HALLUCINOGENIC AGENTS

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Outline

- Review of all hallucinogens with respect to toxicity
- Review of hallucinogens with respect to behavioral manifestations
- Review of best practice for overdose intoxication of these agents

Teaching Points

- There are many different types of hallucinogens, derived from different sources. Lysergic acid diethylamide (LSD) is the prototypical hallucinogen and is the most commonly abused.
- Hallucinogens cause perceptual distortions more than hallucinations, and “bad trips” require varied medical treatment.
- Hallucinogens produce perceptual distortions and cognitive changes with a clear sensorium and without impairment in level of consciousness or attention

Pre-Lecture Exam
Question 1

1. The primary neurotransmitter involved with LSD is

a. GABA
b. Norepinephrine
c. Serotonin
d. Dopamine
e. Acetylcholine

Pre-Lecture Exam Question 2

2. The CNS effects of LSD include

a. Euphoria

b. Labile mood

c. Visual hallucinations

d. Synesthesias

e. All of the above

Pre-Lecture Exam
Question 3

3. The following is not true of how one treats PCP intoxication

a. Diazepam, Lorazepam – for seizure activity
b. Alkalinization the urine – to increase excretion
c. Antipsychotic agents – for psychotic states
d. In cases of extreme overdose with coma – continuous gastric suction, intubation
e. May require physical restraint

Pre-Lecture Exam
Question 4

4. The following is not true of MDMA

a. It is referred to as ecstasy

b. It is promoted by psychotherapists as an adjunct to psychotherapy

c. Use may lead to frank visual hallucinations

d. It usually causes a decrease in blood pressure

e. None of the above (all statements are true)

Pre-Lecture Exam
Question 5

5. Anticholinergics

a. Include SSRI's, MAOI's, and Lithium

b. Produce moist skin, constricted pupils and bradycardia

c. Treatments for overdose include gastric lavage and physostigmine

d. Main psychiatric symptom is paranoid delusions

e. None of the above

Pre-Lecture Exam Question 6

6. With respect to inhalants

a. The common treatment for intoxication are antidepressants

b. Actions are mainly mediated through norepinephrine

c. Are a problem mainly for the elderly

d. Can cause Nystagmus and Muscular incoordination

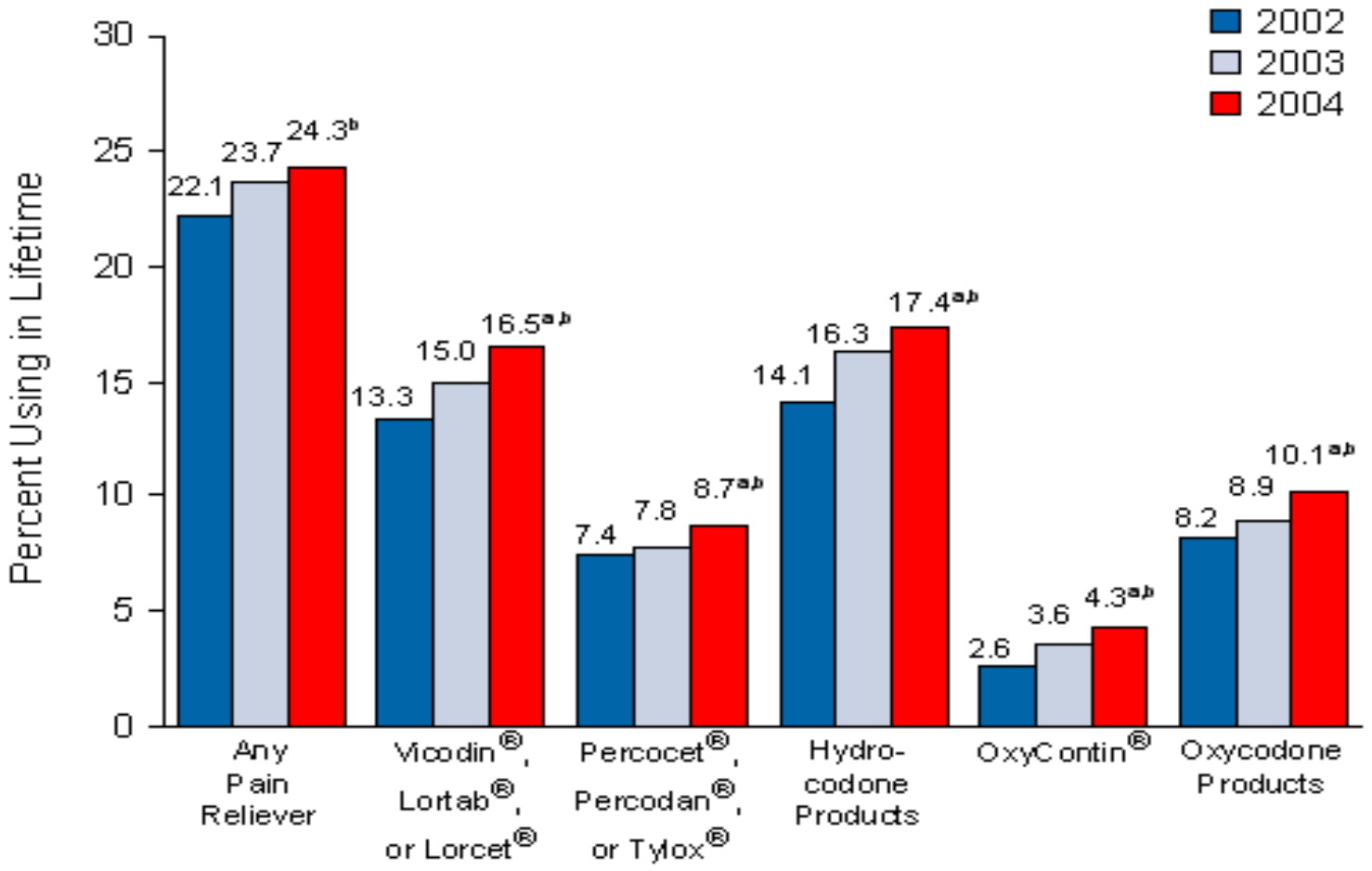
e. Use is not as dangerous as marijuana

EPIDEMIOLOGY

8.8% of the population has used an hallucinogenic agent, according to household surveys

Between 1980 and 1989 the use of hallucinogens declined to about 2 -3%, but increased again in the mid-90's to the 9% range, but has declined slightly recently

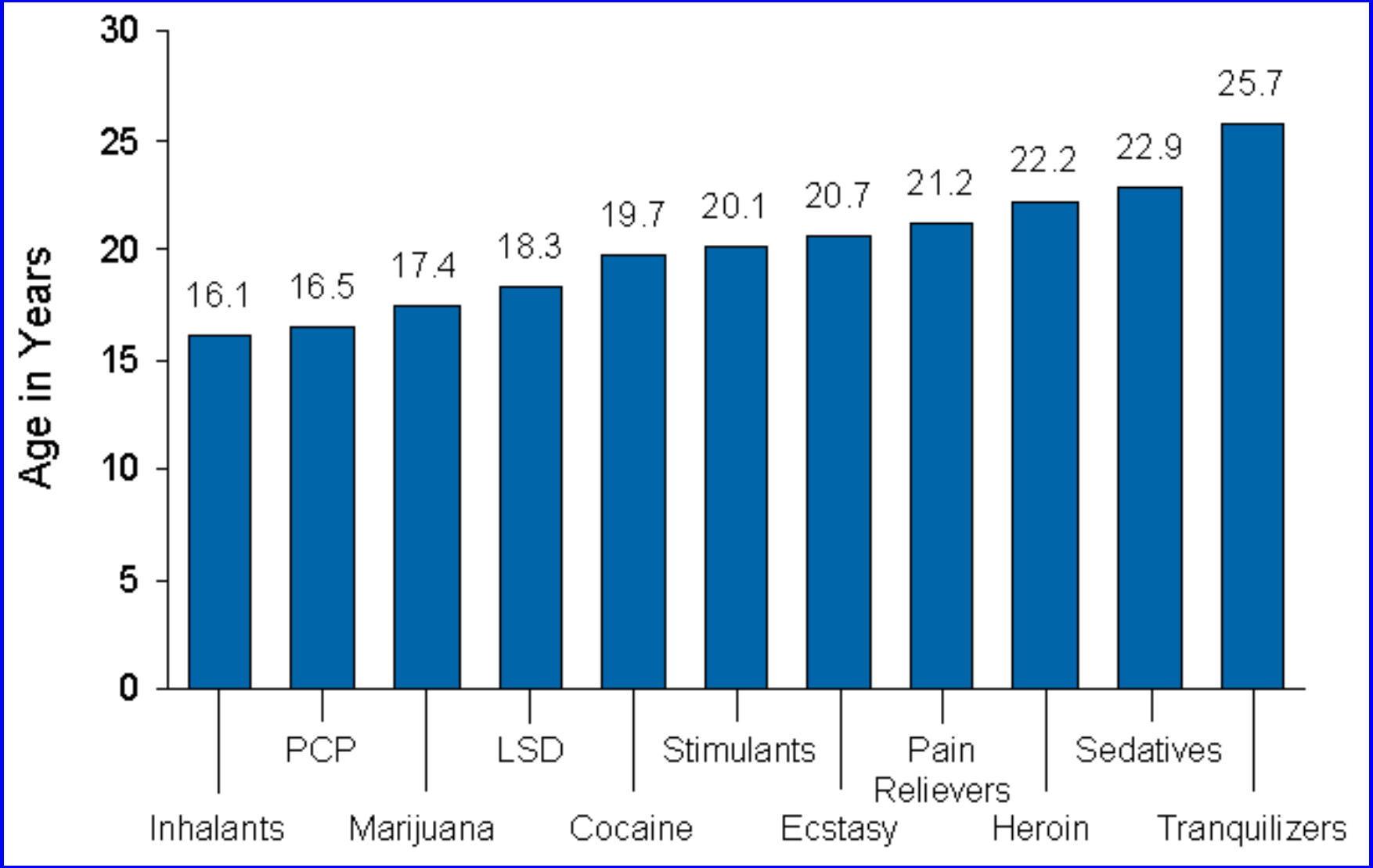
LYSERGIC ACID DIETHYLAMIDE (LSD)



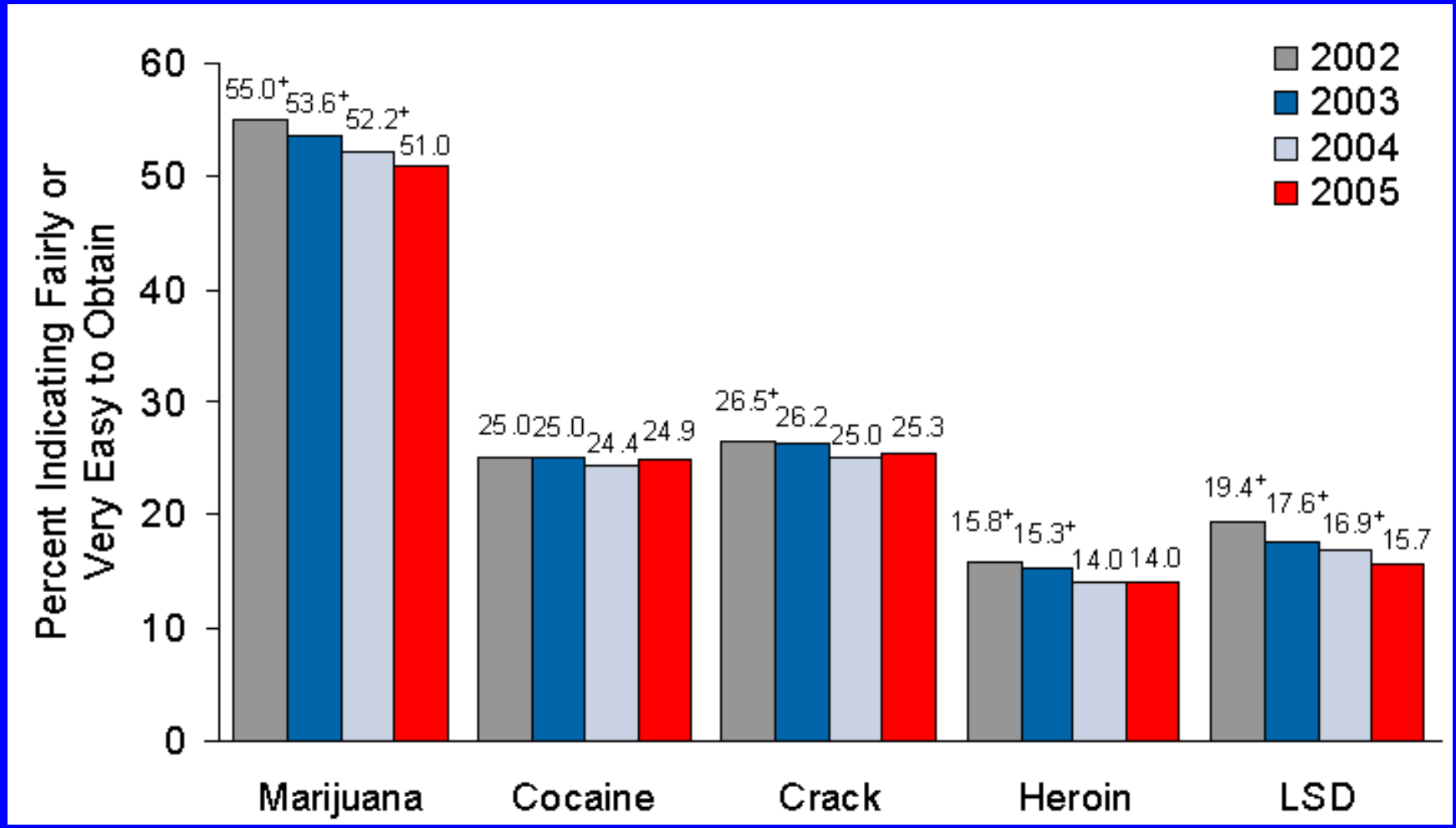
[a] Difference between the 2003 estimate and the 2004 estimate is statistically significant at the .05 level.

[b] Difference between the 2002 estimate and the 2004 estimate is statistically significant at the .05 level.

Age of Initiation of Drug Use



Perceived Availability of Drugs of Abuse



LSD Use - 8th and 10th Graders

	2002	2003	2004	2005
Lifetime	14.4	14.3	14.9	15.1
Past Year	6.8	7.1	7.8	7.8
Past Month	3.1	3.2	3.5	3.2

No current licit use

- Illicit use began on a large scale around 1965, (in LA, 9/65) significantly influenced by Dr. Timothy Leary and his promotion of its use

LYSERGIC ACID DIETHYLAMIDE (LSD) cont'd

Mechanisms of action -

involves primarily, but not exclusively serotonergic systems in particular, the post-synaptic 5HT-2 receptor.

The exact mechanism of action is not known

LYSERGIC ACID DIETHYLAMIDE (LSD) cont'd

Route of administration - usually taken orally

May be provided as a powder, solution, capsule or pill; drops of LSD have been placed on sugar cubes, animal crackers, and blotting paper.

Doses in excess of 35 ug are extremely hallucinogenic;
"street doses" range from 50 to 300 ug.

LYSERGIC ACID DIETHYLAMIDE (LSD) cont'd

Time course and metabolic half-life

Metabolic half-life is approximately 3 hours

BUT the effect of a single dose can last for 4 - 12 hours or more.

The effect of an oral dose can be perceived within 30-60 minutes.

LYSERGIC ACID DIETHYLAMIDE (LSD) cont'd

CNS Effects

- Euphoria
- Labile mood
- Visual hallucinations
- Synesthesias
- Ego fragmentation -

(initially a decrease in normal ego defenses
BUT ego can become overwhelmed ↘
depersonalization)

LYSERGIC ACID DIETHYLAMIDE (LSD) cont'd

Chronic use - no evidence of permanent damage

Psychiatric hazards

Temporary episode of panic - "Bad trip"

Most common is a state of acute panic often accompanied by a fear of imminent insanity.

0.8 - 1.8 per 1000 administrations of LSD

LYSERGIC ACID DIETHYLAMIDE (LSD) cont'd

Precipitation of serious depression, paranoid behavior or prolonged psychotic reaction resembling schizophrenia

Exacerbation of existing psychotic states or conversion of pre-morbid state to frank psychosis

LYSERGIC ACID DIETHYLAMIDE (LSD) cont'd

Hallucinogen Persisting Perceptual Disorder

Flashbacks

- Treatment
  - Diazepam, Lorazepam
  - Interpersonal - reassurance and support

PHENCYCLIDINE (PCP)

(angel dust, peace, crystal, hog, rocket fuel)

Current licit use - no current clinical use;
is used as an animal tranquilizer.

Previous clinical use - general anesthetic to produce dissociative anesthesia-

- produced analgesia
- amnesia
- suppression of laryngeal reflexes
- little CV effect
- little muscle relaxation

PHENCYCLIDINE (PCP), cont'd

But mildest complaints were of graphic nightmares, some patients became delirious and showed near mania when the anesthetic effects wore off.

First appeared in CA in 1960's as pills but numerous reports of psychotic symptoms caused a decline in popularity. Reintroduced in the 1970's as a powder to be smoked or snorted and this time it sold well, especially to young, white polydrug abusers.

PHENCYCLIDINE (PCP)cont'd

Abuse in primarily minority communities in major metropolitan areas - new cases have switched back to primarily white males (between ages 26 and 34). African Americans now have the lowest rates of use of all ethnic groups.

PHENCYCLIDINE (PCP)cont'd

Mechanisms of action - not completely understood

Acts as antagonist of NMDA-glutamate receptors

In animal studies, profound memory disturbances are linked to this receptor antagonism

affinity related to ability to produce PCP-like effects

Other Receptors Involved in PCP Activity

- Presynaptic monoamine receptors - both DA and 5-HT involved.
- Sigma receptor
- K^+ and Na^+ channel receptors

PHENCYCLIDINE (PCP)cont'd

Routes of administration - usually smoked in parsley or marihuana cigarettes.

Time course - onset within 5 minutes, plateau in about one-half hour and remain there from 4-6 hours;
recovery may take 24-48 hours.

PHENCYCLIDINE (PCP)cont'd

CNS Effects

Effects of PCP: 5 mg dose:

sense of intoxication-"euphoria"; "peaceful floating sensation;" "speedy" feeling,

uncommunicative, oblivious, very labile affect,

slurred speech, nystagmus, rolling gait

feelings of numbness in hands and feet

feelings of depersonalization

disordered thoughts

distortions of space and time perceptions

PHENCYCLIDINE (PCP)cont'd

Distortions of body image

Changes in perception of body consistency

Delusions - auditory and visual hallucinations

PHENCYCLIDINE (PCP)cont'd

Larger doses

- drowsiness ---> stupor ---> coma
- feelings of isolation
- hyperacusis; sensitivity to external stimuli
- amnesia
- bizarre, hostile or unusual behavior
- muscle rigidity
- repetitive movements
- excessive salivation WITH loss of gag reflex
- fever
- increased blood pressure and heart rate

PHENCYCLIDINE (PCP)cont'd

Toxicity

- hostility toward others
- confusional periods
- coma, convulsions
- psychotic states - nearly identical to acute schizophrenia
- behavioral problems - talking down is rarely successful
- paranoia

PHENCYCLIDINE (PCP)cont'd

Chronic use - "dulled" thinking and reflexes, loss of impulse control lethargy and depression.

No clear evidence of permanent brain damage, but neurological and cognitive dysfunction persists after 2-3 weeks of abstinence.

PHENCYCLIDINE (PCP)cont'd

Treatment

Diazepam, Lorazepam - for seizure activity

Antipsychotic agents - for psychotic states

Acidification of urine - to increase excretion

May require physical restraint - CAREFUL

In cases of extreme overdose with coma - continuous gastric suction, intubation and maintenance of vital functions

MDMA

ECSTASY

Clinical use - no currently recognized use but promoted as an adjunct to psychotherapy. Has some popularity among groups of psychotherapists

Usually classified as a “Club Drug”

Usual dose - 75-300 mg

MDMA (methylenedioxymethamphetamine) cont'd) (Ecstasy)

Mechanism of action - Believed to be both dopaminergic and serotonergic.

Physiologic effects - not well characterized due to lack of controlled studies.

There is known to be increased blood pressure, increased heart rate, dry mouth, bruxism

MDMA (methylenedioxymethamphetamine) cont'd) (Ecstasy)

CNS effects

- Euphoria - "a loving feeling"
- Loss of boundaries
  - less aware of own boundaries; less distinction between self and others; decreased sense of separation from others
- Decrease or loss of inhibitions
  - decreased defensiveness
- "Promotes intimacy"

MDMA (methylenedioxymethamphetamine) cont'd) (Ecstasy)

Cognitive changes

shift in form and content

slowed thoughts, generalized mental slowing

decreased desire to do mental or physical tasks

Perceptual changes

Visual perceptions are primarily intensified but there may be change in content leading to frank visual hallucinations

Altered time perception

Altered perception of spatial relationships

Increased Anxiety

MDMA (methylenedioxymethamphetamine) cont'd)
(Ecstasy)

Chronic effects - still not known in man. BUT in experimental animals, including non-human primates,
there has been long-lasting, if not permanent, destruction of CNS serotonin pathways. Current evidence in human subjects who have used MDMA also shows permanent destruction of serotonin pathways.

ANTICHOLINERGICS

ATROPINE, DIPHENHYDRAMINE, TRICYCLIC ANTIDEPRESSANTS, MANY OVER-THE -COUNTER SLEEP AIDS, BENZTROPINE

Generally, a side effect rather than the desired effect but occasionally used for the hallucinogenic effects.

Accompanied by delirium, manifested by waxing and waning consciousness, impulsivity, and impaired judgment.

Also accompanied by physiologic signs of anticholinergic toxicity

fever; warm, dry skin; fixed dilated pupils; tachycardia; decreased peristalis; and atonic bladder.

ANTICHOLINERGICS cont'd

Hallucinogenic effects

Misperceptions

Dysphoria

Estrangement and/or depersonalization

Agitation

Visual and auditory hallucinations

Treatment

- Gastric lavage
- Parenteral physostigmine

Inhalants

Toluene
Gasoline
Kerosene
Carbon tetrachloride
Fluorocarbon propellants
Amyl or Butyl nitrates
Nitrous oxide

CNS Effects of Inhalants

Very similar to to effects of alcohol, including actions through the GABA-A receptor complex

Stimulation and disinhibition
Nystagmus
Muscular incoordination
Perceptual distortions --> ? Frank hallucinations

Chronic Use of Inhalants

Toxic effects on various organ systems
depends on agent of choice

CNS damage - related to demyelination,
cerebellar atrophy

Impairments in memory, attention, concentration
and non-verbal intelligence

Treatment of Inhalant Abuse/Dependence

Behavioral

No pharmacological assistance is available

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Answers to Pre and Post-Lecture Exams

1. C
2. E
3. B
4. D
5. B
6. D