

**Project:** Ghana Emergency Medicine Collaborative

**Document Title:** Drugs of Abuse

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# Update on Drugs of Abuse (“some club-drug stuff”)



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# Overview of Topics

- **Gamma hydroxybutyrate (GHB)**
  - GHB
  - GHB Analogs
  - GHB / Analog Withdrawal
- **Ecstasy : MDMA (Methylene dioxymethamphetamine)**



# Overview of Topics

- **Methamphetamine**
- **Dextromethorphan (DM)**
- **Ketamine**
- **Flunitrazepam**
- **Mescaline**
- **Inhalants**
- **Anticholinergics**



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United States Department of Justice, [Wikimedia Commons](#)

**GHB**  
**(Gamma-**  
**hydroxybutyrate)**

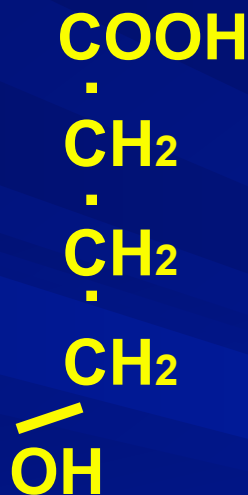
# What is GHB?

- Gamma hydroxybutyrate
- Naturally occurring in brain tissue
  - neurotransmitter-like substance
  - dopamine release in substantia nigra
- Similar structure to GABA
- GABA-B agonist effects
- Approved for narcolepsy 2002
  - Sodium oxybate (Xyrem) Orphan Medical
  - 4.5 gms a night AWP \$739 / month limited to certain pharmacies and physicians

# GHB

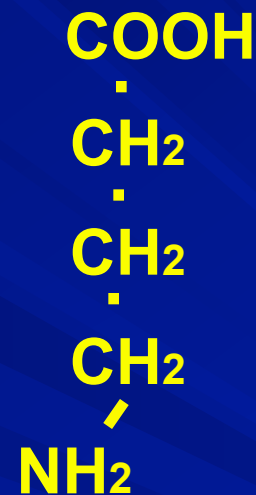
- Investigated as an anesthetic agent :  
caused myoclonus and delirium ; current  
IND for sleep apnea
- Crystalline salt
- Soluble in water and methanol
- Tasteless
- GBL-gamma-butyrolactone & BD-1,4  
butanediol precursor molecules convert to  
GHB in-vivo

# Structure Activity Relationship



**GHB**

**gamma  
hydroxybutyrate**



**GABA**

**gamma  
amino  
butyric acid**

# History of GHB

- 1960's France - Synthesized as an Anesthetic
- 1987 Orphan Drug (IND-narcolepsy) ; USFDA
- 1990-1 Body Builders “Undetectable steroid”  
*Growth hormone stimulator*
- 1992-5 Sleep aid, Rave party, Popularity rises
- 1996 Sexual enhancer, “Date-Rape” Drug
- 1997 Emergence of GHB Analogs  
Emergence of Withdrawal Cases
- 2000 Federal Schedule I status
- 2002 FDA approval for Narcolepsy : Xyrem



# Slang Names : Gamma Hydroxybutyrate

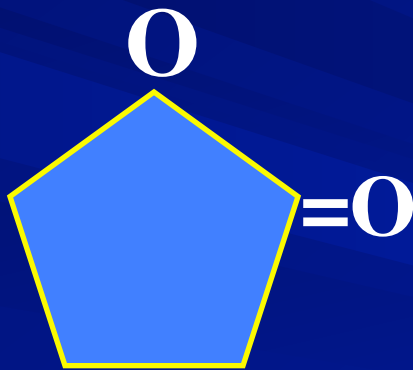
- Cherry meth
- Easy lay
- G, G caps
- Gamma hydrate
- Georgia home boy
- GHB
- GH Beers
- Liquid E
- Liquid X
- Liquid ecstasy
- Natural sleep 500
- Organic Quaalude
- Oxy sleep
- Scoop



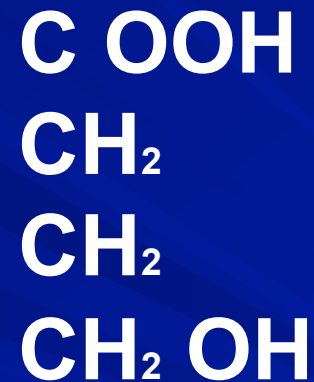
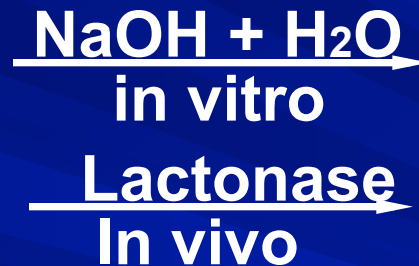
# What are GHB Analogs?

- Organic solvents
  - $\gamma$ -Butyrolactone, 2(3) Dihydrofuranone,
  - 1,4-Butanediol, Tetramethylene Glycol
- Converted to GHB *in vitro* or *in vivo*
  - *In vitro* using NaOH, heat
  - In vivo (Lactonase enzymes) : GBL
  - In vivo (alcohol / aldehyde dehydrogenase)
- Identical clinical effects to GHB

# Conversion : Gamma Butyrolactone (GBL)



GBL



GHB

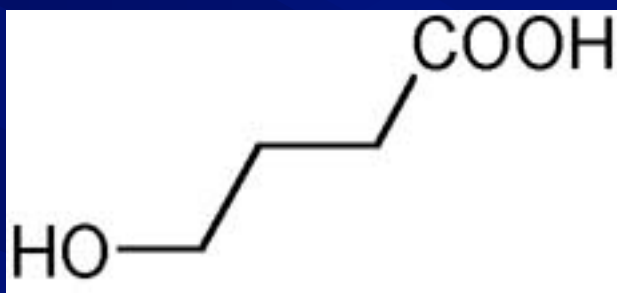
# Gamma Butyrolactone (GBL)



# **Slang Names :**

## **Gamma Butyrolactone or Dihydro Furanone**

- **Blue Nitro**
- **Firewater**
- **Furanone Extreme**
- **Gamma G**
- **GBL**
- **GH Release**
- **Insom-X**
- **Invigorate**
- **Jolt**
- **Liquid Libido**
- **Regenerize**
- **ReneTrient**
- **Revivarant**
- **Revivarant-G**



PD-INEL

Source Undetermined

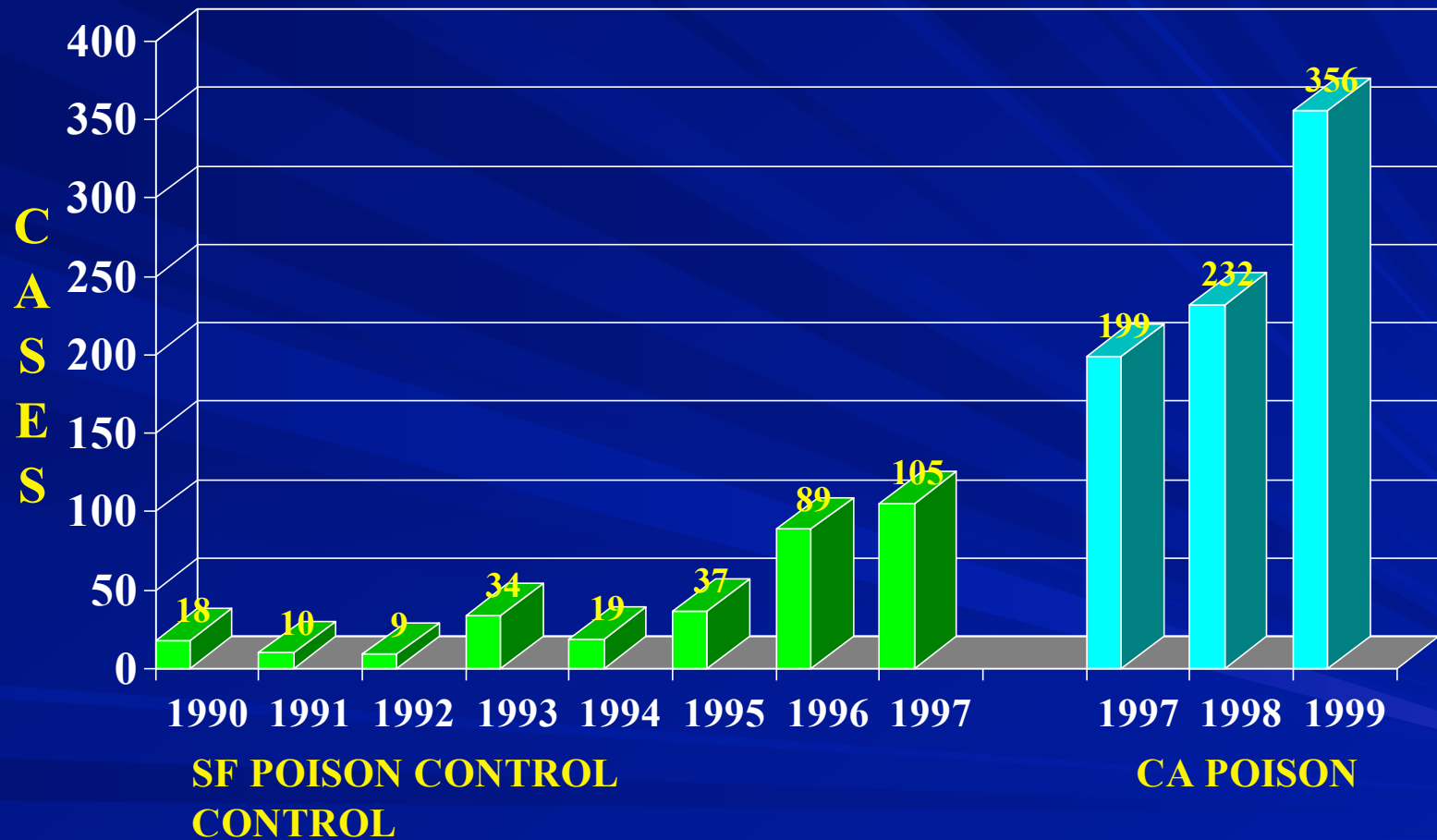
Renewtrient and Blue Nitro, GHB precursors, have been removed from the market.

# **Slang Terms :**

## **1,4 Butanediol or Tetramethylene glycol**

- Biocopia PM
- Borametz
- BVM
- Enliven
- FX
- NRG3
- Inner G
- Thunder Nectar
- Pro G
- Promusol
- Rest-eze
- Revitalize Plus
- Serenity
- SomatoPro

# Incidence : GHB and Precursors





# Pathology

- Structurally similar to GABA
- Stimulates GABA<sub>B</sub> receptors
- Influences dopamine release from substantia nigra
- Readily crosses the BB barrier

# GHB / Analogs : Clinical Presentation

- Vomiting, Coma, Bradycardia
- Myoclonic jerking
- Loss of protective airway reflexes
  - Aspiration risk
- Hypothermia, Mild respiratory acidosis
- HOTN when combined with ethanol

# Effects

## ■ “DESIRED”

- Euphoria
- Mood elevation
- Hallucinations
- *GH-Muscle growth?*
- *Amnesia*

## ■ UNDESIRE

- Decreased HR, RR
- Coma
- Excessive salivation
- Absence-like sz's

# Emergency Department (ED) Course of Gamma Hydroxybutyric Acid (GHB)

## Intoxication Study Acad Emerg Med 2002 Jul;9(7):730-9 Mason

Study	Intubated	Duration of Intubation	Time in ED if Not Admitted	Number Admitted
Chin et al. ( n = 88)	13 %	179 min	NR	11 %
Mahon et al. ( n = 8)	50 %	80 min	NR	0 %
Li et al. ( n = 7)	57 %	210 min	360 min	43 %
Garrison & Mueller ( n = 78)	10 %	NR	180 min	4 %

# Case Study .....

- 26 y/o F with chronic insomnia doubled her dose of Blue Nitro (GBL) : 3 oz.
  - Vomiting within 15 minutes
  - Pt was unresponsive within 30 minutes
  - Myoclonic jerking
  - EMS was called
  - VS: BP 120 / 70, HR 50, RR 22, T 35

# Case Study continued ....

- Unresponsive to pain, GCS 3.
- CT scan normal, glucose 125
- No response to naloxone or flumazenil
- Woke up within 4 hours
- Discharged
- Urine Toxicology screen negative

# GHB / Analogs : Kinetics

- Onset                      15 minutes
  - Immediate conversion of analogs to GHB
- Coma                      within 30 minutes
- Peak                        1 hour
- T 1/2                       Short
- Duration                  1 to 6 hours (Average 2.5 hr)
- Most patients require < 5 hr observation



# Emergence Delirium

- Myoclonic jerking motions
- Confusion, agitation, combativeness
  - Transient symptoms (< 30 minutes)
  - Symptoms worsen with stimulation
- Treatment
  - Supportive Care
  - Minimize stimulation. “Back off”

# GHB / Analogs : Diagnosis

- History of use and circumstances
- Clinical Presentation
- Short Duration
- Role of Laboratory
  - Suspected assault
  - Obtain sample within 12 hours
  - National Medical Laboratories

# GHB / Analogs : Treatment

## ■ Supportive Care

- Approximately 35 % patients require airway protection

## ■ Gastrointestinal Decontamination

- Limited Value
- Consider Charcoal in massive ingestions

## ■ Education regarding Dependence

# **GHB Dependence : Case Study**

- **29 year old male started taking GHB for the “anabolic effects” 2 yrs ago**
- **Gradually increased dose to 4 to 6 “capfuls” every 4 hours**
- **Discontinued the GHB cold turkey**
- **Arrived in ED 24 hr after his last dose**

# **Case Study continued ....**

- Patient was highly agitated**
- Visual and auditory hallucinations**
- Delusional, paranoid**
- Tremulous, diaphoretic**
  
- VS: HR 110, BP 160 / 112, T 99.1**

# Case Study continued ...

- Patient received :
  - Ativan : 90 mg in the first 24 hours
  - Phenobarbital, Haloperidol
- 10 day withdrawal course
- Discharged symptom and drug free

# GHB Withdrawal

- Similar to ETOH and sedative-hypnotic withdrawal.
- Symptoms start within a few hours of discontinuation.
- Seen with long-term use or daily use.



# GHB Withdrawal : Clinical Presentation

- Onset : 1 to 6 hours
- Progression of sx's over 1 to 3 days
- Symptoms
  - Agitation, hallucinations, paranoia
  - Tremulous, diaphoretic
  - Tachycardic, hypertensive
  - Hyperthermia, Rhabdomyolysis possible
- Duration : 5 to 15 days

# GHB Withdrawal : Management

- ***AGGRESSIVE TREATMENT EARLY***
- **Benzodiazepines**
  - High doses may be required
- **Barbiturates**
- **Antipsychotics**
- **Unproven Therapy**
  - **Baclofen (GABA-B agonist)**

# Stimulants of Abuse

- **Methamphetamine**
- **Methylene dioxymethamphetamine :  
MDMA (Ecstasy)**
- **Cocaine**
- **Ketamine / PCP (phencyclidine)**
- **Dextromethorphan**

# Rave Party : Case Study ...

- 18 year old F was at a Rave party with a friend. She was drinking ethanol and using the following:
  - Midnight      1 tablet of Ecstasy
  - 3 am            Snorted 1 line of Ketamine
  - 5 am            Drank a “capful” of GHB
- At 6:30 am patient found slumped in bathroom, cyanotic. EMS called.

# Case Study continued ....

- In ED, comatose but not cyanotic.
- Intubated for airway protection.
- No response to flumazenil or narcan
- VS: HR 58, BP 110 / 60, RR 16, p 5mm, T 37
- ICU admission. Woke up at 12 hours
- Extubated, discharged

# Ketamine : Clinical Presentation

- **Dissociative anesthetic**
- **Clinical Presentation**
  - Separation of perception and sensation
  - Nystagmus, hallucinations, lethargy, sz
  - tachycardia, HTN, RR depression
  - hyperthermia
- **Duration**
  - 2 to 4 hours

# Ketamine Treatment

- Supportive
- Sedation



# Phencyclidine Effects

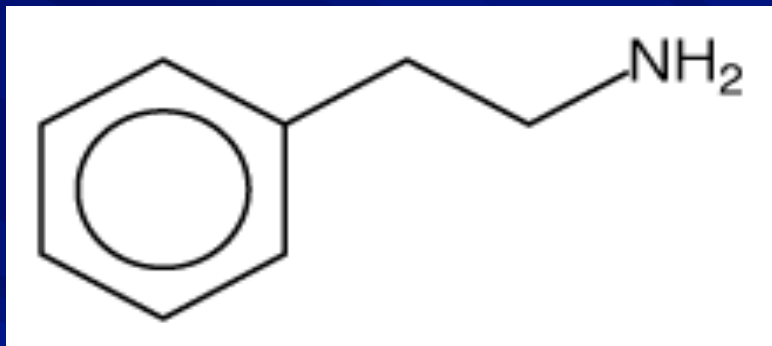
- Tremors, agitation, hallucinations : visual and auditory.
- Tachycardia, HTN.
- Wernicke-Korsakoff syndrome.

**Treatment is same as for ketamine**

# Methamphetamine

- First synthesized by a Japanese pharmacologist in 1893
- Ephedrine most common precursor
- Red phosphorus-hydriotic acid most common reduction method.
- D-isomer : CNS stimulant effects.
- L-isomer : peripheral sympathomimetic activity.

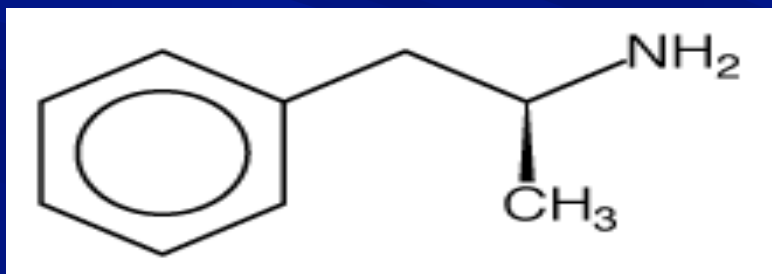
# Structures



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Source Undetermined

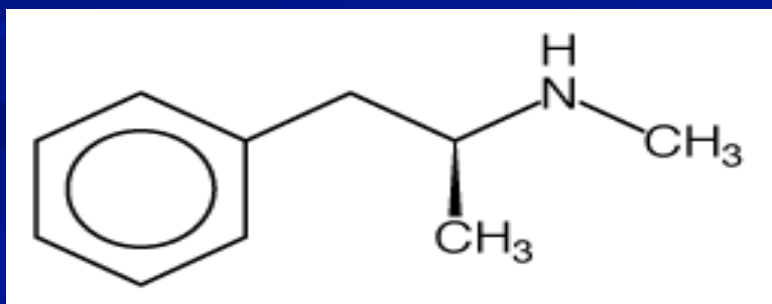
■ Phenethylamine



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Source Undetermined

■ Amphetamine

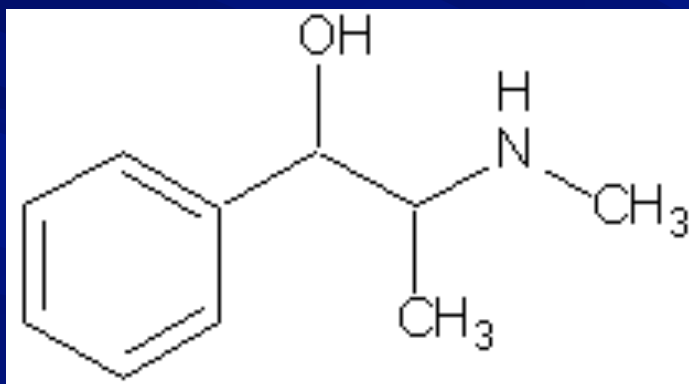


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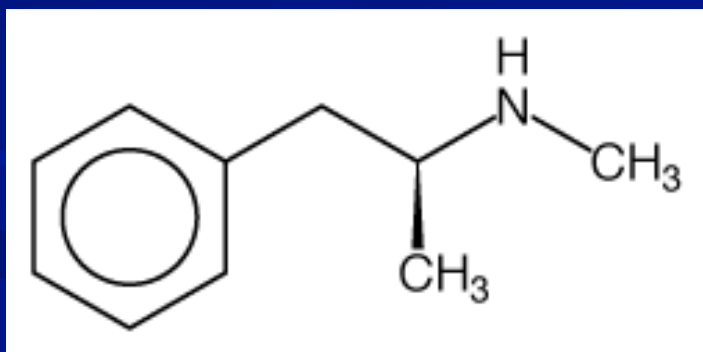
■ Methamphetamine

# Production



 Source Undetermined

■ Ephedrine

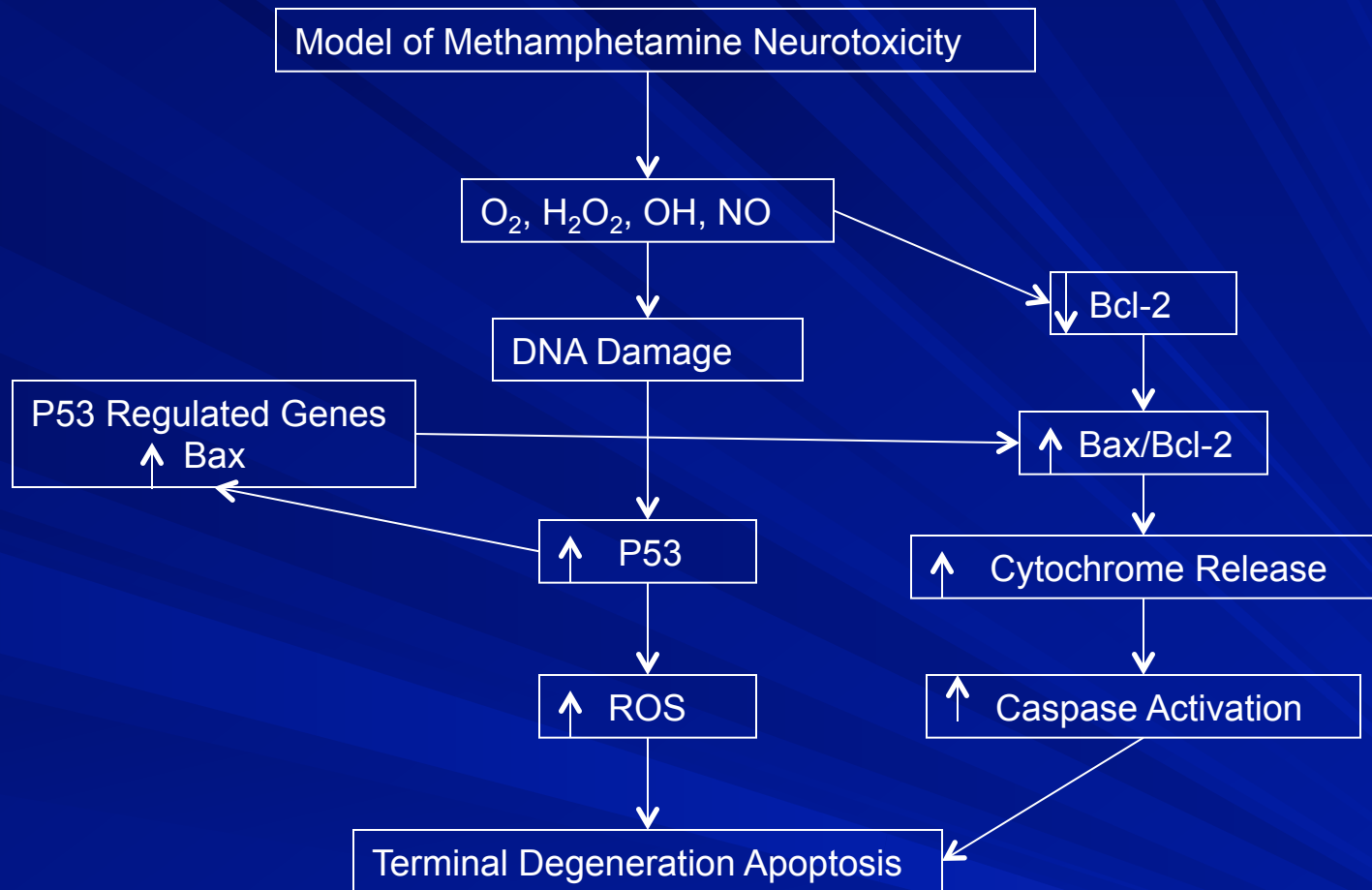


 Source Undetermined

■ Methamphetamine

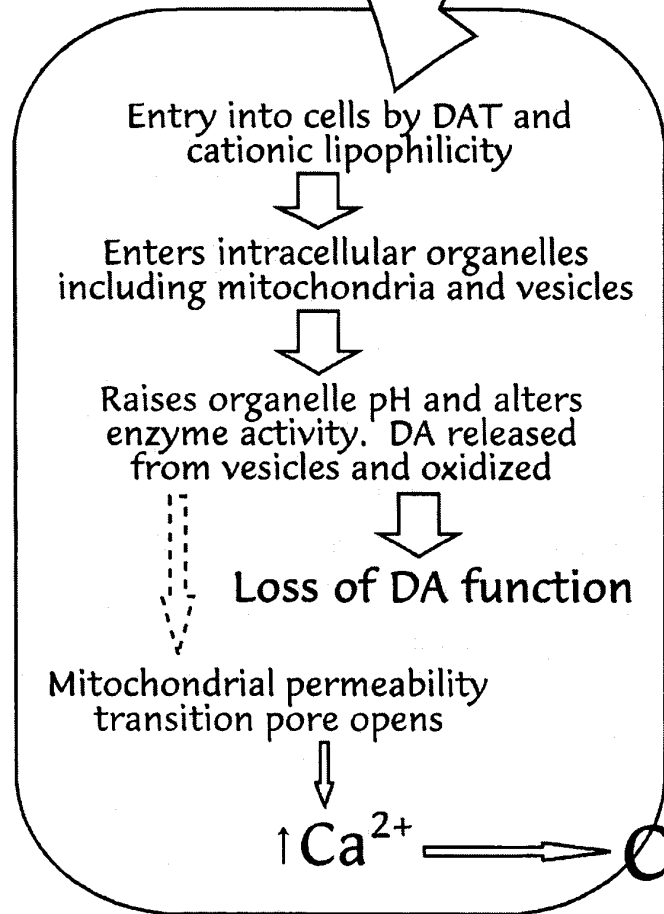
# Pathology

- Increase release of neurotransmitters from nerve terminals.
- Serotonergic and dopaminergic ATP decrease.
- 5HT and D2 depletion.
- Apoptosis
- Endothelial injury.
- Reactive oxygen species.



## A: Acute overdose toxic model

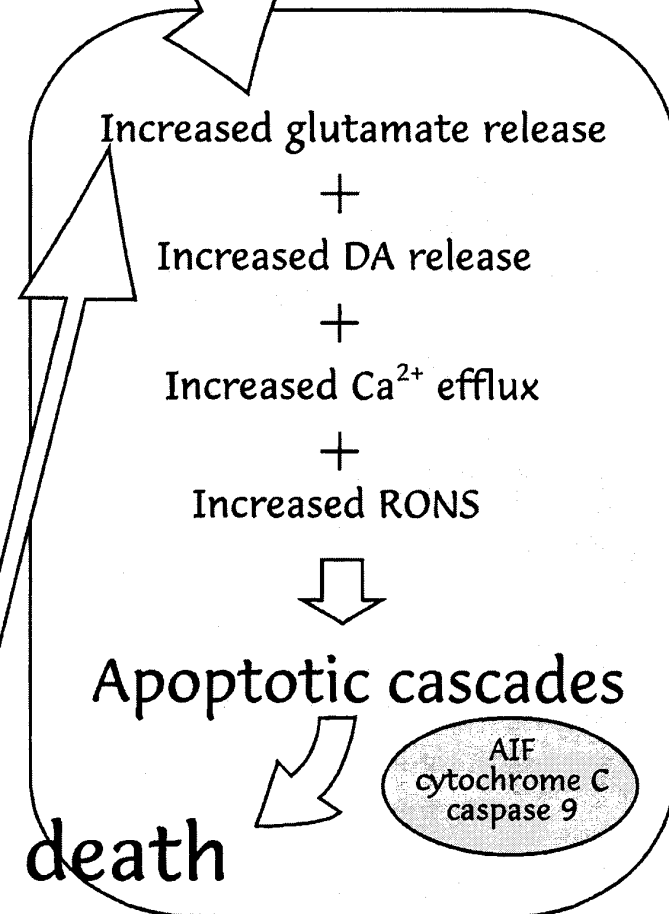
e.g. 4 X 5 mg/kg



MA

## B: Chronic binge (continuous) model

e.g. 15 mg/kg/day X 14 days



Cell death



# Signs and Symptoms

## ■ Action phase

- Skin picking
- Head banging
- Pacing
- Paranoid psychosis
- Extreme suspiciousness

## ■ Resolution phase

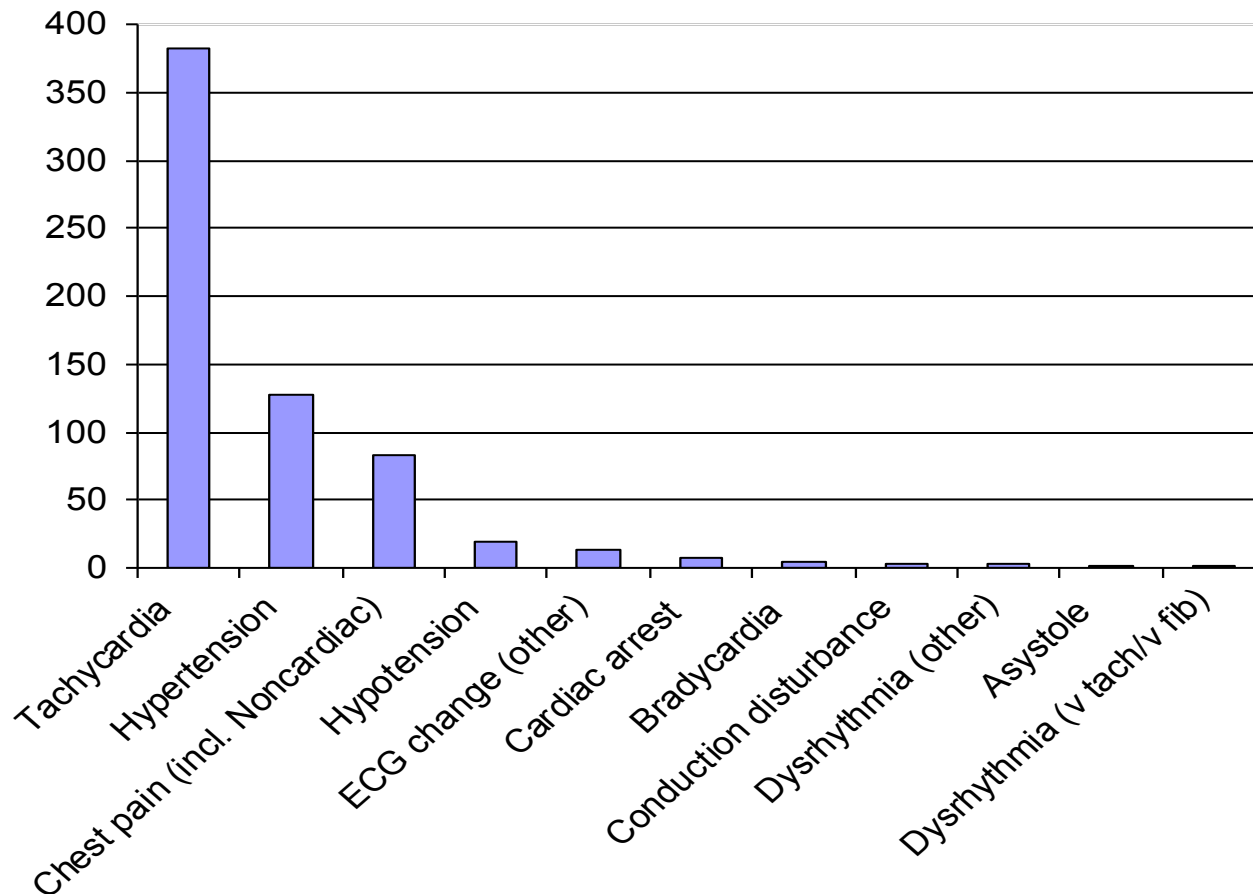
- Exhaustion
- Fatigue
- Sleep
- Depression

# Other Signs and Symptoms

- Pulmonary hypertension
- Dyspnea
- Pleuritic chest pain
- Anorexia/weight loss
- Ulcers
- Rhabdomyolysis

# TESS DATA

**Methamphetamine Exposures Without Concomitants, 2001  
(Cardiovascular Effects)**



# Methamphetamine and the ED

- 6 months UCDCMC ED ending February 1997
- 461 methamphetamine (+) patients
- Caucasian males without health insurance
- Increase use of ambulances and acute hospitalization
- Significant association with trauma : blunt 33 % and penetrating 4 %
- Altered LOC (23 %), Abd pain (13 %), suicide (8 %), chest pain (8 %), skin infections (6 %)
- Richards, et al., West J Med 1999 ; 170:198-202

# **Methamphetamine and Trauma**

- **UCDMC Level 1 Trauma Center**
- **Retrospective Study 1989 to 1994**
- **Results :**
  - **18,004 pts ; 3.1 / 1000 population per year**
  - **+ methamphetamine defined as urine > 1000 ng / ml**
  - **Rates increased from 7.4 to 13.4 %**
  - **Cocaine rates 5.8 to 6.2 %**

# Methamphetamine and Trauma

- Decrease in ethanol from 43 % to 35 %
- Meth (+) most common in Caucasian or Hispanic
- Cocaine (+) most common African American
- Meth (+) in MVA or MCA' s
- Cocaine (+) in assaults, GSW' s or stab wounds
- Schermer and Wisner, J Am Coll Surg 1999; 189: 442-449



# Treatment

- Don't forget to r/o other causes :
  - Look-alike diseases : e.g. Pheo, scorpion bites.
  - Drugs : e.g. LSD, psilocybin-hallucinations, etc.
  - Elevated temperature : e.g. malignant hyperthermia, NMS, anticholinergic syndrome.
  - Seizures : e.g. cocaine, ETOH withdrawal.
  - CVS : e.g. GHB withdrawal.



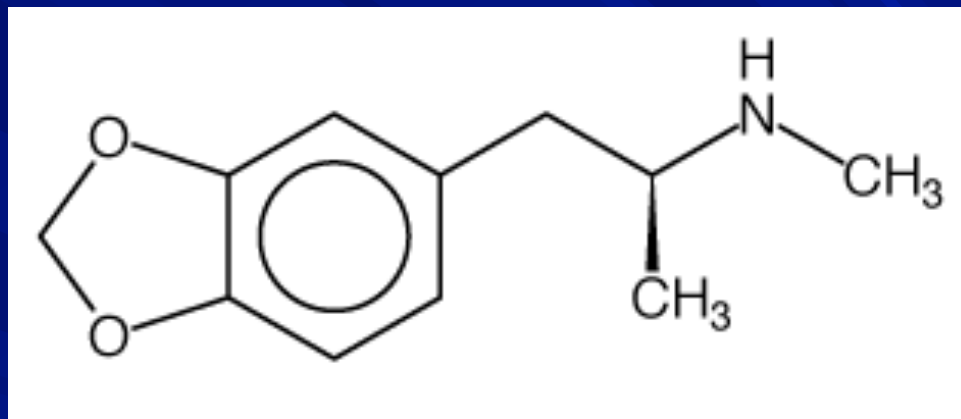
# Treatment (cont.)

- **Control stimulant effects**
- **Decontamination**
- **Control hyperthermia : how ?**
- **Control seizures : how ?**
- **Be careful of physical restraints.**
- **Treat psychiatric conditions.**

# What is Ecstasy (MDMA) ?

- 3,4-Methylenedioxymethamphetamine
- Sympathetic effects mild in low doses
- Potent releaser of serotonin
- Overdose
  - Symptoms similar to amphetamines
  - Risk of serotonin syndrome
  - Risk of hyponatremia
    - SIADH and / or increased water intake

# MDMA



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Source Undetermined



 PD-GOV

Drug Enforcement Agency,  
[Wikimedia Commons](#)

# History of Ecstasy

- 1914      Patented as Appetite suppressant
  - *Never Marketed*
- 1970's      Use by psychiatrists
- 1980's      "LSD of the 60's"
- 1990's      Increasing abuse, Rave party use
- 2000      Continuing abuse
- Illicit adulterants common



# Illicit Ecstasy Tablets



# Pathology

- Similar to other amphetamines in causing release of catecholamines.
- Alpha and beta-adrenergic agonist.
- Can cause SIADH by an unclear mechanism.

# Effects

## ■ DESIRED

- Increased energy
- Euphoria
- Empathy
- Visual hallucinations

## ■ UNDESIRE

- Jaw clenching
- Paranoia
- Hot / cold flashes
- Hyperpyrexia
- Seizures



# Clinical Signs and Symptoms

- Rhabdomyolysis
- Hyponatremia
- DIC
- Renal failure
- Hepatotoxicity
- Aplastic anemia : rare

# Illicit MDMA Adulterants

- Assayed tablets have contained :
  - MDMA
  - MDMA with Caffeine
  - Dextromethorphan 122 to 143 mg / tablet
  - Caffeine
  - Ephedrine, Pseudoephedrine, PPA
  - Placebo

# Treatment

- **Similar to amphetamines and derivatives**
- **Controlling cerebral edema from hyponatremia important.**
- **Pneumomediastinum also an issue**
- **Controlling hyperthermia predicts survival in several studies**

# Dextromethorphan : Case Study .....

- 14 year old M ingested 30 Coricidin tablets to get high. At 2.5 hours :
  - Lethargic, slurred speech, hallucinating
  - Flushed , tremulous
  - Nystagmus present
  - VS : HR 114, BP 170 / 100, T 97.8, p 7mm

# Dextromethorphan (DXMF) Abuse

- Many DXMF containing OTC products
- Coricidin : many combinations
  - DXMF 30 mg, CTM, APAP, PPA, etc.
- Teenage DXMF abuse is rising
- Easy OTC availability

# Dextromethorphan

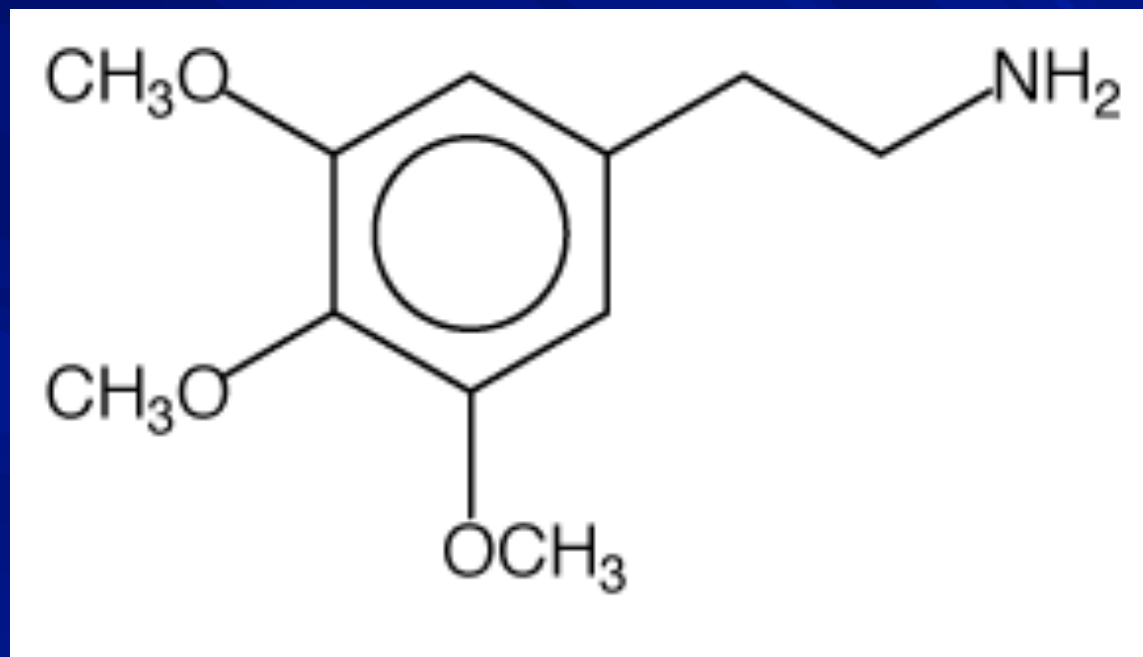
- Therapeutic doses : mild CNS effects
- High doses : significant CNS effects
- Specific DXMF receptors (opiate - sigma)
  - Anticholinergic-like symptoms
  - Hallucinations, delusion, dysphoria
- Opiate kappa and mu receptors
  - Opiate effects

# **Dextromethorphan : Treatment**

- **Gastrointestinal decontamination**
- **Narcan may be useful**
- **Supportive Care**
- **Laboratory**
  - **Rule out aspirin and acetaminophen**



# Mescaline



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Source Undetermined

# Characteristics

- Derived from peyote cactus.
- Hallucinogen.
- Can mimic an acute gastroenteritis

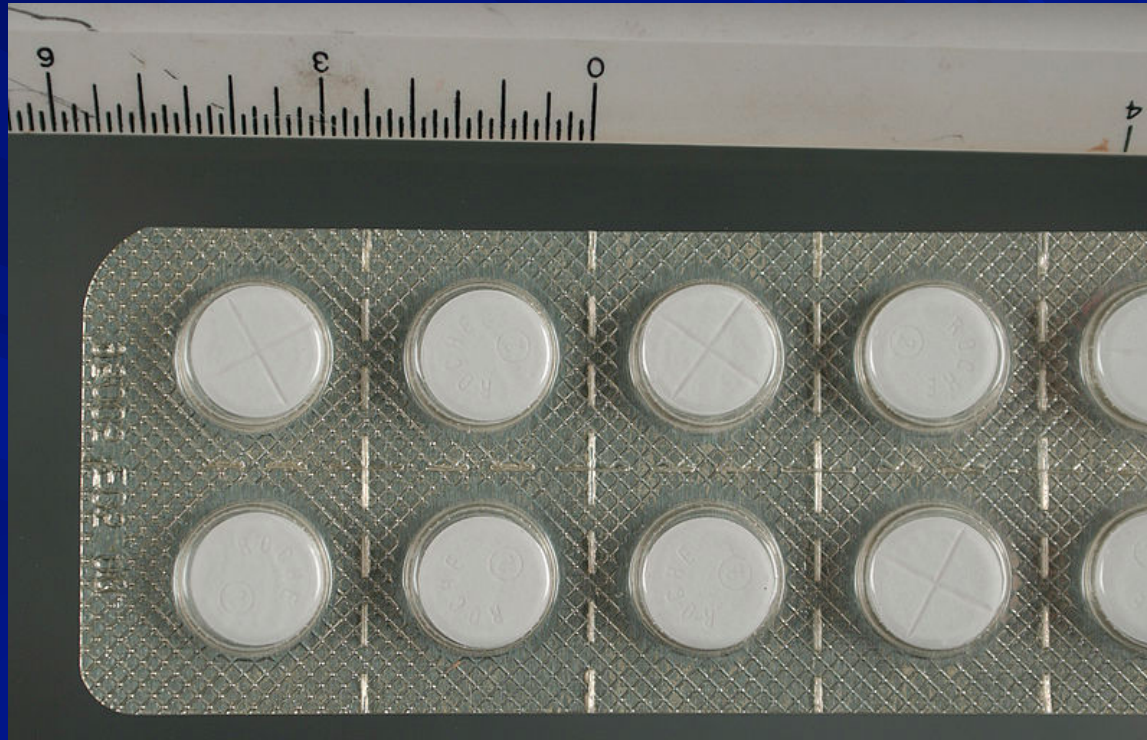
# Mescaline Treatment

- Supportive

# Flunitrazepam

- Used throughout Europe.
- Not approved in the US.
- One of the “date-rape” drugs.
- By weight 10x more potent than diazepam.
- Produces effects within 15 mins.

# Flunitrazepam tablets



PD-GOV

Drug Enforcement Agency, [Wikimedia Commons](#)

New Rohypnol tablets include a dye that make the drug visible if slipped into a drink

# Pathology

- A benzodiazapine working on the GABA<sub>A</sub> receptor.
- Lipid soluble rapidly crossing the BB barrier.



# Effects

## ■ “DESIRED”

- Euphoria
- Hallucinations
- Disinhibition
- SM relaxation
- Sedation
- *Memory impairment*

## ■ UNDESIRE

- Hypotension
- Drowsiness
- Apnea
- Urinary retention
- Tremors

# Treatment

- Supportive care.

AC, lavage (use with caution, may be contraindicated)

Benzodiazepine antagonists  
(flumazenil) :

**NO!!** (very few indications).

# Inhalant Abuse

- Freon Propellants
- Xylene, Toluene
- Gasoline Fumes



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United States Department of Defense,  
[Wikimedia Commons](#)

# Anticholinergic Abuse

- Antihistamines
- Jimson Weed
- Anticholinergic Syndrome:
  - Mad as a hatter
  - Blind as a bat
  - Hot as Hades
  - Dry as a bone
  - Red as a beet

# Summary

- **GHB / GHB Analogs**
  - Classic Symptoms in Overdose
  - Withdrawal Symptoms
- **Rave Parties**
  - Multiple drugs commonly used
- **Rising OTC Dextromethorphan Use**
  - Rule out aspirin and acetaminophen

# Summary

- **Methamphetamine is a major problem**
- **Older drugs of abuse have not gone away**
  - **PCP**
  - **LSD**
  - **Heroin**
  - **Cocaine**
  - **Ethanol**
  - **Marijuana**