet identified
- Conclusion: no medications proven effective to reduce cocaine withdrawal sx

(de Lima et al. 2002 *Addiction*)

Cocaine Pharmacotherapy for Abstinence Initiation, Use Reduction, or Relapse Prevention

- Many medications tried
- Most common categories: antidepressants, dopaminergic agents, mood stabilizers
- Aim to reduce abstinence symptoms or craving
- Or aim to block/reduce subjective effects of cocaine
- Most recent positive studies: phenytoin, propranolol, methamphetamine, modafinil, topiramate,
 - and especially disulfiram
- Conclusion: No medication has yet shown reproducible efficacy in the treatment of cocaine dependence

Medications for Cocaine Tx

Dopamine agonists

Lima Reisser AARL, et al. (2003) Dopamine agonists for cocaine dependence. *Cochrane Database of Systematic Reviews*, Issue 2.

- 17 studies, 1224 participants
- Amantadine, bromocriptine, and pergolide were evaluated.
- Main outcomes were urine cocaine metabolites and retention in treatment
- No significant differences between interventions.
- Current evidence does not support clinical use of dopamine agonists in cocaine dependence.

Anticonvulsants

Minozzi S, et al. (2008) Anticonvulsants for cocaine dependence. *Cochrane Database of Systematic Reviews*, Issue 2.

- 15 studies (1066 participants)
- anticonvulsants studied: carbamazepine, gabapentin, lamotrigine, phenytoin, tiagabine, topiramate, valproate.
- No significant differences for any of the efficacy measures comparing any anticonvulsants with placebo.
- Placebo superior to gabapentin in diminishing dropouts, and superior to phenytoin for side effects,
- no current evidence supporting clinical use of anticonvulsants in cocaine dependence.

Antipsychotics

Amato L, et al. (2007) Antipsychotic medications for cocaine dependence. *Cochrane Database of Systematic Reviews*, Issue 3.

- 7 small studies were included (293 participants)
- the antipsychotic drugs studied were risperidone, olanzapine and haloperidol.
- No significant differences were found for any of the efficacy measures comparing any antipsychotic with placebo. Risperidone was found to be superior to placebo in diminishing the number of dropouts,
- no current evidence supporting clinical use of antipsychotics in cocaine dependence.

Conclusions

Pharmacotherapy of Cocaine Withdrawal, Abstinence, or Relapse Prevention in 2008

- No medication has been consistently shown to be useful
- Available pharmacotherapies are much less robust in effects than psychotherapeutic and psychosocial interventions

De Lima et al. 2002 Addiction

Methamphetamine

Amphetamines: History

- First synthesized in 1887; first available in the U.S. as benzedrine inhaler (OTC) in 1932
- Other forms of amphetamines became available by prescription starting in 1939; but widespread availability of amphetamines for nonmedical uses continued through the 1960s until tighter regulation of manufacture and prescription occurred in 1972
- Medical uses: narcolepsy, obesity, ADHD, depression

(Source: McCance-Katz, AAAP 1999)

Medical Use of Stimulants

- Attention deficit (hyperactivity) disorder
- Narcolepsy
- Appetite suppression for weight loss
- Decongestion
- Bronchodilation (ephedrine)
- Depression (esp. geriatric, medically ill)
- Reduce fatigue, drowsiness

Federal Schedule of Controlled Substances, Schedule II Stimulants

- Criteria:
 - High potential for abuse
 - Accepted medical use with severe restrictions
 - Abuse may lead to severe psychological or physical dependence
- Examples:
 - cocaine, amphetamine, methamphetamine, methylphenidate, phenmetrazine

Epidemiology: Methamphetamine

- Recent increase, after steady decline until 1991 (DAWN data)
- Spread of MA particularly extensive in Western US
- Ethnic differences from cocaine users: fewer African Americans
- Gay men in US metropolitan areas particularly affected

(NIDA 1992; USDHHS/SAMHSA 1995)

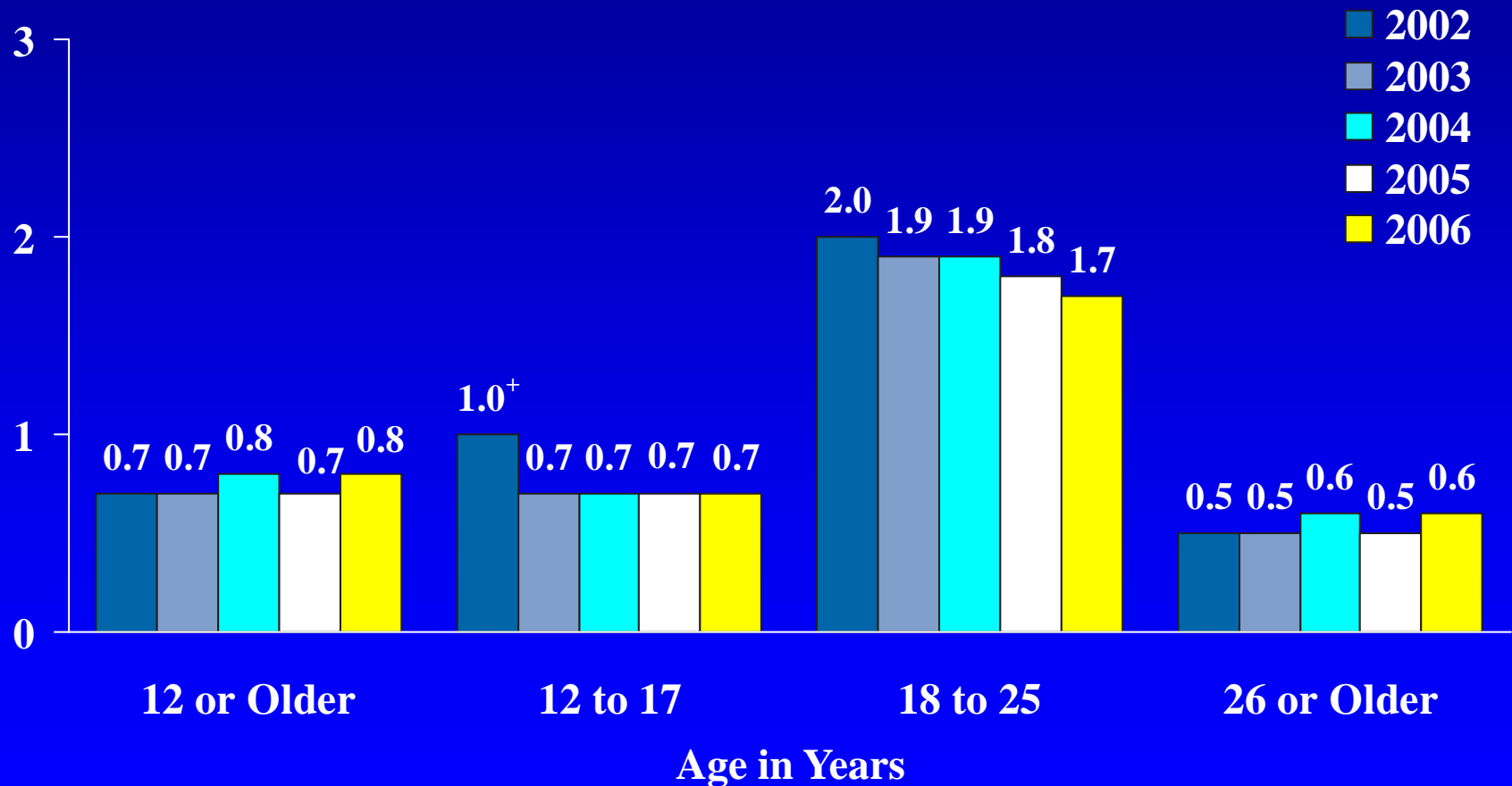
Prevalence of Methamphetamine Use

2000 National Household Survey on Drug Abuse

- 4.0% of U.S. population >12 yo report ever using MA
- 0.5% report using MA within the past year
- 0.2% report using within the past month
- Most common in 18-25 yo age group
- 245,000 received treatment for stimulants in past year

Past Year Methamphetamine Use among Persons Aged 12+, by Age: 2002-2006

Percent Using in Past Year

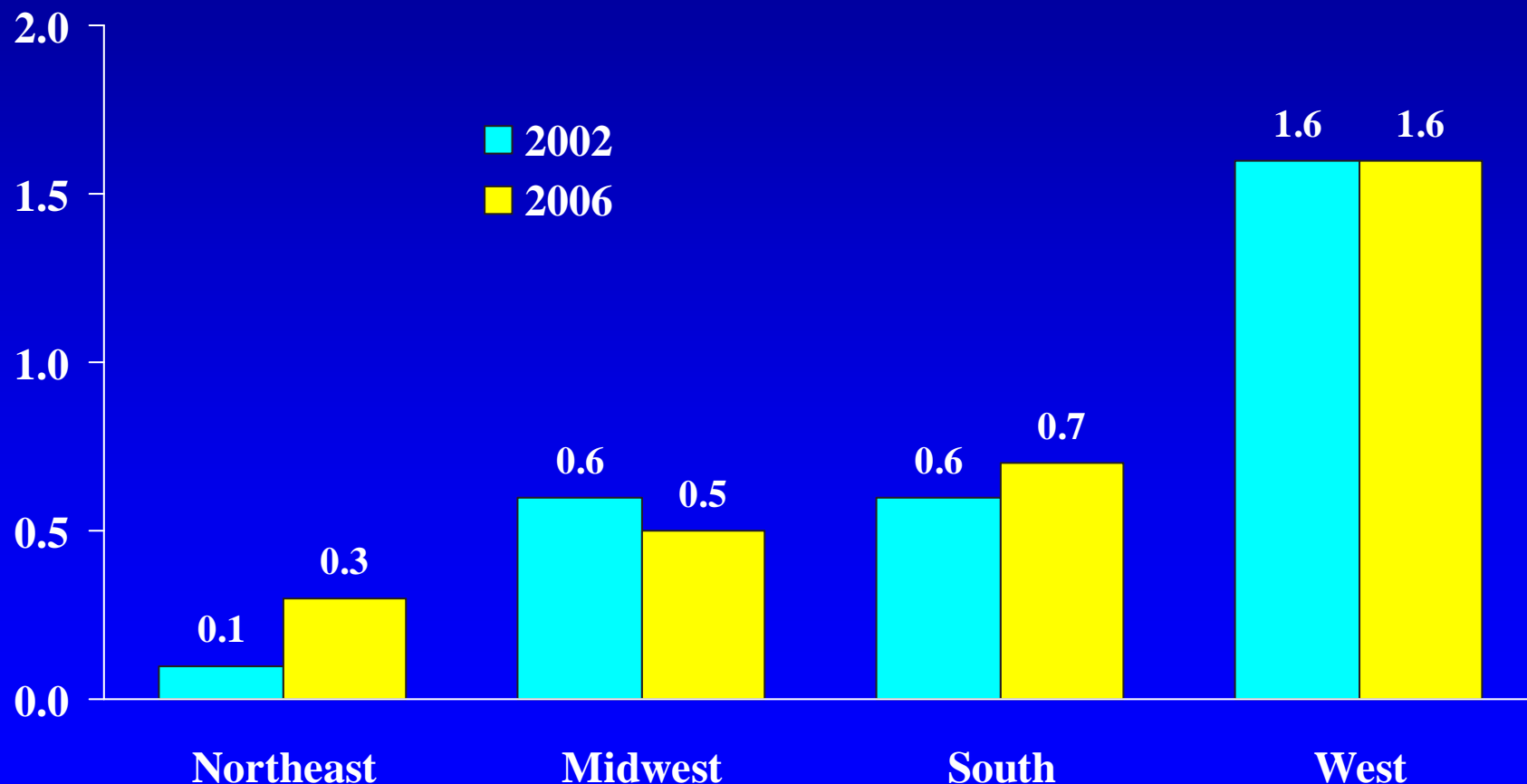


Note: Estimates are based on new 2006 questions. 2002-2005 estimates are adjusted for comparability.

+ Difference between this estimate and the 2006 estimate is statistically significant at the .05 level.

Past Year Methamphetamine Use among Persons Aged 12+, by Region: 2002 and 2006

Percent Using in Past Year



Note: Estimates are based on new 2006 questions. 2002 estimates are adjusted for comparability.

+ Difference between this estimate and the 2006 estimate is statistically significant at the .05 level.

Demographic Characteristics of DAWN ED Mentions for 2000: Methamphetamine

- N = 14,923 ED mentions
- Gender: Male 54.5%
- Race/Ethnicity:
 - White: 73.8%
 - Black 2.5%
 - Hispanic 13.2%
 - Unknown 10.5%
- Age:
 - 12-17 years: 8.9%
 - 18-25: 31.2%
 - 26-34 31.5%
 - 35 and older 27.9%

Mechanisms of methamphetamine's acute actions: enhanced monoaminergic neurotransmission

- Methamphetamine (MA) is an indirect catecholamine and 5-HT agonist
- MA releases newly synthesized (versus stored) DA, NE, & 5-HT (King & Ellinwood 1997)
 - MA enters neuronal membranes through membrane transporters and storage vesicles via vesicle transporters
- May deplete catecholamines and 5-HT

Pharmacology: Methamphetamine

- Mostly release of monoamines; lesser reuptake inhibition of DA, NE & 5-HT
- lesser MAOI effects
- Overall, tolerance develops rapidly, but sensitization can also occur (e.g. to psychosis)

MA Pharmacokinetics

- Absorption rapid after oral and other routes
- MA $\frac{1}{2}$ life= 11-12 hrs IV or smoked (Karch 1996)
- metabolism: MA→amphetamine by CYP450 2D6; multiple other routes
- drug interactions: CYP450 2D6 blockers such as fluoxetine could potentially prolong MA presence in blood, but no evidence yet
- acidification of urine hastens excretion
- duration of effects: 10-12 hrs (vs 30-50 minutes for cocaine)

MA Chronic Neurochemical Effects in Animals

- Decreased DA stores
- Decreased DA uptake sites, decreased DA transporters
- Decreased tyrosine hydroxylase & tryptophan hydroxylase activity

MA Clinical presentation

- Patterns of use
 - frequency: often weekend binge pattern -- binges 12-24 hrs to 2-3 days; accompanied by rapid tolerance
 - amount varies enormously from 10 mg to 1 gram or more/day
 - route of administration: intranasal, oral, IV, rectal, smoked
 - “ICE”-- purified form of d-isomer, often in large crystals, not the “free base” form, which is liquid at room temp & has very limited use (SAMSHA, 1997)
 - binges followed by crash, with depression, fatigue, hypersomnolence, craving

Methamphetamine Effects in Humans

- At low doses:
 - wakefulness
 - increased physical activity
 - anorexia
 - increased respiration
 - hyperthermia
 - euphoria
 - hypersexuality
- At higher doses:
 - anxiety
 - irritability
 - insomnia
 - confusion
 - tremor
 - seizures
 - delusions
 - hallucinations
 - aggressiveness

(adapted from NIDA Infobox 016, 1998)

Amphetamines: intoxication

- MSE
 - Euphoria, hyperactivity (motoric & verbal), hypersexuality initially, insomnia, anorexia.
 - Confusion rare
 - Persecutory delusions (paranoia) and hallucinosis (aud, vis, & tactile), agitation
 - Elev BP, HR, Temp
- Hyperthermia
- Rigidity
- Seizures

Methamphetamine's Medical, Public Health, Psychiatric Effects

- Medical
 - CNS
 - Cardiovascular
 - Pulmonary
- Public Health
 - HIV
 - Hepatitis B & C
 - STDs
 - TB
- Psychiatric
 - Psychosis
 - Mood & anxiety disorders

MA Psychiatric Morbidity

(Baberg 1996)

- psychosis
 - acute--classically paranoid, persecutory delusions, ideas of reference, heightened awareness of environment
 - chronic--can persist after acute episode or recur with little or no further MA use
 - pathophysiology uncertain
- mood disorders
 - mania during intoxication
 - depression during withdrawal

MA Medical Morbidity

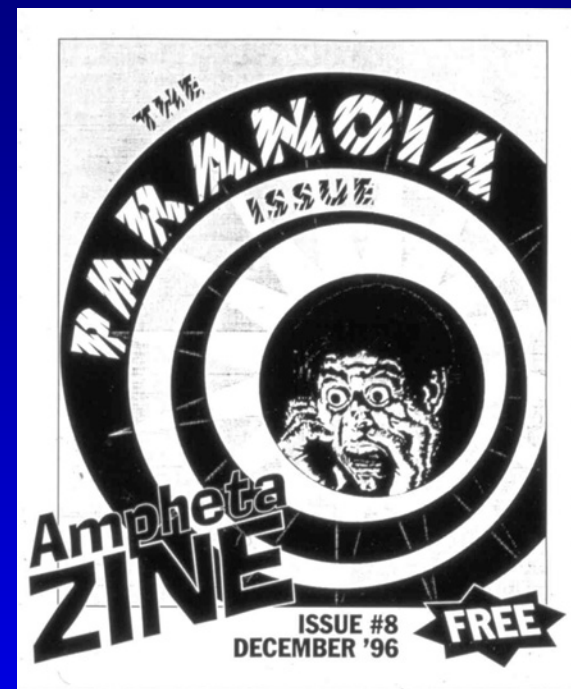
- High dose acute intoxication
 - ventricular irritability
 - hypertension
 - MI
 - hyperthermia (hyperpyrexia)
 - rhabdomyolysis
 - seizures
 - stroke

Methamphetamine Neurotoxicity

- **History**
 - PCA-related 5HT depletion 1st shown in early 60s
 - more recently shown with MDMA, etc
- **5-HT depletion**
 - rapid decrease in 5HT synthesis
 - persistent in animals \geq 110 da
- **DA depletion**
 - decreased brain DA concentration & decreased DA uptake sites

Amphetamine Psychosis

- History
 - 1st reported 1938
- characteristics
 - clear consciousness
 - occasionally confused
 - relatively little formal thought disorder
 - persecutory delusions
 - occasionally nonparanoid & disorganized
 - hallucinations -- all modalities
 - persistent psychosis of long duration is possible
- sensitization
 - psychosis of increased duration
 - induced by lower doses--increased vulnerability
 - spontaneous psychosis



Management of Amphetamine Intoxication

- Confirm diagnosis by urine toxicology screen
- If ingestion is oral, use gastric lavage and activated charcoal; avoid ipecac emesis due to risk of seizure, arrhythmia, or hypertensive crisis
- For seizures use diazepam acutely
- For psychosis/agitation use diazepam, back up with antipsychotic if needed
- Hyperthermia; external cooling

(Source: McCance-Katz, AAP 1999)

Methamphetamine

lack of medical treatments

- Few clinical trials have tested pharmacotherapies for methamphetamine dependence
- Controlled trials with
 - imipramine, fluoxetine, and amlodipine have been negative
 - most recent promising treatments: bupropion, modafinil
- No pharmacological treatments have been shown to be effective

Methamphetamine: Psychosocial Therapies

- Matrix Model (Shoptaw, Rawson, et al)
- Possible utility of contingency management
- Self-help groups, e.g. Crystal Meth Anonymous (CMA)