

ECSTASY, GHB, KETAMINE, PCP , Dextromethorphan and Designer Drugs

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Award

Conflicts of Interest

- The speaker has no conflicts of interest to disclose regarding this topic.

“A pill for every ill”





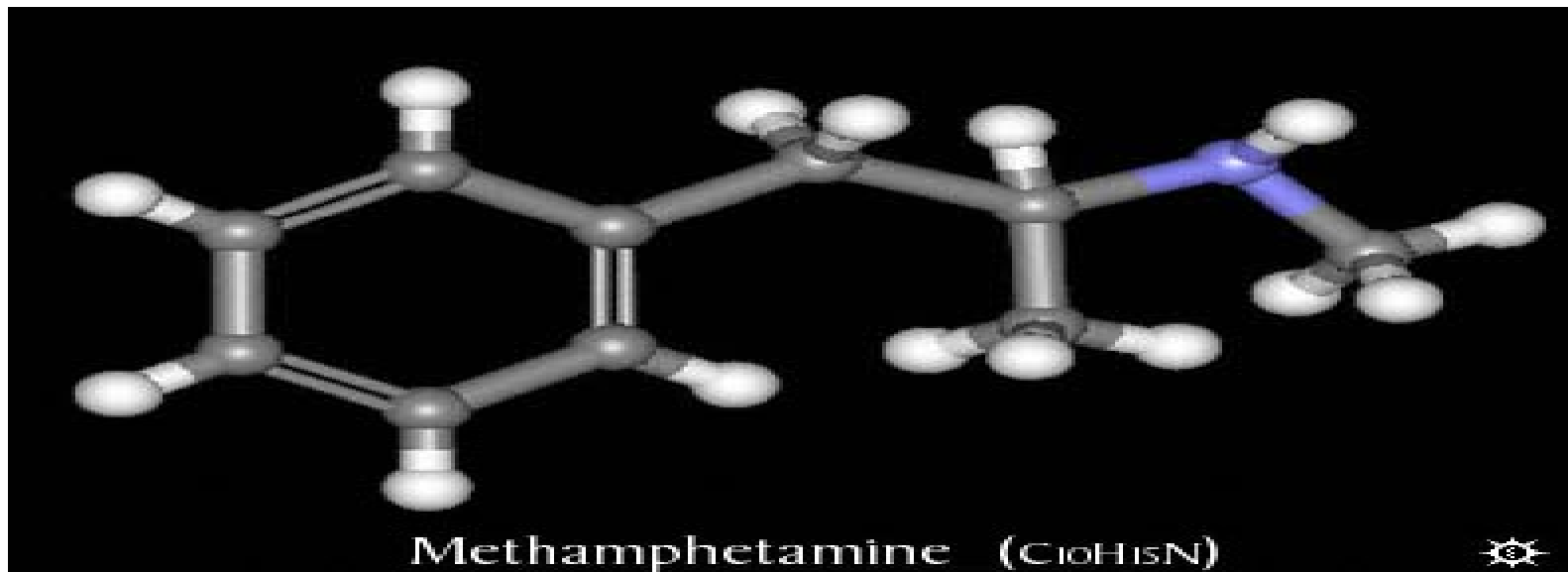
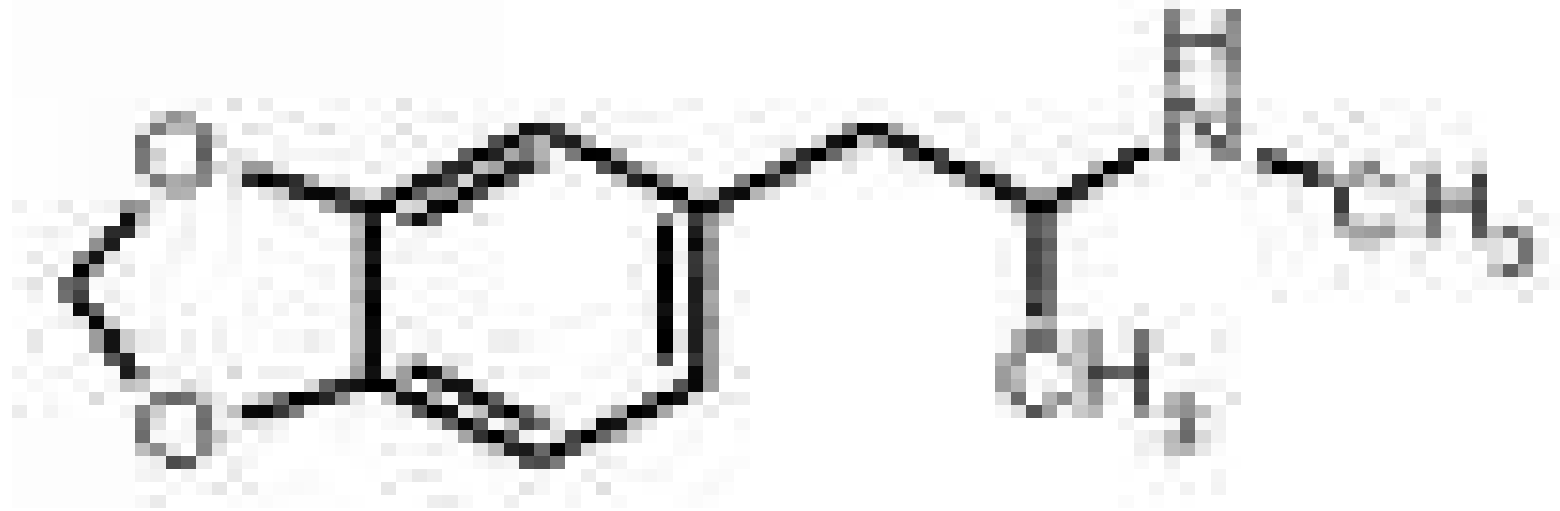
144 Ecstasy (MDMA) Tablets
photographer unknown



Ecstasy

- MDMA 3,4 –
methylenedioxyamphetamine
- Substituted phenethylamines
- Hallucinogenic amphetamine
 - Similar to mescaline
- Historical use in psychotherapy
- DEA ban on MDMA in 1985
- MDMA often adulterated

MDMA and Methamphetamine



MDMA Use by Students

Monitoring the Future Survey, 2007

Between 2005 and 2007, abuse of MDMA increased among 12th-graders, from 3.0 percent to 4.5 percent

	8th Grade	10th Grade	12th Grade
Lifetime	2.3%	5.2%	6.5%
Past Year	1.5	3.5	4.5
Past Month	0.6	1.2	1.6

MDMA/Ecstasy Background

- 1914: E. Merck Pharmaceutical company obtained a patent for MDMA in Germany
- 1950's: The US Army conducts animal experiments with MDMA
- 1965: Alexander Shulgin a chemist at DOW predicts that MDMA is psychoactive
- 1970's and early 1980's: thought to Improve interpersonal communications and enhance emotional awareness
 - Adjunct to psychotherapy

Rochester, JA, & Kirchner, JT. (1999). Ecstasy (3,4-methylenedioxymethamphetamine): history, neurochemistry, and toxicology. The journal of the American Board of Family Practice, 12(2), 137-42.

MDMA/Ecstasy Background

- 1985: MDMA Schedule 1 Controlled Substance by DEA
 - Increasing use and concern over potential neurological damage
- 1990's and 2000: Popularity increased at "Raves" or dance parties
- 2004-2007: Ongoing placebo controlled trial of "MDMA-Assisted Psychotherapy in People With Posttraumatic Stress Disorder"
 - <http://www.maps.org/research/mdma/protocol/>

MDMA Mechanism of Action

- Potent release of brain serotonin and inhibition of serotonin reuptake
- MDMA does NOT cause release of serotonin via exocytosis of serotonin containing secretory vesicles
MDMA causes a reverse in the direction of the normal inward bound serotonin reuptake channel and is taken up into the cell via the serotonin uptake channel and/or through diffusion across the membrane.
- Within the cell MDMA is known to deplete stores of tryptophan hydroxylase (TPH) via acute oxidative inactivation.

MDMA Mechanism of Action

- MDMA has biphasic effect on serotonergic neurons in rats:
- Acutely serotonin levels fall 3 to 6 hours after drug and return to near normal by 24 hours; Depletion secondary to serotonin secretion from the neurons:
- Levels decrease again by 1 week Long-term depletion occurs because of toxic degeneration of the serotonergic nerve terminals

Amphetamine-Like Effects of MDMA

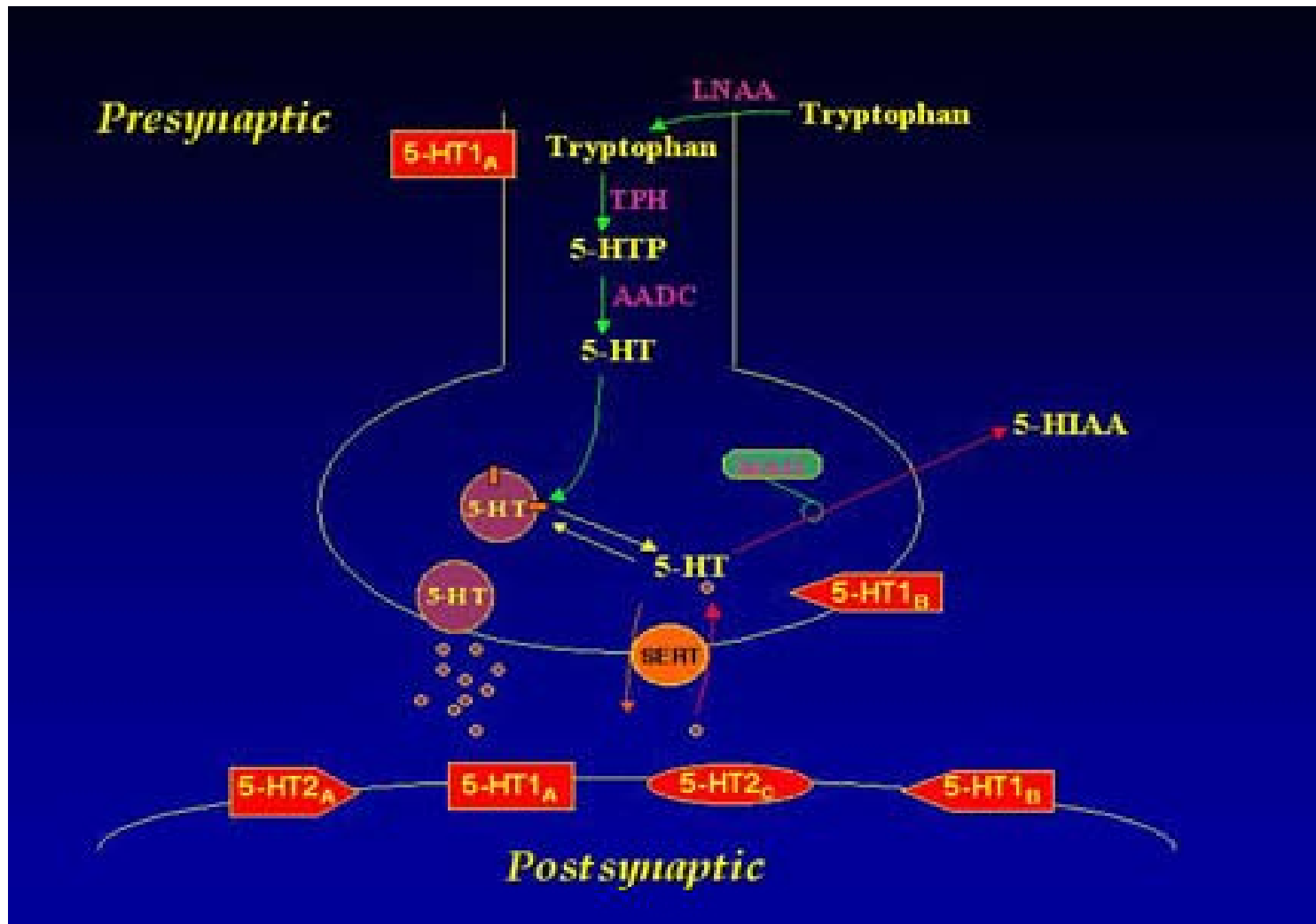


Figure 1: Schematic Diagram of a Serotonergic Synapse

Image: www.chem.psu.edu/images/research/andrewsfig1.html

MDMA

- Dose concentration 50 to 300 mg
- Cost \$15 - 25 per tablet
- Onset 20 to 40 minutes
- Plasma half life 7.6 hours
- Street names: e, Adam, X, XTC
- Drug class: Enactogen - Empathogen, entheogenic – “the god within”

Subjective Effects of MDMA

- Altered time perception
- Increased ability to interact with others
- Decreased defensiveness
- Changes in visual perceptions
- Increased awareness of emotions
- Decreased aggression
- Decreased restlessness
- Less impulsive

Leister M et al, J of Nerv Ment Dis, 1992; 180 345-352

McDowell & Kleber, Psychiatric Annals 1994; 24 127-130

MDMA Adverse Effects

- Mydriasis
- Marked rise in plasma cortisol and prolactin concentrations
- Increase in BP and heart rate
- Bruxism
- Increased restlessness
- Increased anxiety – panic
- Depressed mood
- Nystagmus
- Motor tics
- Headaches
- Anhedonia
- Lethargy
- Anorexia
- Decreased motivation

Leister M et al, J of Nerv Ment Dis, 1992; 180 345-352

McDowell & Kleber, Psychiatric Annals 1994; 24 127-130

de la Torre R et al Ann N Y Acad Sci. 2000 Sep;914:225-37



MDMA Adverse Effects

- Hyperpyrexia, rhabdomyolysis and multi-organ failure
 - Prolonged exertion
 - Warm environment
 - Prolonged repetitive activity
 - Disregard for body signals (thirst, exhaustion)
 - Increased muscle tone
- Serotonin syndrome
 - Rapid onset, confusion, diaphoresis, diarrhea, increased muscle tone, rigidity, cardiovascular instability, tremor, myoclonus, muscle contraction

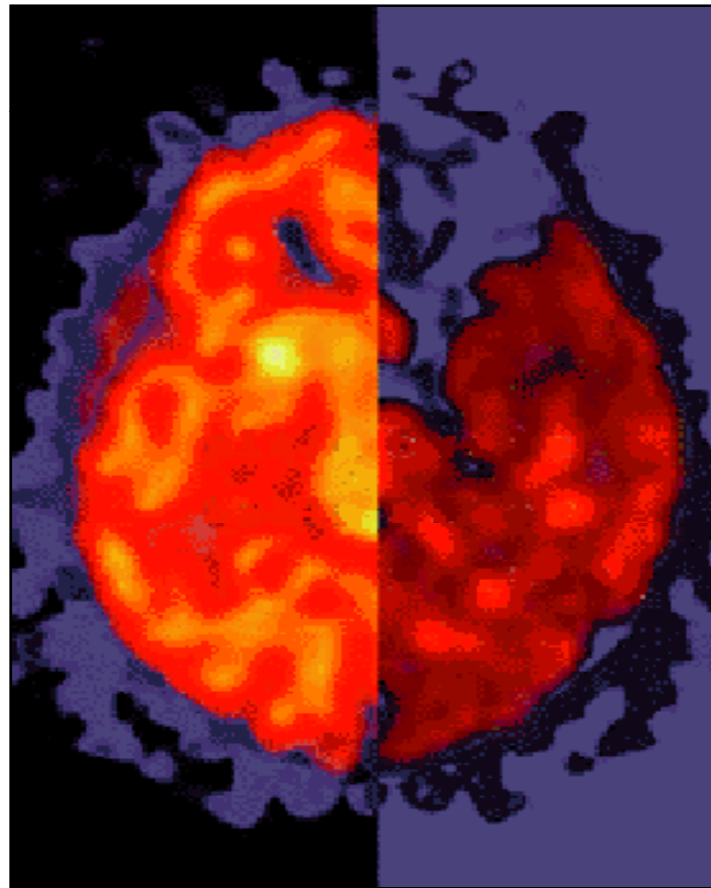
Hall & Henry Br J of Anaes 96 (6) 2006

MDMA Adverse Effects

- Serious acute illness are relatively rare
- Dilutional hyponatremia – cerebral edema
- Liver failure
 - In some cases it is a function of hyperpyrexia, shock and DIC
 - Other case reports of liver failure independent of hyperthermia
- Impaired driving – maybe fatal

PET Scans

New studies suggest long-term MDMA usage may lead to permanent brain damage



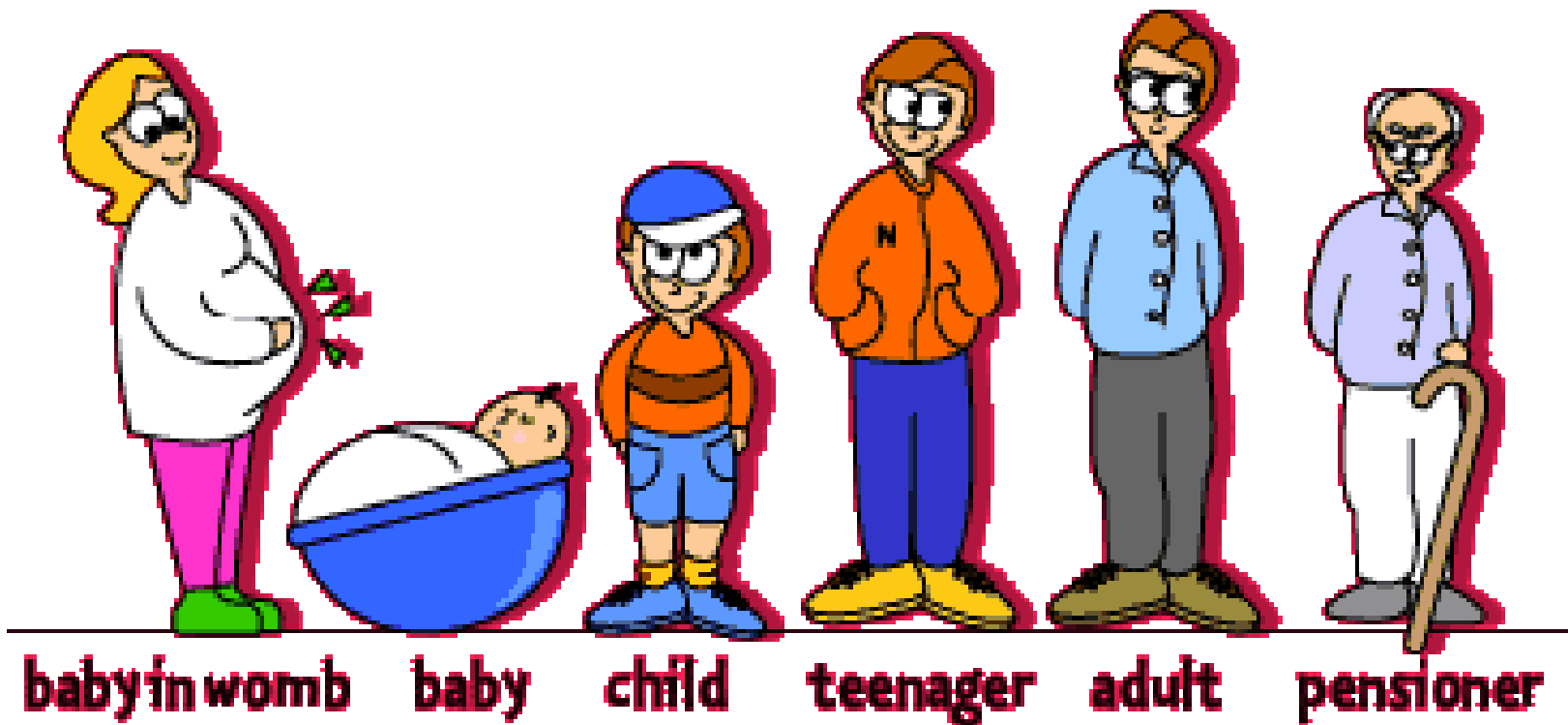
Drug users:
darker=less
serotonin activity

MDMA Research Used Wrong Drug

George Ricaurte, et al. Science September 2002 - paper retracted 1 year later

- People taking MDMA for just one night might later develop Parkinson's disease
- Indicated that 3 consecutive doses of MDMA given to squirrel monkeys and baboons caused damage to dopaminergic neurons
- Animals were injected with MDMA at three-hour intervals to mimic the way humans take the drug; 2 of 10 died within hours after developing hyperthermia
Retraction stated team discovered that all but one of the animals received methamphetamine

What is the impact of Ecstasy on the brain across the lifespan?



MDMA and psychiatric Disorders

- Much of the literature is from case reports:
- Patient developed florid paranoid psychosis after long-term MDMA use and EEG changes intermittent paroxysmal discharges
- Patient developed atypical paranoid psychosis with Fregoli syndrome (delusional disorder) and complex-partial seizures with secondary generalization after first dose

Vecellio M, Schopper C, Modestin J. J Psychopharmacol. 2003 Sep;17(3):342-5.

- Temporal pathway - childhood symptoms of anxiety and depression may precede use of MDMA

Anja C Huizink et al BMJ 2006;332:825-828

Guillot C, Greenway D. J Psychopharmacol. 2006 May;20(3):411-6.

MDMA and Cognitive Problems

- Multiple studies suggest memory and cognitive deficits proportional to the amount and duration of use
 - Verbal memory
 - working memory
 - Episodic memory tasks
 - Attention
 - Frontal-executive function
- Do SSRI's provide neuroprotection?

Quednow BB, et al J Psychopharmacol. 2006 May;20(3):373-84.

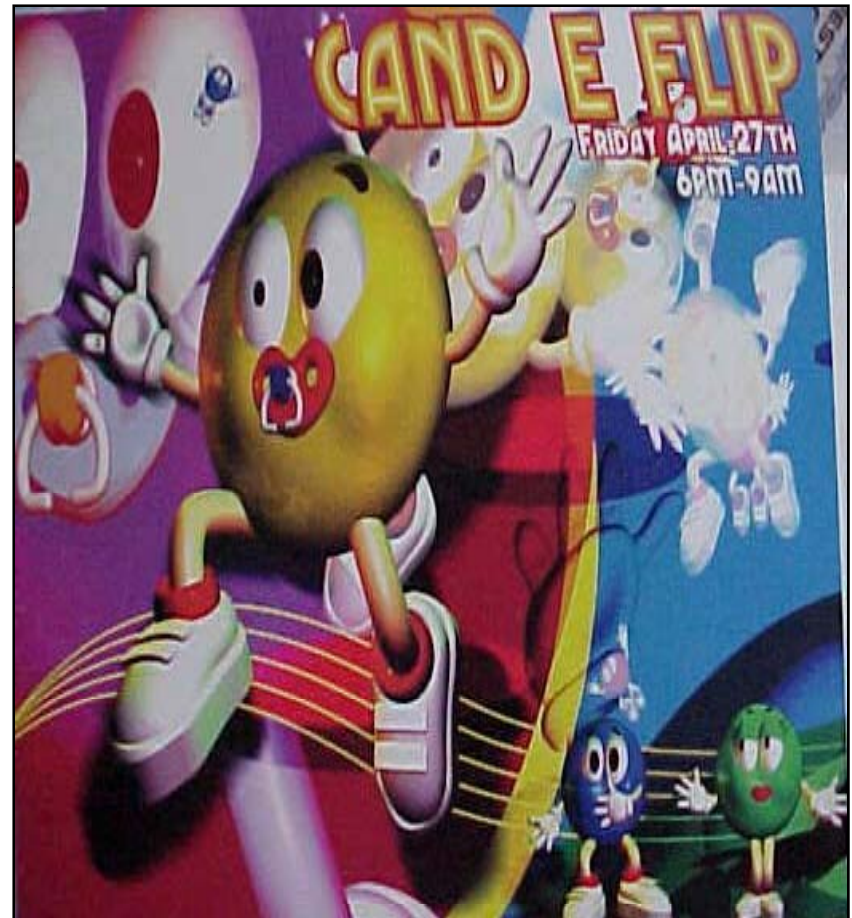
Thomasius R, et al J Psychopharmacol. 2006 Mar;20(2):211-25. Review.

Reneman Let al . J Psychopharmacol. 2006 May;20(3):389-99

Parrott J Psychopharmacol. 2006 Mar;20(2):147-63

De-coding the Message

- “Y” replaced by “E”
- “E” & “X” may be capitalized, hyphenated or underlined to accentuate it.
- “Drop & Roll” refers to dropping pills & rolling on MDMA.





GHB Trends in Use

Monitoring the Future (MTF) Survey

According to results of the 2007 MTF survey

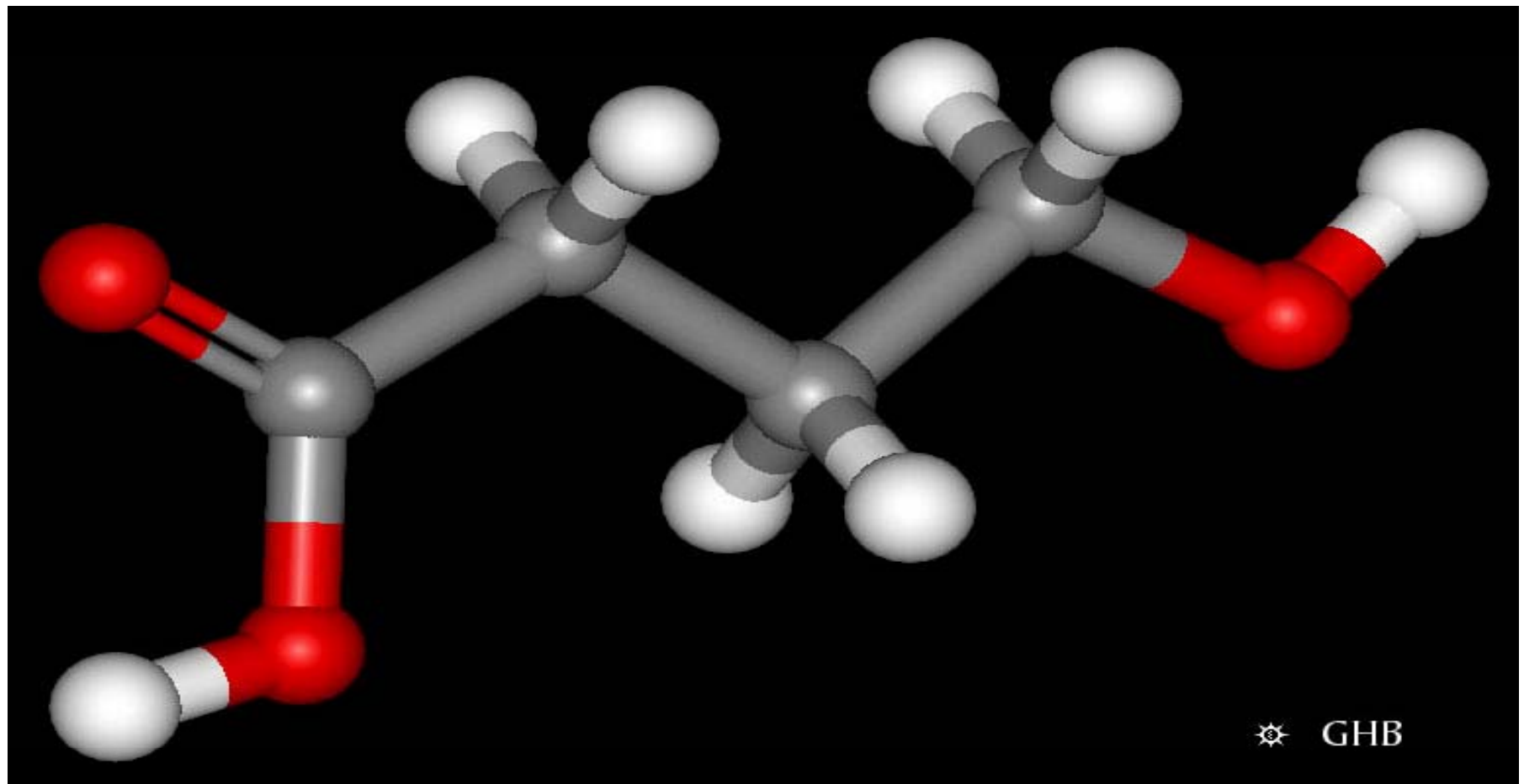
0.7 percent of students in the 8th grade reported past-year use of GHB

0.6 percent of the students in 10 th grade

0.9 percent of the students in 12 th grade

This is consistent with use reported in 2006

GHB



GHB Background

- 1960: Studied for induction of a sleep-like state with cardiovascular stability
- 1963: Naturally occurring chemical in the human brain
- 1960's Anesthetic, abandoned because of poor analgesic effects

GHB Background

- 1970's: first studied for treatment of narcolepsy/cataplexy
- 1980's: marketed as a “fat burner and muscle developer”
 - Takahara et al Stimulatory effects of GHB on growth hormone and prolactin release in humans *Journal of Clinical Endocrinology & Metabolism* 1977;44(5)1014
- 1990: GHB banned from OTC sales
- 1990s: GHB replaced by precursor GBL gamma-butyrolactone

ROBERT KENNEDY'S

May 1993

MUSCLEMAG

International

ING HEALTH LESS UE

**PLUS -
HOT OFF THE PRESS!
SPRING
SHAPE-UP
POSTER
FREE!!**

**START
NOW!**

BASIC BODYBUILDING
FOR WOMEN

**"HOW I
IMPROVED
MY BACK"**

LEE LABRADA

**ROUND OUT
YOUR BUNS**

AND ADD FLEX APPEAL!

**THE PROS
SPEAK OUT!**

ABSORBING STUFF!

**"I MADE MY
LEGS GROW
AND GROW!"**

MICHAEL FRANCOIS

**HE'S THE NEW
MR. AMERICA!**
FULL CONTEST REPORT INSIDE!



© 1993 M&M Publications

131

PLUS: TOTAL SHAPE TRAINING ZULAK TELLS HOW

GHB Background

- 1990's: Studied for treatment of opiate and alcohol withdrawal and maintenance therapy for alcohol dependence
- 1999 FDA recall of GBL containing products – replaced by 1,4-butanediol
- 1999 FDA declared 1,4-BD a Class I Health Hazard

GHB Background

- 2000: GHB implicated in drug facilitated sexual assault: President Clinton signed the Hillary J. Farias and Samantha Reid Date-Rape Drug Prohibition Act
- 2002: Zyrem (sodium oxybate) is approved for the treatment of cataplexy in patients with narcolepsy as a Schedule III but Schedule I for illicit use
- 2005: FDA approves Zyrem indication for the treatment of excessive **daytime** sleepiness in patients with narcolepsy
- 2005: Phase II trial of Zyrem for the treatment of fibromyalgia

GHB analogs: gamma butyrolactone (GBL) and 1,4 butanediol (BD)

- Both are common industrial solvents used to produce polyurethane, engine degreasers, nail polish remover
- When ingested, both are rapidly transformed to GHB, with the same recreational and toxic effects



DEA's Operation Webslinger



Looking for GHB online?

GHB Survey Study

- Convenient sample - recruited by a news paper advertisement
- 120 callers
- 42 came in for an interview
- Male 76%
- Caucasian 73%
- Heterosexual 70%
- Employed 69%



GHB/GBL Analogs and Reported Uses

- **Gamma-Butylactone**
- **2(3H) Furanone dihydro**
- **1,4 Butanediol**
- **Sodium oxybate**
- **ZYREM**
- Improve sleep
- Insomnia
- Dancing
- Avoid drug testing
- Antidepressant
- Antianxiety
- Socialize
- Weight lifting

GHB/GBL Preparations

- Blue Nitro
- Blue Nitro Vitality
- G3
- Gamma G
- GHRE
- Invigorate
- Jolt
- Remforce
- Renewtrient
- Revitalize Plus
- Revivarant
- Serenity
- Solar Water
- SomatoPro
- Thunder Nectar
- Verve
- Weight Belt Cleaner
- ZEN
- www.ashesonthesea.com/ghb/analogs.htm#trinka2

GHB

- Water-soluble four-carbon molecule
- Formed from the precursor gamma-butyrolactone (GBL)
- Recipe: GBL, heat to dissolve with sodium hydroxide
- Often sold as clear salty liquid
- Dose is the number of caps



GHB Pharmacology

- Cap concentration varies 500mg-5g
 - Jo Ellen Dyer SF Poison Control Center
- Rapidly absorbed, peak conc 20-60 min
- Half life is 20 minutes
- Almost completely oxidized to carbon dioxide
- Readily crosses the blood brain barrier and placenta

GHB Mechanism of Action

- Neurotransmitter or neuromodulator in mammalian brain
- Structurally related to GABA (gamma-aminobutyric acid) and is a metabolite of GABA
 - It does not bind to GABA_A receptors; bind noncompetitively to GABA_B but only when present in amounts larger than occur naturally
- High and low-affinity GHB receptor sites that are highly specific for GHB and whose distribution differs from GABA receptors

GHB Use (Survey Study N=42)

- **How often do you use GHB**
 - **Every day** **21.4%**
 - **1-6 days/ week** **35.7%**
 - **1X/month or less** **42.9%**
- **How many times per day**
 - **Once** **28.6%**
 - **2-3 times** **42.9%**
 - **4 or more** **28.6%**
- **How much do you use at a time?**
 - **< 1 capful** **9.5%**
 - **1-3 capfuls** **73.8%**
 - **> 3 capfuls** **14.3%**
 - **Other** **2.4%**

GHB Dosing

- Sleep studies - 50 - 60 mg/kg/night 2 doses
- Alcohol studies - 50 - 150 mg/kg day divided doses
- Sodium Oxybate - 4.5 grams initial dose ½ at bedtime, ½ 2-4 hours later
- Titrate 1.5 grams q 2 weeks Max 9 grams
- Solution 500 mg/ml 1 month supply \$750
- Central Pharmacy Xyrem Risk management System

Scrima L, et al, 1989 Biol Psychiatry; Lammers G et al, 1993 Sleep; Gallimberti L et al, 1992 Alcoholism; Moncini M, 2000 Alcohol

Subjective Effects of GHB

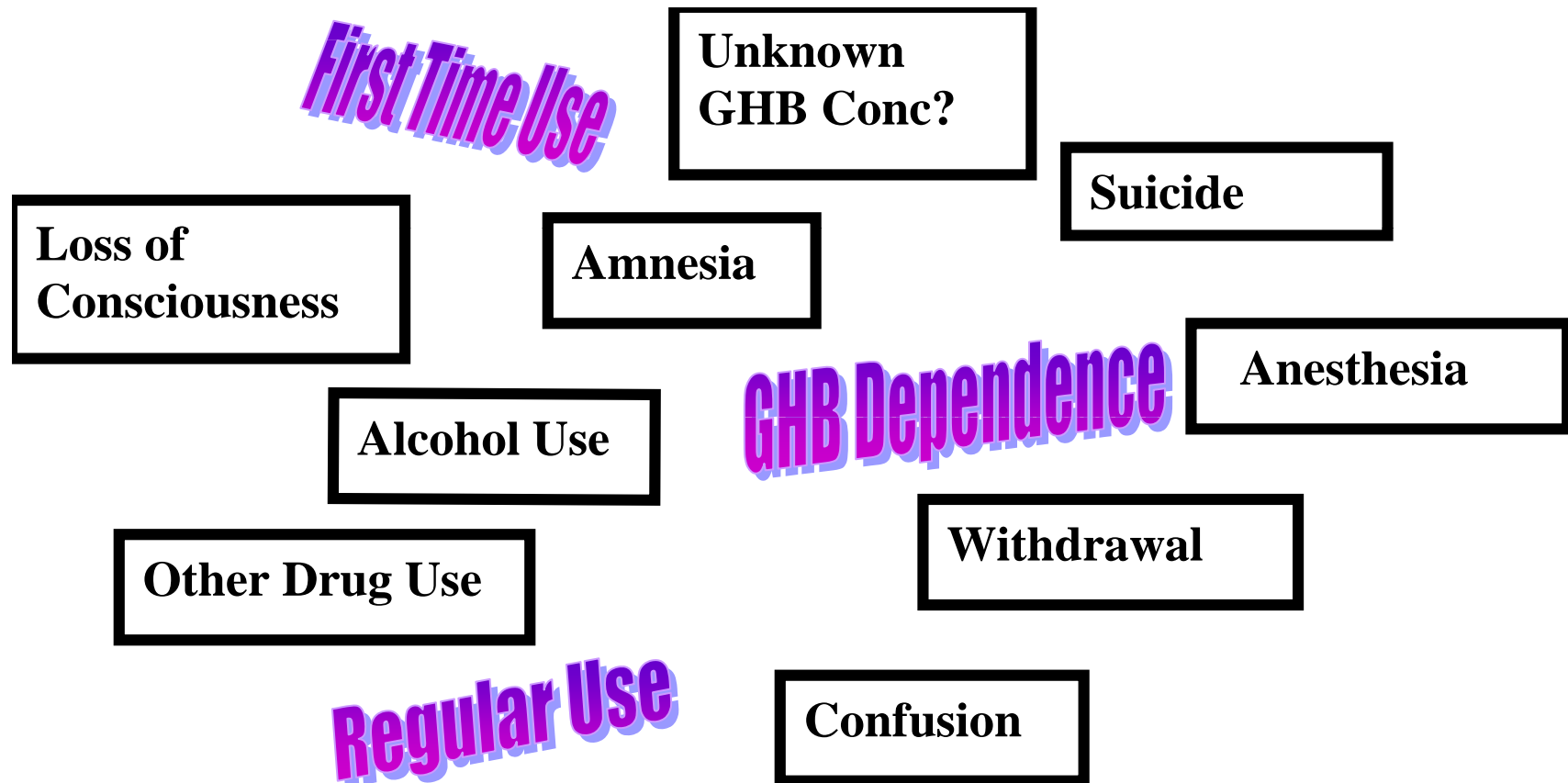
Reported by > 50% of participants

- Euphoria
- Increased sexuality
- Well-being
- Relaxation
- Talkative
- Tranquility
- Tranquility
- Drowsy
- Optimism
- Increased energy
- Giddiness
- Increased sensitivity to sound
- Feeling silly
- Sweaty
- Loss of consciousness

Adverse Effects Associated GHB

- Nausea
- Vomiting
- Enuresis
- Feeling drunk
- Disorientation
- Confusion
- Respiratory depression in combination with other depressants
- Sleep walking
- Sleep paralysis
- Cataplexy
- Headache
- Blurred vision
- Dizziness
- Coma
- Overdose

Factors Associated With GHB Overdose





when sleep is safe and desired. Ensure that those around you are aware that you may be unarousable and that this is normal. Higher doses will result in proportionally longer periods of deep sleep. Excessive doses may result in sweating, muscle spasms, vomiting, bedwetting, and diarrhea. Unless drugs or alcohol have been taken with Blue Nitro the only treatment necessary is to SLEEP IT OFF! A call for help may result in uninformed emergency medical personnel using expensive, unnecessary and potentially dangerous methods of arousal.

- KEEP OUT OF REACH OF CHILDREN
- DO NOT COMBINE WITH DRUGS OR ALCOHOL



GHB Abuse

Tolerance

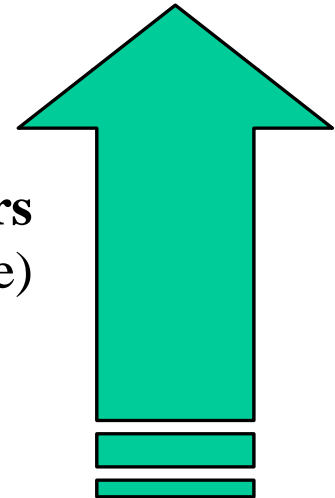
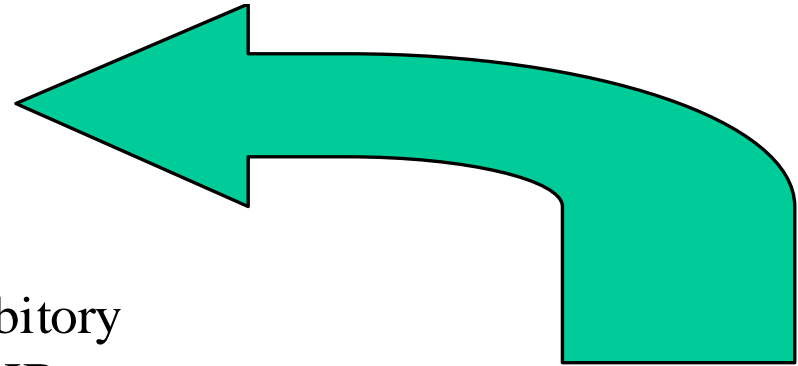
Down regulation of inhibitory
GABA-A, GABA-B, GHB receptors

Decreased GHB Consumption

Dysinhibition of Excitatory Neurotransmitters
(Glutamate, NMDA, Norepinephrine, Dopamine)

Withdrawal

Anxiety Restlessness Insomnia Tremor Confusion
Delirium Hallucinations Tachycardia Hypertension
Nausea Vomiting Diaphoresis



Temporal Pattern of the Symptoms of GHB Withdrawal

SYMPTOMS:	Early (1-24 hours)	Progressive (1-6 days)	Episodic when waning (7-14 days)
Anxiety/ Restlessness	++	+++	++
Insomnia	+++	+++	++
Tremor	+	++	+
Confusion	++	+++	++
Delirium	++	+++	+++
Auditory/Visual hallucinations	+	+++	++
Tachycardia	+	++	+
Hypertension	+	++	+
Nausea	++	+	+
Vomiting	++	+	0
Diaphoresis	+	++	+

Key: Mild = +, Moderate = ++, Severe = +++

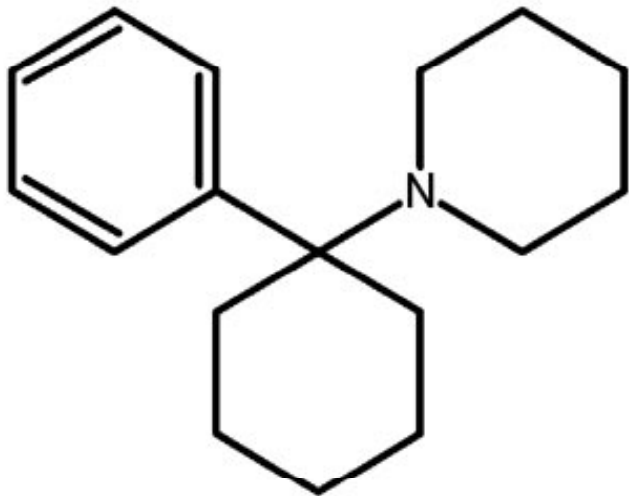
GHB Withdrawal Clinical Concerns

- Patients present to the ER with anxiety, confusion and hallucinations - early manifestation withdrawal
- Antipsychotic are started and high dose benzodiazepines or barbiturates are delayed
- Agitated delirium develops with dehydration
- Restraints are need for the patient safety
- Autonomic changes independent of withdrawal severity
- Treatment setting: psychiatry, ICU, medical floor?
- Recommendation: start treatment early with benzodiazepines – load to sedation – patients are generally resistant to the sedative effects

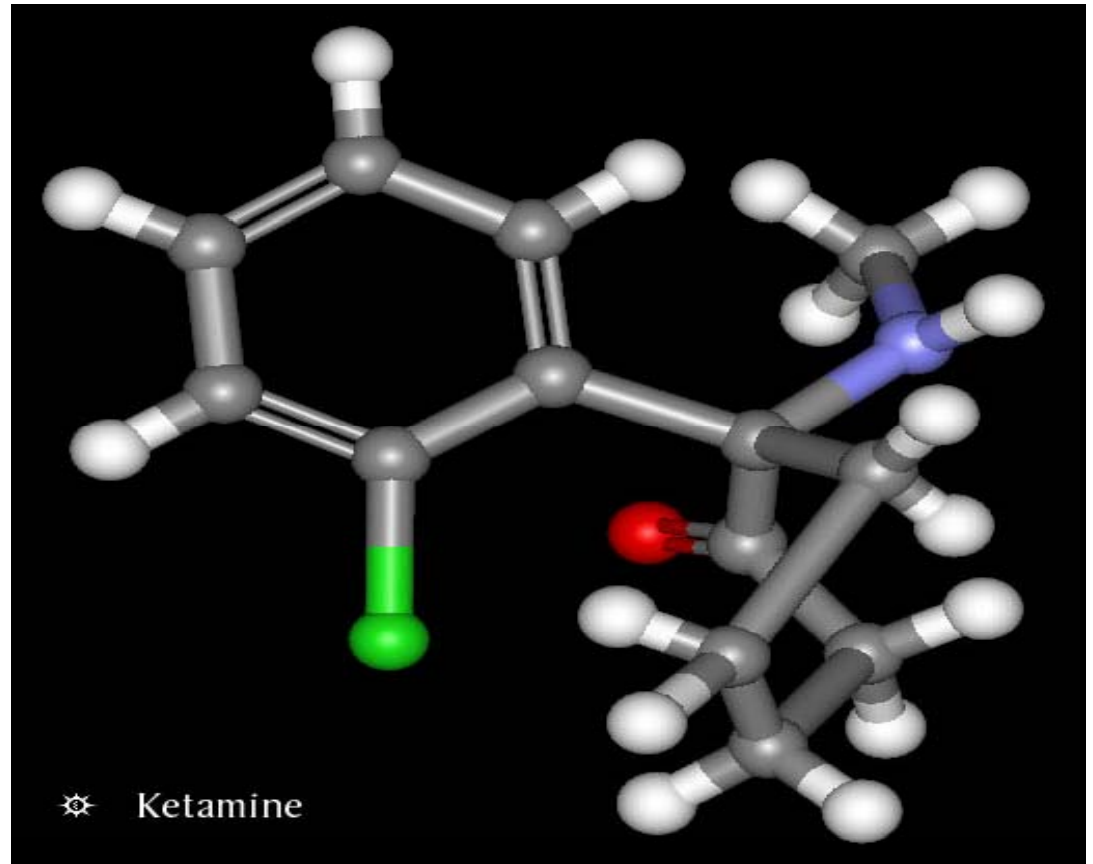
GHB -like Drugs Summary


- Evolving drug distribution system
 - Designed to defy FDA ban
 - Marketed as health aids
 - Internet sales
 - Sold by some body builders and personal trainers
- Drugs effects – amnesia, hypnotic ,anxiolytic, myorelaxant, anesthetic
- GHB tolerance, dependence and withdrawal
- Major toxicity - Overdose

Ketamine and PCP



Phencyclidine (C₁₇H₂₅N)
Image by Erowid, © 2002 Erowid.org



 Ketamine

Take a little 'K' and

Meet the

“K- Monster”



Ketamine Trends

- Past-year use of ketamine did not change significantly from 2006 to 2007
- Use was reported by 1.0% of 8th-graders
- Use was reported by 0.8% of 10th graders
- Use was reported by 1.3% of 12th graders in 2007

Ketamine Background

- 1962: Developed and initially promoted as a fast acting anesthetic
- 1970's: Approved for human use by federal government, and as a result became popular as a battlefield anesthetic
- Dissociative anesthesia – catalepsy, catatonia and amnesia but not necessarily complete unconsciousness
- Late 1970's and early 1980's: Abuse began to increase across the country, especially among certain sub-cultures (e.g., mind explorers and New Age spiritualists)

Ketamine Background

- Mid-1980s: Another increase in the social-recreational use in the dance or rave cultures
- 1999: Classified as a Schedule III controlled substance in August 1999, creating more stringent controls of the drug
- Late 1990s: Ketamine and the treatment of pain
 - Low dose ketamine infusion
 - Ketamine tablets
 - Intranasal ketamine

Ketamine Properties

- Central nervous system depressant
- N-methyl-D-aspartate (NMDA) antagonist
- Rapid acting-acting dissociative anesthetic
- Sedative-hypnotic, analgesic and hallucinogenic properties
- Structurally similar to:
 - PCP
 - Dextromethorphan



Ketamine – Users Report

- Dissociative effects called a “K-hole” – your brain is active but your body isn’t, “like you’re in a tunnel, your hear echoes, you’re in a semi-conscious state”
- Used at rave/dance club scene, “not as popular now”
- “Like living inside a big cotton ball,” “everything is in slow motion”
- Flashbacks
- K-land desired state



Ketamine Mechanism of Action

- *N*-methyl-D-aspartate (NMDA) receptor antagonist
Binds NMDA receptor causing a blockade of calcium flow through these channels - Blockade of calcium associated with altered perception, memory, and cognition
- Some evidence suggests that ketamine can inhibit the reuptake of dopamine and norepinephrine
- NMDA blockade is associated with increased dopamine release in prefrontal cortex and midbrain
- NMDA blockade has also been linked to activation of serotonin systems, particularly serotonin 1A receptors

Ketamine

- Administration: intranasal, oral, smoked, injected
- 10 ml vials provide 5 doses
- Sell for \$20 a dosage unit
- Rapid onset of effects
- Duration of effects 4-6 hours
- Street names:
 - Special K
 - Vitamin K
 - KitKat
 - Blind squid
 - Super acid



Ketamine Effects

- Muscle spasm
- Blurred vision
- Nystagmus
- lack of coordination
- Dizziness
- Slurred speech
- Psychological effects
- Tolerance
- Dependence
- Anesthesia
- Cataplexy
- Immobility
- Tachycardia
- Increased blood pressure
- Profound insensitivity to pain
- Amnesia, slurred speech



Toxicity and Adverse Effects

- Emergence reactions : common during recovery, include unpleasant dreams , confusion, hallucinations and irrational behavior (children less susceptible), reduced by prior administration of a benzodiazepine
- “Out-of-body” state/experience : a psychological dissociation, “near death experience”
- “Flashbacks”

Phencyclidine – Trends

- In the **2005 Monitoring the Future (MTF) Survey**, 2.4% of HS seniors reported lifetime use of PCP, 1.3% reported annual use of PCP, and 0.7% reported 30-day use of PCP.
- In the **2004 National Survey on Drug Use and Health (NSDUH)**, lifetime use of PCP went down for 18 to 25 year olds. Males showed significant decreases in lifetime use from 2003. Females showed significant declines in past year use. Lifetime use among 12- or 13-year-olds, however, was up significantly in 2004, from 0.1% in 2003 to 0.3%.
- In the **2003 National Survey on Drug Use and Health (NSDUH)**, 3% of the population 12 years and older used PCP at least once.

Phencyclidine Background

- Chemical name phenylcyclohexylpiperidine
 - It is synthetic arylcyclohexylamine
- Sernyl introduced as anesthetic in clinical trials in 1957
 - Drug induced amnesia, analgesia, anesthesia, catalepsy postoperative delirium and acute psychotic reactions
- A dissociative anesthetic - Schedule II drug
- NMDA receptor antagonist
- Powder, pill and liquid forms - sprayed onto leafy material, i.e. marijuana, mint, oregano, parsley, or ginger leaves, then smoked

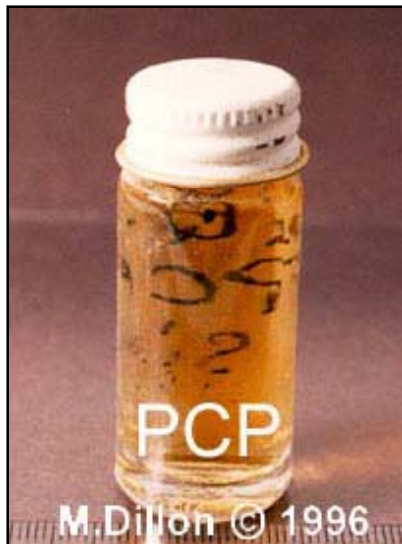
Phencyclidine Street names

- Slang terms for PCP:

- Angel Dust
- Hog
- Ozone
- Rocket Fuel
- Shermans
- Wack

- Slang terms for PCP combined with marijuana:

- Killer Joints
- Crystal Super Grass
- Fry
- Lovelies
- Wets
- Waters



Phencyclidine Effects

- Changes in body image, loss of boundaries, and depersonalization, altering mood states in an unpredictable fashion
- Small doses produce a numbness in the extremities and intoxication; staggering, unsteady gait, slurred speech, bloodshot eyes
- Moderate doses (50-100mg intranasally, or 1-2mg/kg intramuscularly or intravenously), will produce analgesia and anesthesia
- High doses may lead to convulsions

Phencyclidine Adverse Effects

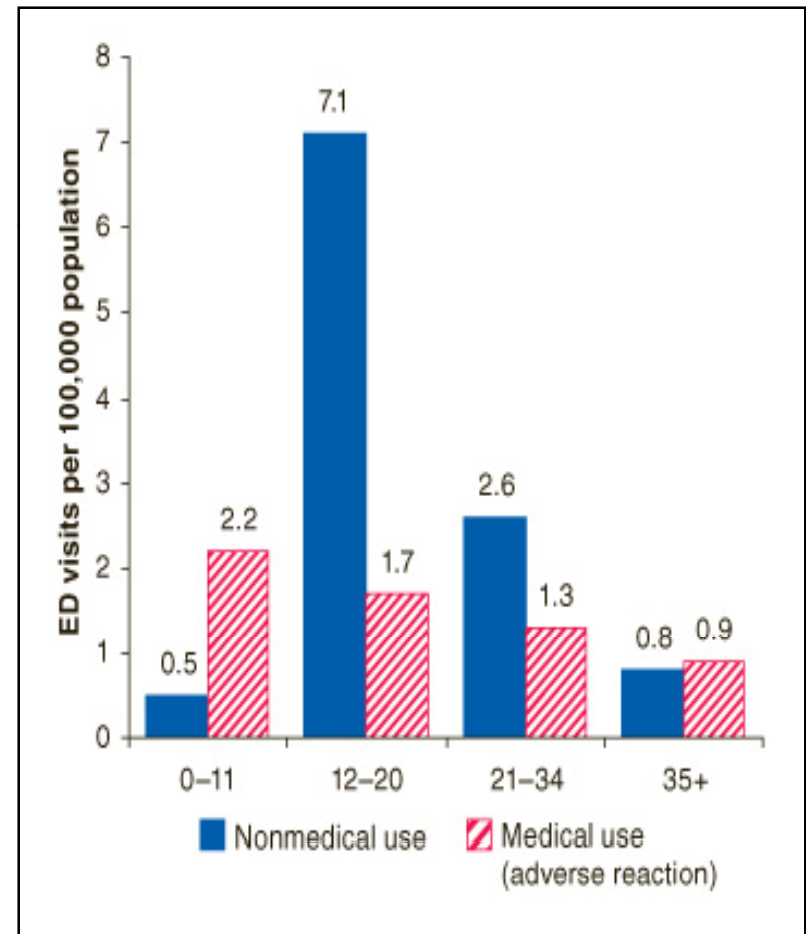
- Symptoms can be recalled by the mnemonic device RED DANES:
 - Rage
 - Erythema (redness of skin)
 - Dilated Pupils
 - Delusions
 - Amnesia
 - Nystagmus
 - Excitation
 - Skin dry

Phencyclidine Toxicity

- PCP toxicity is manifested by a stuporous, comatose state in which the patient is responsive only to deep pain
- Many deaths associated exclusively with PCP intoxication have been reported in the US
- In most cases, circumstantial evidence suggested that death was secondary to the behavioral toxicity of PCP

Dextromethorphan Trends

- Poison control experts point to a four-fold increase in abuse cases since 2000.
- Target population:
 - School-aged youth and young adults
 - Dance club or “rave” scene



Dextromethorphan Trends

- According to the **2004 Drug Abuse Warning Network (DAWN)**, an estimated 12,584 emergency department (ED) visits involved pharmaceuticals containing dextromethorphan (DXM).
- The rate of ED visits resulting from nonmedical use of DXM for those aged 12 to 20 was 7.1 visits per 100,000 population compared with 2.6 visits or fewer per 100,000 for other age groups.
- Alcohol was implicated in about a third (36%) of ED visits involving non-medical use of DXM for those aged 18 to 20 and in 13 percent of visits for those aged 12 to 17.

Dextromethorphan – Background

- Oral cough suppressant available in the US without a prescription
- Ingredient in >125 nonprescription cough and cold medications
- 1954 - FDA approved as a cough suppressant
- 1970s - added to cough syrups - less addictive than codeine
- Some states have statutes and bills related to state regulations of DXM

Dextromethorphan Use

- Typical dose (1/2 an 8-ounce bottle) drink the liquid very quickly – to avoid vomiting
 - Recommended dose 15 to 30 mg 3 to 6 times a day
 - Large doses (e.g. 100 to 2000 mg),
- Internet sales of DXM alone
- Acid-base extraction technique to “free-base,” or extract, the DXM from the unwanted guaifenesin, coloring agents, sweeteners, and alcohol in cold preparations

Hendrickson & Cloutier. “Crystal Dex:” Free-Base Dextromethorphan J of Emerg Med, 2007

Dextromethorphan Street Names

- Slang terms for DXM intoxication:
 - Dexing
 - Robo Tripping
 - High produced by abuse of the cough syrup Robitussin which contains DXM
 - Skittling
 - Taking extremely large doses of cough medicine to get high
- Slang terms for DXM:
 - Dex
 - CM
 - Poor Man's PCP
 - Red Devils
 - Robo
 - Skittles
 - Cough medicine pills are often red or brightly colored and resemble Skittles candy
 - Syrup
 - Triple C's (C-C-C)
 - Tussin
 - Velvet
 - Vitamin D

DXM Pharmacology

- Dextromethorphan is 3-Methoxy-17-methylmorphinan monohydrate, which is the d-isomer of levophenol, a codeine analogue and opioid analgesic
- NMDA-receptor antagonist
- Dextromethorphan reduces coughing by elevating the threshold for the NMDA-mediated cough reflex
- DXM increases the release and inhibits the reuptake of serotonin

Psychotropic effects of DXM are altered by the CYP2D6 polymorphism

- Extensive metabolizers (EMs) and poor metabolizers (PMs) of CYP2D6 substrates
- All EMs tolerated higher doses of DXM
- EMs also reported greater abuse potential compared with PMs
- Plasma kinetics profoundly differ between EMs and PMs
- PMs had greater psychomotor impairment
- PMs reported greater sedation and dysphoria

Zawertailo et al, 1998

Dextromethorphan Effects

- Euphoric or dreamlike state
- Hallucinations
- Separation from self
- Feelings of detachment
- Cognitive and motor impairment
- Distorted perceptions of sight and sound
- Dizziness
- Lightheadedness
- Drowsiness
- Nervousness
- Restlessness



Dextromethorphan Effects (cont'd)

- Toxic state: confusion, paranoia, panic attacks, impaired judgment, blurred vision, dizziness, excessive sweating, slurred speech, seizures, fever, abdominal pain, nausea, and vomiting
- Toxicity of combination products
 - acetaminophen
- Tolerance and dependence
- Serotonin syndrome when combined with other Rx or OTC medications

Designer Drugs



Tryptamines Designer Drugs

- Monoamine alkaloid
- Found in fungi, plants and animals
 - Psilocybin (mushrooms)
- DMT: N,N-dimethyltryptamine: active orally only when combined with an MAOI
- Ayahuasca - prepared from the [Banisteriopsis spp.](#) vine, usually mixed with the leaves of the Psychotria bush -brew contains MAO inhibiting harmala alkaloids



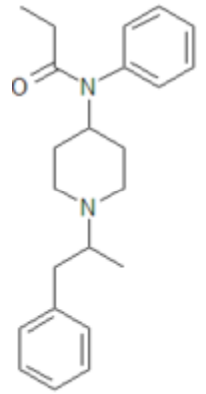
Tryptamines Designer Drugs

- Chemically related to the amino acid tryptophan
- Endogenous tryptamines
 - Serotonin: 5-HT
 - Melatonin : N-acetyl-5-methoxytryptamine
- Monoamine oxidase (MAO) is the inactivation pathway of most tryptamines
- Harmine and harmaline – MAOI activity allows oral use of tryptamines
- Synthetic DMT available
 - Smoked
 - Injected
- Substituted tryptamines
 - 5-MeO-DiPT (Foxy)
 - AMT

Phenethylamine – Designer Drugs

- Biosynthesized from the
- Phenethylamine is a natural compound biosynthesized from the amino acid phenylalanine by decarboxylation
- Substituted phenethylamines
 - Broad class of compounds
- Stimulants
 - Dextroamphetamine
- Hallucinogens
 - Mescaline
 - 2C-B synthetic drug
- Empathogens
 - MDMA
 - MDA

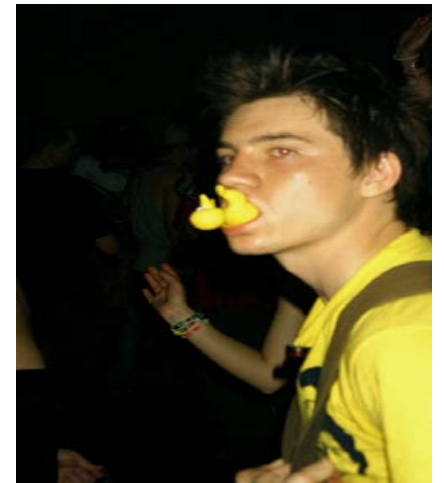
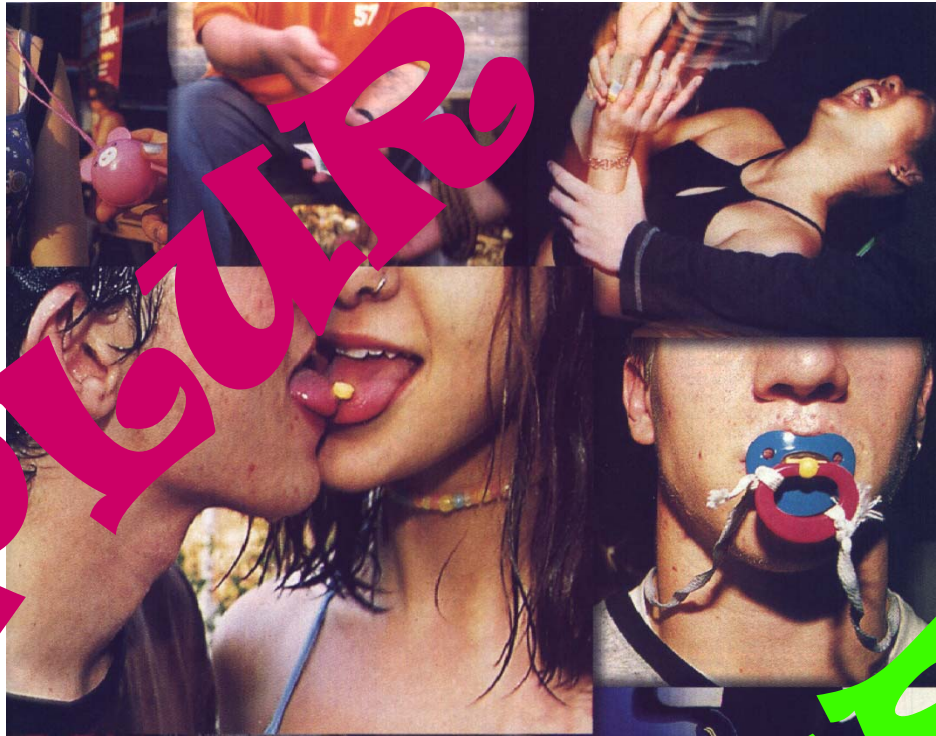
Alpha-methylfentanyl



- Alpha-methylfentanyl is a simple analog of fentanyl, but twice as potent
- Various fentanyl analogs are diluted with large amounts of lactose or mannitol so the amount of active drug present is exceedingly small and therefore contributes nothing to the color, odor, or taste of the sample.
- The color of the samples ranges from pure white ("Persian White"), to an off-white or light tan ("China White," "synthetic heroin," or "fentanyl"), to light or dark brown ("Mexican Brown").
- Currently, the only illicit fentanyl available is the fentanyl/benzylfentanyl mixture.
- Usually smoked or snorted
- "Designer drugs" is a term that has been used recently to describe synthetic drugs of abuse. Alpha-methylfentanyl, and all other analogs of fentanyl, would be considered "Designer Drugs"

RAVE

- All night dance party
- Electronically synthesized repetitive loud (techno) 'mind-numbing' music
- Dress: "Lack of pretense" - baggy pants, glow sticks, infant toys, pacifiers, beads
- Diminished distinction based on physicality and sexual orientation
- Description of atmosphere: "safety, acceptance, hyper connectivity"
- Philosophy "Peace, Love, Unity and Respect"



Pluris
Pluris

Raves Today—Big Business

- Music, Venue, People, Drugs
- Noncommercial music - Independent artist distribute directly to DJs
- DJ can be the main draw for rave audience
- Now held in legal spaces: concert halls, sports centers, parking lots Called: Venues or Concerts not Raves
- Many raves held on Holidays such as Valentines Day, Halloween and News Years Eve
- Usually no age restriction (no alcohol)
- Kids don't live in small towns...They live in the Wide Web World . It is easy to find a rave near you!
 - www.raves.com/ www.bluelight.nu/bluelight/

E y e C a n d y



Conclusion Club Drugs

- Ecstasy
- GHB
- Ketamine
- PCP
- Dextromethorpan
- Designer Drugs
- Rave Culture



Jefferson Airplane

One pill makes you larger

And one pill makes you small

And the ones that mother gives you

Don't do anything at all

Go ask Alice

When she's ten feet tall

And if you go chasing rabbits

And you know you're going to fall

Tell them a hookah smoking

caterpillar has given you the call

Call Alice

When she was just small