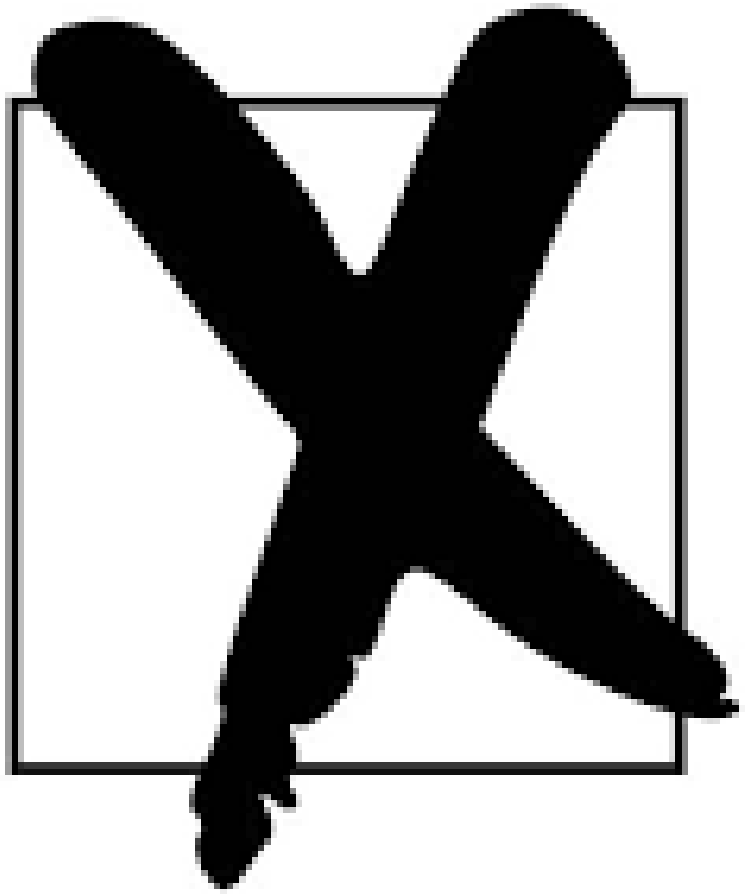
# Stimulants, Hallucinogens and Club Drugs


**Rob Campbell, MD, FASAM**
**Clinical Faculty, University of Louisville**
**The Ohio State University,**
**Departments of Psychiatry**
**Ohio University College of Medicine**
**Staff Psychiatrist**
**Twin Valley Behavioral Health**
**Columbus, Ohio**



None of the above

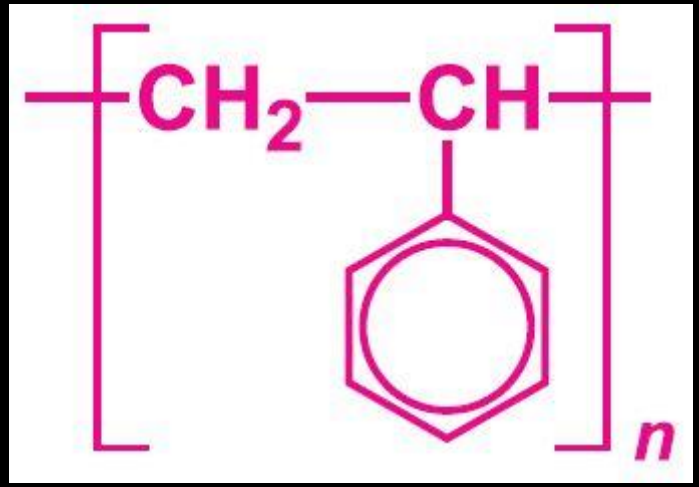
# Objectives

- 1. Understand the pharmacology of stimulants , hallucinogens, and club drugs
- 2. Learn which substances belong in each category
- 3. Learn the side effects and complications of each substance as how it affects organ systems in the body

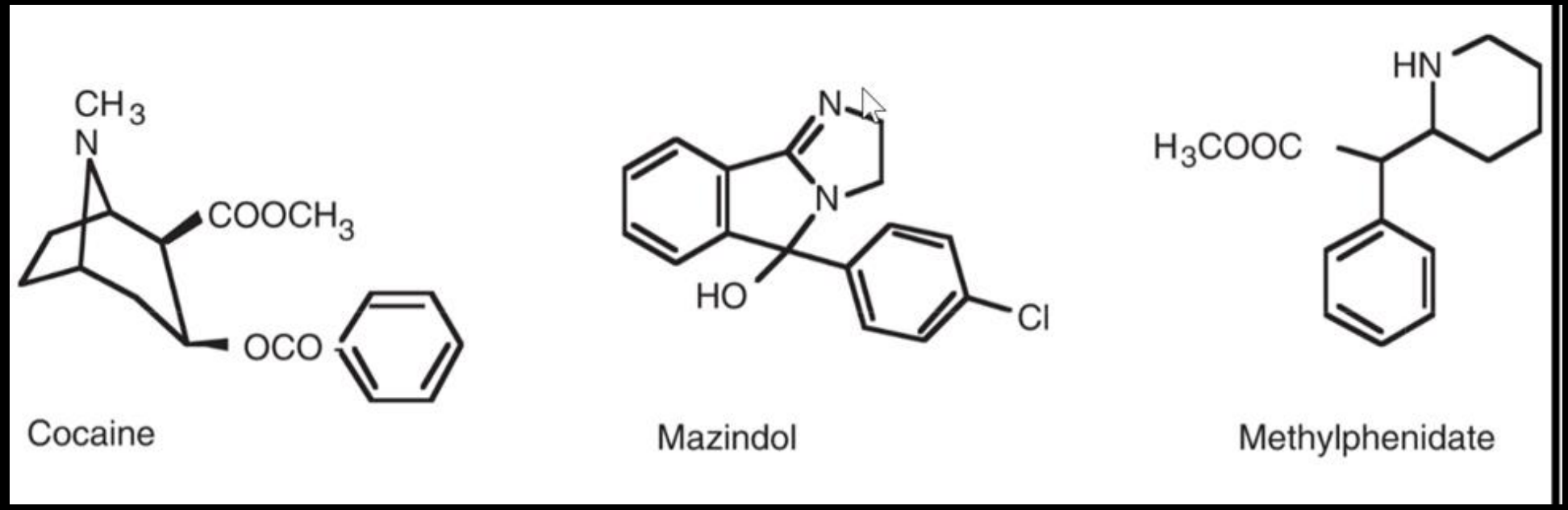
# Stimulants: DEFINITION

- Stimulants are a class of drugs that stimulate activity in the CNS and sympathetic PNS
- Enhance neurotransmitter activity at catecholaminergic synapses

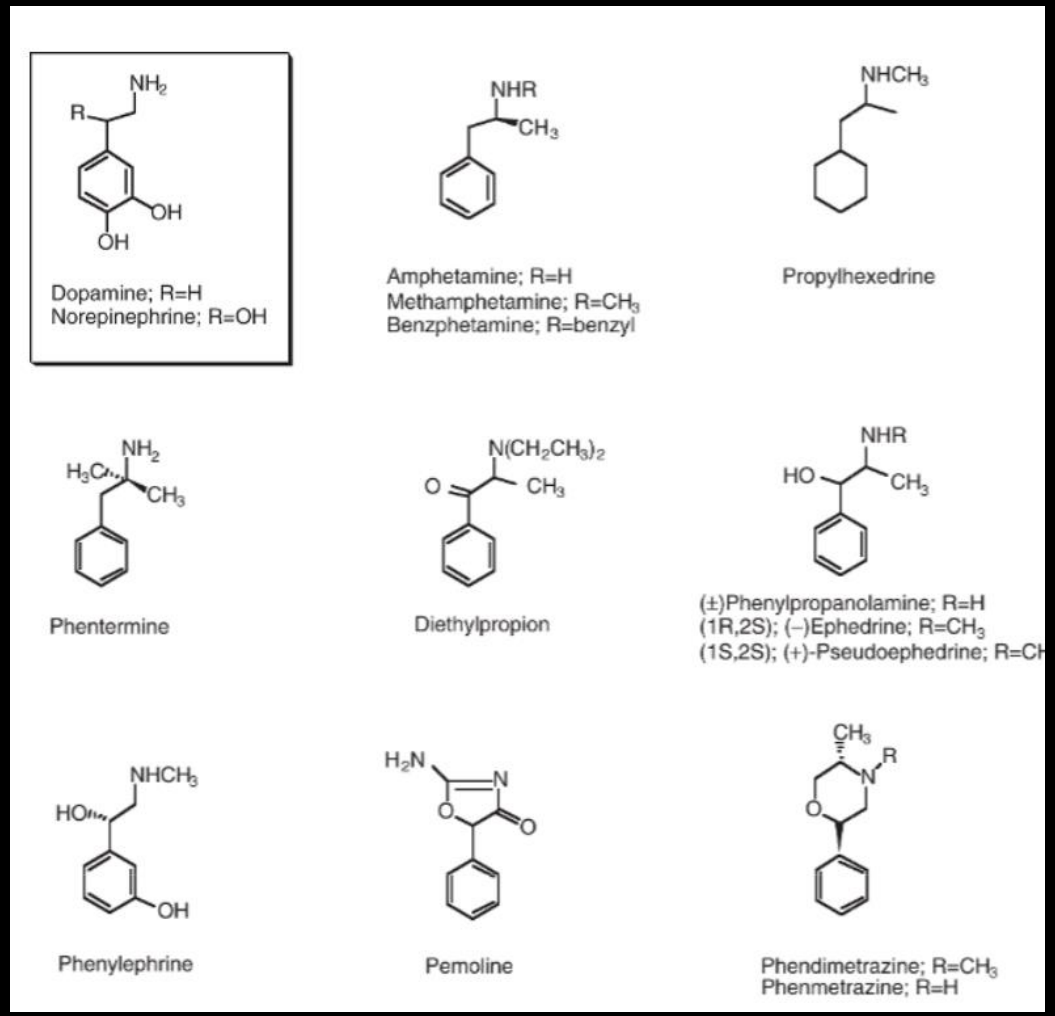
# The Culprit?…the phenylethylamine structure



# SUBSTANCES INCLUDED: Chemical structures of cocaine, mazindol, and methylphenidate



# Chemical structures of endogenous catecholamine neurotransmitters vs the amphetamines…



# Overview of the stimulants….

- All stimulants share the same range of psychological and physiological effects while differing in **potency** and **pharmacokinetic characteristics**
- 3, 4-methylenedioxymethamphetamine (MDMA, "Ecstasy"), a structural analog of methamphetamine with both **stimulant** and **hallucinogenic** characteristics, will be considered with the club drugs later in this presentation

# Mechanism of action…

**TABLE 10-4 NEUROPHARMACOLOGIC ACTIONS OF SELECTED STIMULANTS**

| | CATECHOLAMINE | | SEROTONIN | | | |
|---|---|---|---|---|---|---|
| | TRANSPORTER BLOCKER | TRANSPORTER SUBSTRATE (RELEASER) | TRANSPORTER BLOCKER | TRANSPORTER SUBSTRATE (RELEASER) | MAO INHIBITION | NA CHANNEL BLOCKER |
| Amphetamine | ++ | +++ | 0 | + | + | 0 |
| Cocaine | +++ | 0 | +++ | 0 | 0 | +++ |
| Ephedrine[a] | + | ++ | 0 | 0 | 0 | 0 |
| Mazindol | +++ | 0 | + | 0 | 0 | 0 |
| Methamphetamine | ++ | +++ | + | ++ | + | 0 |
| Methylphenidate | +++ | 0 | + | 0 | 0 | 0 |
| Phentermine | + | ++ | 0 | 0 | + | 0 |

[a]Also a direct agonist at adrenergic (norepinephrine) receptors.
MAO, monoamine oxidase; 0, no effect; +, marginal effect; ++, substantial effect; +++, predominant effect.
Based on data from Rothman RB, Baumann MH, Dersch CM, et al. Amphetamine-type central nervous system stimulants release norepinephrine more potently than they release dopamine and serotonin. *Synapse* 2001;39:32–41 (256); Howell LL, Kimmel HL. Monoamine transporters and psychostimulant addiction. *Biochem Pharmacol* 2008;75:196–217 (219).

Table 10-4 Neuropharmacologic Actions of Selected Stimulants

# FORMULATIONS: Plant-Derived Stimulants…

- **Cocaine:**

✓ Alkaloid tropane **ester**

✓ Chemical structure similar to **scopolamine** and other plant alkaloids

✓ Occurs in leaves of the coca bush, ***Erythroxylum coca***, which grows at altitudes of 1,500 to 6,000 feet in the Andean region of South America (chiefly Colombia, Peru, and Bolivia)

✓ The leaf contains cocaine (0.2% to 1%) and more than a dozen other tropane alkaloids (such as **benzoylecgonine, methylecgonine, ecgonine, and cinnamoylcocaine**), most of which are of unknown pharmacologic activity

✓ Another *Erythroxylum* species, *E. novogranatense*, contains lesser amounts of cocaine and greater levels of other alkaloids

✓ Available for street use in two forms:

➢ **Base:** low melting point → easily smoked → small particles mostly + true cocaine vapor reach alveoli, relatively insoluble in H2O (i.e., can't dissolve for IV use). "Crack" cocaine is a ba**se ("Smokers")**

➢ **Salt:** high melting point, heating it for smoking destroys it, highly water soluble so ideal for IVDA and facilitating absorption across mucous membranes ("**Shooters" and "Snorters")**

Cocaine is usually cut to enhance dealer profits, and common cutting agents include:

- **Inert fillers that look like cocaine:**

✓ **Dextrose, lactose, mannitol, or starch**

- **Active chemicals that mimic the local anesthetic effect of cocaine:**

✓ **Benzocaine, lidocaine, or procaine**

- **Active chemicals that provide some psychoactive effect:**

✓ **Ephedrine, amphetamine, caffeine, or phencyclidine (PCP)**

- The veterinary antihelminthic agent **levamisole** is increasingly common as a cocaine adulterant and is found in more than 60% of analyzed street cocaine samples in the United States.

➢ Cocaine adulterated with levamisole → agranulocytosis and cutaneous vasculitis

- Street cocaine may also contain contaminants from the preparation process (such as **benzene, acetone, or sodium bicarbonate**)

# More drugs from the plants…

- **Ephedrine and pseudoephedrine:**

✓ Naturally occurring alkaloids with a phenylethylamine chemical structure

✓ Found in several *Ephedraceae* species

✓ **Ephedra** is a preparation of dried young branches of Ephedra species, typically containing 1% to 3% ephedrine

✓ This may be converted into a capsule, tincture, liquid extract, or tea.

✓ Ephedra products are widely used in East Asia and North America; they appear in the pharmacopoeias of China, Japan, and Germany.

✓ Often advertised as legal versions of or alternatives to the more strictly regulated manufactured stimulants

✓ May appeal to consumers as safer than synthetic stimulants because they are “natural” or “herbal”

✓ Ephedra alkaloids have same range of psychological and physiologic effects as do cocaine and amphetamines

✓ Limited evidence of their efficacy for weight loss in obese individuals

❖ ***Ephedra use has been associated with severe cardiovascular and central nervous system (CNS) effects, including death, leading to its banning from the US market in 2006***

# And more plant derived stimulants…

- **Khat:**

✓ Common term for preparations of the ***Catha edulis***

✓ Native to East Africa and the southern Arabian peninsula

✓ Fresh khat leaves contain at least two stimulant alkaloids with **phenylethylamine** chemical structures: **cathinone** (present at 1% to 3%) and **cathine** (norpseudoephedrine)

✓ Pure **cathinone** is a Schedule I controlled substance; **cathine** is in Schedule IV

✓ **Cathinone** displays neuropharmacological potency similar to **amphetamines**

✓ Recreational use of potent synthetic cathinone congeners such as **mephedrone**, **methylone**, and **3,4-methylenedioxypyrovalerone,** often marketed as "**bath salts**," has increased markedly around the world in the past decade

✓ Khat use was a widely accepted social custom for centuries, apparently predating the use of coffee (caffeine)

✓ Leaves are used in the same way as coca leaves in South America, that is, chewed and kept in the cheek for several hours

✓ Less often, the leaves are brewed into tea or crushed with honey to make a paste: Moderate use reduces fatigue and appetite

✓ Compulsive use may result in **manic behavior** or **psychotic symptoms** such as **paranoia** or **hallucinations**

✓ Khat loses much of its potency within 2 days of harvesting, as cathinone is converted to the much less potent cathine

✓ Some khat use is found among immigrant communities in Europe, but there appears to be negligible use of khat in the United States

✓ **Methcathinone** is widely abused in Russia and the Baltic area.

# Synthetic stimulants…Rx

**TABLE 10-1 STIMULANTS AVAILABLE BY PRESCRIPTION IN THE UNITED STATES**

| DRUG | TRADE NAME | STREET NAME | CSA SCHEDULE | TYPICAL INDICATIONS | ORAL DOSE (MG/D) |
|---|---|---|---|---|---|
| Amphetamine (as *d*-isomer or racemic mixture) | Adderall, Dexedrine, Dextrostat, generic | Amp, bennies, dex, black beauties | II | ADHD, narcolepsy, weight control, depression[a] | 2.5–60 |
| Lisdexamfetamine (L-lysine-*d*-amphetamine | Vyvanse | — | II | ADHD | 30–70 |
| Benzphetamine | Didrex | — | III | Weight control | 25–150 |
| Cocaine | — | Coke, crack, flake, snow | II | Local or topical anesthetic | — |
| Diethylpropion | Tenuate | — | IV | Weight control | 75–100 |
| Mazindol | Sanorex, Mazanor | — | IV | Weight control | 1–3 |
| Methamphetamine | Adipex, Desoxyn, Methedrine | Ice, meth, speed, crank, crystal | II | ADHD, weight control | 5–40<br>10–15 |
| Methylphenidate (as *d*-isomer or racemic mixture) | Ritalin, Focalin, Concerta | Rits, Vitamin R | II | ADHD, narcolepsy | 10–60<br>10–60 |
| Modafinil | Provigil | | IV | Narcolepsy | 100–400 |
| *R*-Modafinil | Nuvigil | | IV | Narcolepsy | 150–250 |
| Phendimetrazine | Bontril, Plegine | | III | Weight control | 35–105 |
| Phenmetrazine | Preludin | | II | Weight control | 25–75 |
| Phentermine | Adipex-P, Fastin, Ionamin | — | IV | Weight control | 15–90 |

[a]Not labeled for this indication by the U.S. Food and Drug Administration.
ADHD, attention deficit/hyperactivity disorder; CSA, the U.S. Controlled Substances Act.

Table 10-1 Stimulants Available by Prescription in the United States

# Synthetic stimulants… OTC

**TABLE 10-2 STIMULANTS AVAILABLE AS OVER-THE-COUNTER PREPARATIONS IN THE UNITED STATES**

| DRUG | TRADE NAME | INDICATIONS | TYPICAL ORAL DOSE (MG/D) |
|---|---|---|---|
| Caffeine | (Various) | Weight control, alertness | 50–250 |
| Ephedrine | Marax, Quadrinal | Decongestant, bronchodilation | 50–100 |
| Phenylephrine | Comhist, Dristan, Neo-Synephrine | Decongestant | 40–60 |
| Pseudoephedrine | Sudafed, Sine-Aid | Decongestant | 90–240 |
| Propylhexedrine | Benzedrex, Dristan, Obesin | Decongestant, weight control | 50–150 |

Table 10-2 Stimulants Available as Over-the-Counter Preparations in the United States

# Clinical uses…

- Cocaine is used clinically only as a local or topical anesthetic, chiefly for eye, ear, nose, or throat surgery or procedures
- Other prescription stimulants generally are used for one of the several FDA-approved indications:

✓ ADHD in both children and adults

✓ Narcolepsy and excessive daytime sleepiness

✓ Appetite suppression to promote weight loss in exogenous obesity

- OTC stimulants generally used for:

✓ Decongestion and bronchodilation in the treatment of asthma, upper respiratory infections, allergic rhinitis, sinusitis, or bronchitis and for

✓ Appetite suppression to promote weight loss in exogenous obesity (both of which are FDA-approved indications)

# Nonmedical use, abuse, and dependence..

- All stimulants have a potential for misuse, abuse, and dependence, varying only in their potency
- **Cocaine**, **amphetamine**, and **methamphetamine** have high abuse potential, as reflected in their placement in Schedule II

# Epidemiology…

- Substantial geographic and sociodemographic differences in the epidemiology of stimulant use exists
- 2011 →17 million cocaine users worldwide, representing 0.4% of the 15- to 64-year-old population
- Use is increasing virtually everywhere globally
- In 2011 → 33.7 million global nonmedical users of synthetic amphetamine-type stimulants (primarily amphetamine and methamphetamine)

# PHARMACOKINETICS: Absorption and Distribution

- **Route of administration** has major effect on the pharmacokinetic characteristics of stimulants
- **Smoked** stimulants (such as cocaine base or methamphetamine) are rapidly absorbed through the lungs and probably reach the brain in **6 to 8 seconds**
- **Intravenous** administration produces peak brain uptake in **4 to 7 minutes**
- Greatest cocaine uptake occurs in the **striatum** (caudate, putamen, and nucleus accumbens)
- The rapid offset after rapid onset often is experienced as a “crash” by users of smoked or intravenous stimulants
- Heavy cocaine users have about 20% less brain cocaine uptake than do healthy nonusers
- Intranasal and oral stimulants have a slower absorption and onset of effect (30 to 45 minutes), a longer peak effect, and a more gradual decline from peak.

# Metabolism…

- **Cocaine:**

✓95% is metabolized by hydrolysis of **ester** bonds to **benzoylecgonine** (the primary urinary metabolite) and **ecgonine methyl ester** by the action of **carboxylesterases** in the liver and **butyrylcholinesterase** in the liver, plasma, brain, lung

✓Remaining 5% of cocaine is N-demethylated to **norcocaine** by CYP3A4

✓Norcocaine has some pharmacologic actions similar to those of cocaine and is hepatotoxic.

- **Amphetamines:**

✓Metabolized in the liver via three different pathways:

- **Deamination** to **inactive** metabolites,
- **Oxidation** to **norephedrine** and other active metabolites
- **Para-hydroxylation** to active metabolites
- Amphetamine itself is the initial metabolite of methamphetamine.

# Elimination:

- Stimulants and their metabolites are largely eliminated in the urine
- **Benzoylecgonine** is the cocaine metabolite found in highest concentration in urine for several days after cocaine use.
- **Benzoylecgonine,** NOT cocaine, is compound measured in routine urine drug tests for cocaine.
- GI absorption and urinary elimination of amphetamines are **HIGHLY pH dependent**
- Acidification of the GI tract or urine substantially **decreases absorption** and **increases excretion**,
- Conversely, alkalinization of the GI tract or urine **increases GI absorption** and **reduces excretion** to negligible levels.
- **This fact is exploited by drug users who take large doses of sodium bicarbonate to prolong the action of amphetamines and reduce the amount of drug present in the urine for detection by drug tests**

❖***Meth addict + UGI bleeding: think Alka Seltzer and check salicylate levels too!!***

# DRUG–DRUG INTERACTIONS…

- **Amphetamines:**

✓ Area of clinical concern is with other stimulants or with other medications that also enhance catecholamine activity

✓ **Overstimulation → cardiac arrhythmia, hypertension, seizure, cardiovascular collapse, and death**

✓ A major potential for interaction is with **MAOIs**

✓ Potent prescription stimulants, such as amphetamine and methamphetamine, **should not be used within 2 weeks of MAOI use**

✓ Stimulants should be used cautiously in conjunction with **tricyclic antidepressants**, many of which block presynaptic reuptake of catecholamines.

- **Cocaine:**

✓ Cocaine + alcohol → **cocaethylene**

✓ **Cocaethylene** action similar to, but less potent than, cocaine, with a longer half-life.

✓ Cocaethylene may contribute to more severe or longer-lasting toxic effects of cocaine when it is used along with alcohol

# Intoxication…

- **Initial effects:**

✓ Increased energy, alertness, and sociability

✓ Elation or euphoria

✓ Decreased fatigue, need for sleep, and appetite

- Intense pleasurable feeling has been described as a “total body orgasm”
- These effects may occur after:

✓ 5 to 20 mg of oral amphetamine, methamphetamine, or methylphenidate;

✓ 100 to 200 mg of oral cocaine = 40 to 100 mg of intranasal cocaine = 15 to 25 mg of IV or smoked cocaine

✓ Such single oral doses of stimulants **improve cognitive** and **psychomotor performance** in subjects whose performance has been impaired by fatigue, sleep deprivation, or alcohol, especially in tasks that require focused and sustained attention (vigilance)

# Intoxication…

- Stimulant effects often progress to include dysphoric effects:

✓ Anxiety
✓ Irritability
✓ Panic Attacks
✓ Interpersonal Sensitivity
✓ Hypervigilance
✓ Suspiciousness
✓ Paranoia
✓ Grandiosity
✓ Impaired Judgment
✓ Psychotic symptoms such as delusions and hallucinations

- 10% to 40% of stimulant users may have sleep disturbance and weight loss

✓ 25% may experience severe paranoia and/or hallucinations
✓ Proportion of stimulant users experiencing paranoia or psychotic symptoms varies with intensity and duration of use and degree of dependence and **has been as high as 100% in some studies**

# Psychotic behavior…

- Patients with stimulant-induced psychosis may closely resemble those with acute schizophrenia
- Both conditions share the presumed pathophysiology of excessive brain dopamine activity
- Cocaine-induced psychosis may differ from acute schizophrenic psychosis in being marked by **less** thought disorder and bizarre delusions and fewer negative symptoms such as alogia and inattention
- Stimulant-induced hallucinations may be auditory, visual, or somatosensory
- Tactile hallucinations are especially typical of stimulant psychosis and include the sensation of something (e.g., insects) crawling under the skin (“formication,” “cocaine bugs”).
- Parallel behavioral effects include restlessness, agitation, tremor, dyskinesia, and repetitive or stereotyped behaviors such as picking at the skin or foraging for drugs (“punding,” “hung-up activity”)
- Associated physiologic effects include tachycardia, pupil dilation, diaphoresis, and nausea, reflecting stimulation of the sympathetic nervous system.

# Chronic effects…

- Chronic cocaine or amphetamine abuse → cognitive impairment that may persist for at least several months of abstinence
- Most affected are visuomotor performance, attention, inhibitory control, and verbal memory.
- Several studies have found abnormalities of behavioral regulation and risk–reward decision making. This type of impairment is associated with lesions of the frontal cortex
- Chronic cocaine use is associated with decreased gray and white matter volumes in the frontal cortex of the brain
- Chronic amphetamine or methamphetamine use (either oral or intravenous) can cause a psychotic syndrome (with paranoia and hallucinations) that may persist for years after the last drug use, even in persons with no personal or family history of psychiatric disorder
- Methamphetamine-induced psychosis may be associated with focal perfusion deficits in the frontal, parietal, and temporal lobes of the cerebral cortex
- Psychotic flashbacks have been reported in methamphetamine abusers up to 2 years after their last drug use and often are precipitated by threatening experiences
- A persisting psychosis after cocaine use has not been reported, except in patients with an underlying psychiatric disorder (such as schizophrenia or bipolar disorder)

# Withdrawal…

- Cessation of stimulant use may result in a withdrawal syndrome that does not have prominent physiologic features and is not life threatening
- Withdrawal symptoms generally are the opposite of those associated with stimulant intoxication and include:

✓ Depressed Mood

✓ Anhedonia

✓ Fatigue

✓ Difficulty Concentrating

✓ Increased Total Sleep And Rapid Eye Movement Sleep Duration (But With Poor Sleep Quality)

✓ Increased Appetite.

- An early report of cocaine withdrawal among 30 outpatients described a complex triphasic syndrome lasting several days to weeks

- Human brain imaging studies suggest a modest increase in dopamine transporter binding during early cocaine withdrawal, followed by a decrease after 11 to 30 days of abstinence

# Cardiovascular system…

- Stimulants act acutely on the cardiovascular system both directly by:
- ✓ Increasing adrenergic activity at sympathetic nerve terminals
- ✓ Via the CNS to increase heart rate, blood pressure, and systemic vascular resistance
- Stimulant-induced increases in heart rate and blood pressure are significantly correlated with increases in plasma norepinephrine and epinephrine concentrations
- Cocaine-induced tachycardia is blocked by beta-adrenergic receptor blockade (propranolol) but not by muscarinic receptor blockade (atropine) further suggesting a sympathetic role.
- The resulting increase in myocardial oxygen demand, often accompanied by decreased coronary blood flow (from vasospasm and vasoconstriction), may cause acute myocardial infarction, even in young persons without atherosclerosis.
- This process may be promoted by cocaine-induced increases in circulating activated platelets, platelet aggregation, and thromboxane synthesis.

# Cardiovascular system…

- Cocaine use is a factor in about one-fourth of nonfatal heart attacks in persons younger than 45 years
- Frequent cocaine users are up to seven times more likely to have a nonfatal heart attack than are nonusers
- Postmortem studies suggest that chronic cocaine use is associated with higher levels of coronary atherosclerosis
- Cocaine use is associated with cardiac arrhythmias (such as ventricular tachycardia or fibrillation) and sudden death
- Chronic cocaine or amphetamine use is associated with **cardiomyopathy** and **myocarditis**
- Cocaine-associated cases of dilated cardiomyopathy and myocardial fibrosis may be due to direct toxic effects of high concentrations of circulating norepinephrine.
- Cocaine-associated myocarditis (whose acute symptoms may mimic myocardial infarction) may be a direct toxic effect of cocaine or a hypersensitivity effect.
- Autopsy series of current cocaine users have found myocarditis in up to 20%.

# Pulmonary…

- **Smoked cocaine produces both acute and chronic pulmonary toxicity**
- **Acute respiratory symptoms may develop in up to half of users within minutes to several hours after smoking.**
- **Symptoms include:**

✓ Productive cough
✓ Shortness of breath
✓ Chest pain
✓ Hemoptysis
✓ Exacerbation of asthma

- **More severe, and rarer, acute effects include:**

✓ Pulmonary edema,
✓ Pulmonary hemorrhage
✓ Pneumothorax and/or pneumomediastinum
✓ Thermal airway injury
✓ Pulmonary edema also has been reported after intravenous cocaine use

# Other systems…

- **Renal:**

✓ Stimulants have little direct toxic effect on the kidneys.

✓ Acute renal failure can occur as a result of renal ischemia or infarction, malignant hypertension, or rhabdomyolysis

✓ Release of myoglobin during rhabdomyolysis may cause renal tubular obstruction or direct myoglobin damage to renal tubules.

✓ Intrarenal arterial constriction with resulting renal medullary ischemia also may contribute to renal tubular damage

- **GI:**

✓ Cocaine reduces gastric motility and delays gastric emptying

✓ Major gastrointestinal effects of cocaine use are due to vasoconstriction and ischemia:

✓ Gastroduodenal ulceration and perforation,

✓ Intestinal infarction and perforation, and

✓ Ischemic colitis

✓ Concealing cocaine by swallowing large packets (“body packing”) may result in severe acute toxicity if the wrapping deteriorates and allows cocaine into the gastrointestinal tract

- Chronic changes in the endocrine and musculoskeletal system as well as the liver have also been noted

# Treatment of acute intoxication…

**TABLE 46-2 TREATMENT OF ACUTE STIMULANT INTOXICATION**

| CLINICAL PROBLEM | MODERATE SYNDROME | SEVERE SYNDROME |
|---|---|---|
| Anxiety; agitation | Provide reassurance; place in a quiet, nonthreatening environment. | Diazepam (10–30 mg PO, 2–10 mg IM, IV) or lorazepam (2–4 mg PO, IM, IV); may repeat every 1–3 h |
| Paranoia; psychosis | Place in a quiet, nonthreatening environment; benzodiazepines for sedation | High-potency antipsychotic (e.g., haloperidol) or second-generation antipsychotic |
| Hyperthermia | Monitor body temperature; place in a cool room. | If temperature >102°F (oral), use external cooling with cold water, ice packs, hypothermic blanket; if >106°F, use internal cooling; epigastric lavage with iced saline |
| Seizures | Diazepam (2–20 mg IV, <5 mg/min) or lorazepam (2–8 mg) | For status epilepticus: IV diazepam or phenytoin (15–20 mg/kg IV, <150 mg/min) or phenobarbital (25–50 mg IV) |
| Hypertension | Monitor blood pressure closely; benzodiazepines for sedation | If diastolic >120 for 15 min, give phentolamine (2–10 mg IV over 10 min). |
| Cardiac arrhythmia | Monitor electrocardiogram, vital signs; benzodiazepines for sedation | As appropriate for specific rhythm, based on advanced cardiac life support criteria |
| Myocardial infarction | Benzodiazepines for sedation; supplemental oxygen; sublingual nitroglycerin for vasodilation; aspirin for anticlotting; morphine for pain | Give nitrates IV for coronary artery dilation; phentolamine (2–10 mg IV) to control blood pressure; thrombolysis, angioplasty (if clot confirmed and no hemorrhage) |
| Rhabdomyolysis | IV hydration to maintain urine output >2 mL/kg/h | Force diuresis with aggressive intravenous hydration |
| Increased urinary drug excretion | Cranberry juice (8 oz TID) or ammonium chloride (500 mg PO every 3–4 h) until urine pH < 6.6 (if renal and hepatic function are normal) | Same as for moderate intoxication |
| Recent (few hours) oral drug ingestion | Activated charcoal orally or gastric lavage via nasogastric tube (if patient is awake and cooperative) | Gastric lavage via nasogastric tube after endotracheal intubation (if patient is unconscious) |

Table 46-2 Treatment of Acute Stimulant Intoxication

# Pharmacology of hallucinogens…

- Hallucinogens are chemically divergent substances primarily used for their potential to profoundly alter the processing of cognitive, perceptual, and emotional understanding of self and reality

**TABLE 14-1 MAJOR HALLUCINOGENS (PARTIAL LIST)**

| CLASS | CHEMICAL NAME | COMMON OR STREET NAME | SOURCE | DOSAGE | ROUTE | DURATION OF ACTION | MAJOR NEUROBIOLOGIC TARGET | NOTES |
|---|---|---|---|---|---|---|---|---|
| Indolealkylamines | LSD | LSD, acid, blotter | Synthetic | 50–200 µg | PO | 8–14 h | 5-$HT_{2A}$ partial agonist | Distributed on small squares of blotting paper, drops of liquid, gel caps, small pills |
| | Psilocybin | Magic mushrooms, shrooms | *Psilocybe cubensis*, *Psilocybe azurescens*, and many other subspecies; synthesis | 10–50 mg, 1–5-g dried mushroom; quite variable | PO | 4–8 h | 5-$HT_{2A}$ partial agonist | Psilocybin is converted in the body to psilocin, the actual active hallucinogen. Continued shamanic use in Mexico. Bruising of mushroom turns blue. |
| | DMT | DMT, yopo, cohoba, "businessman's trip" | *Psychotria viridis*, *Anadenanthera peregrina*, *Mimosa hostilis*, and many other natural sources; synthesis | 5–40 mg | Smoked, inhaled snuff | 30–60 min | 5-$HT_{2A}$ partial agonist | Continued Amazonian shamanic use |
| | Ibogaine | Ibogaine | *Tabernanthe iboga* | 200–300 mg | PO | 12+ h | Likely 5-$HT_{2A}$ partial agonist | Religious sacrament; long-acting metabolites may contribute to purported antiopioid withdrawal benefits. |
| Phenylalkylamines | 3,4,5-Trimethoxyphenethylamine | Mescaline, peyote, San Pedro | *Lophophora williamsii*, *Echinopsis pachanoi*, other cacti; synthesis | 200–500 mg, 10–20 g or 5–10 dried peyote buttons, 1-kg fresh *E. pachanoi* | PO | 6–12 h | 5-$HT_{2A}$ partial agonist | Religious sacrament |
| Entactogenic phenylalkylamines | 3,4-Methylenedioxymethamphetamine | MDMA, ecstasy, X, XTC, rolls, molly | Synthesis | 80–150 mg | PO | 4–6 h | 5-HT release and depletion | Mildly hallucinogenic at high doses |
| | 3,4-Methylenedioxyamphetamine | MDA, love drug, Adam | Synthesis | 75–160 mg | PO | 4–8 h | 5-HT release and depletion | |
| | 4-Bromo-2,5-dimethoxyphenethylamine | 2C-B, nexus | Synthesis | 5–30 mg | PO | 4–8 h | Unknown | |
| Other | Salvinorin A | Salvia, sally D, diviner's sage | *Salvia divinorum* | 250–750 mg (smoked), 2–10 g dried leaves (PO) | Smoked, PO | 30–60 min (smoked), 1–3 h (PO) | Kappa opioid selective agonist | Atypical hallucinogen; no longer found in the wild |

# Methods of use and abuse…

- No other recreational drug class (such as alcohol, opiates, or cannabis) enjoys a philosophical underpinning in Western society as does LSD
- For LSD users, the psychedelic experience is about **enhancing and expanding perception** in order to see the world "as it really is"
- More than 10,000 subjects received LSD (and other hallucinogens) from 1950 to the mid-1960s in controlled research settings, resulting in several thousand research papers
- During this time, the most prevalent substances were called "psychedelic drugs," used for:

✓ Enhancing creativity

✓ Deschematizing perceptual processes

✓ Inducting "experimental psychoses"

✓ Education of psychiatric staff through temporary self-experience of quasipsychotic states

✓ Experimental exploration of religious and mystical experiences

# Methods of use and abuse…

- Another important application was psycholytic therapy, where lower dosages (of LSD or psilocybin) were used to induce a dream-like state with affective and sensory activation to access unconscious material for therapeutic processing in psychoanalytic settings
- These therapeutic approaches were later abandoned, not for reasons of safety or lack of efficacy, but because of criminalization of the substances.
- Currently, there is renewed interest in **psilocybin** and **LSD** as experimental tools for elucidating neural mechanisms of consciousness for the treatment of cluster headache and in psychotherapy with the terminally ill
- Beyond a few experimental applications, no clinical use of DMT, mescaline, or Salvorinum A (Salvia) has been documented
- Recent studies of the psychotherapeutic utility of MDMA report significant clinical improvement in double-blind, placebo-controlled trials of MDMA-assisted psychotherapy for patients with PTSD

# Historical features…

- Psychoactive substances derived from plant materials have been used ritualistically for millennia
- Hallucinogens were primarily used for religious and shamanic purposes
- Hallucinogens play a prominent role in the cultures of Mesoamerican people
- **Psilocybin**-containing mushrooms were originally employed as shamanic sacraments by some native tribes of Mexico
- ***Ayahuasca*** remains an important spiritual medicine of many native people of the Amazon basin
- **Peyote** cactus containing the hallucinogen **mescaline**, has been venerated for over 3,000 years by the indigenous ethnic groups of Northern Mexico
- **Mescaline** is the sacrament of the Native American Church (NAC) in the United States and Canada, the largest faith among native people of North America with some 500,000 adherents

# Epidemiology…

- The 2010 National Survey on Drug Use and Health (NSDUH) estimated that almost 37.5 million Americans (14.8%) over age 12 ingested a hallucinogen at least once in their lifetime
- LSD is still the most widely used hallucinogenic drug; 23.3 million Americans used LSD at least once in their lifetime
- Since the 1970s, there is no decline in its use, especially in the United States and central Europe
- ***Psilocybe*** mushrooms appear to be the most common hallucinogen consumed in the among new hallucinogen users
- The mescaline-containing peyote cactus plant use is protected by the American Indian Religious Freedom Act of 1994 and is almost solely consumed in religious prayer services of the NAC
- ***Salvia divinorum*** is still legal in much of the United States, and an estimated 1.8 million people in the United States have tried this plant

# Subjective effects…

**TABLE 14-2 HALLUCINOGEN[a] INTOXICATION MAY INCLUDE A CLUSTER OF THE FOLLOWING**

| PHYSICAL EFFECTS[b] | PSYCHOLOGICAL EFFECTS |
|---|---|
| **Typical (mild to very mild):** | **Typical:** |
| Tachycardia | Intensification and lability of affect with euphoria, anxiety, depression, and/or cathartic expressions |
| Palpitation | Dream-like state |
| Slight hypertension or hypotension | Sensory activation with illusion, pseudohallucination,[c] hallucination, and/or synesthesia |
| Diaphoresis | Altered experience of time and space |
| Slight hyperthermia | Altered body image |
| Motor incoordination | Increased suggestibility |
| Tremor | Lassitude/indifference/detachment |
| Hyperreflexia | Acute cognitive alterations with loosening of association, inability for goal-directed thinking, and memory disturbance |
| Altered neuroendocrine functioning | **"Positive":** |
| **Typical (mild to strong):** | Sense of perceiving deeper layers of the world, oneself, and others ("consciousness expansion") |
| Mydriasis | Mystical experience |
| Arousal | Sense of profound discovery/healing |
| Insomnia | **"Negative":** |
| **Occasional:** | Psychosomatic complaint |
| Nausea | Impaired judgment |
| Vomiting | Derealization |
| Diarrhea | Depersonalization |
| Blurred vision | Megalomania |
| Nystagmus | Impulsivity |
| Piloerection | Odd behavior |
| Salivation | Paranoid ideation |
| | Suicidal ideation |

# Mechanisms of action…

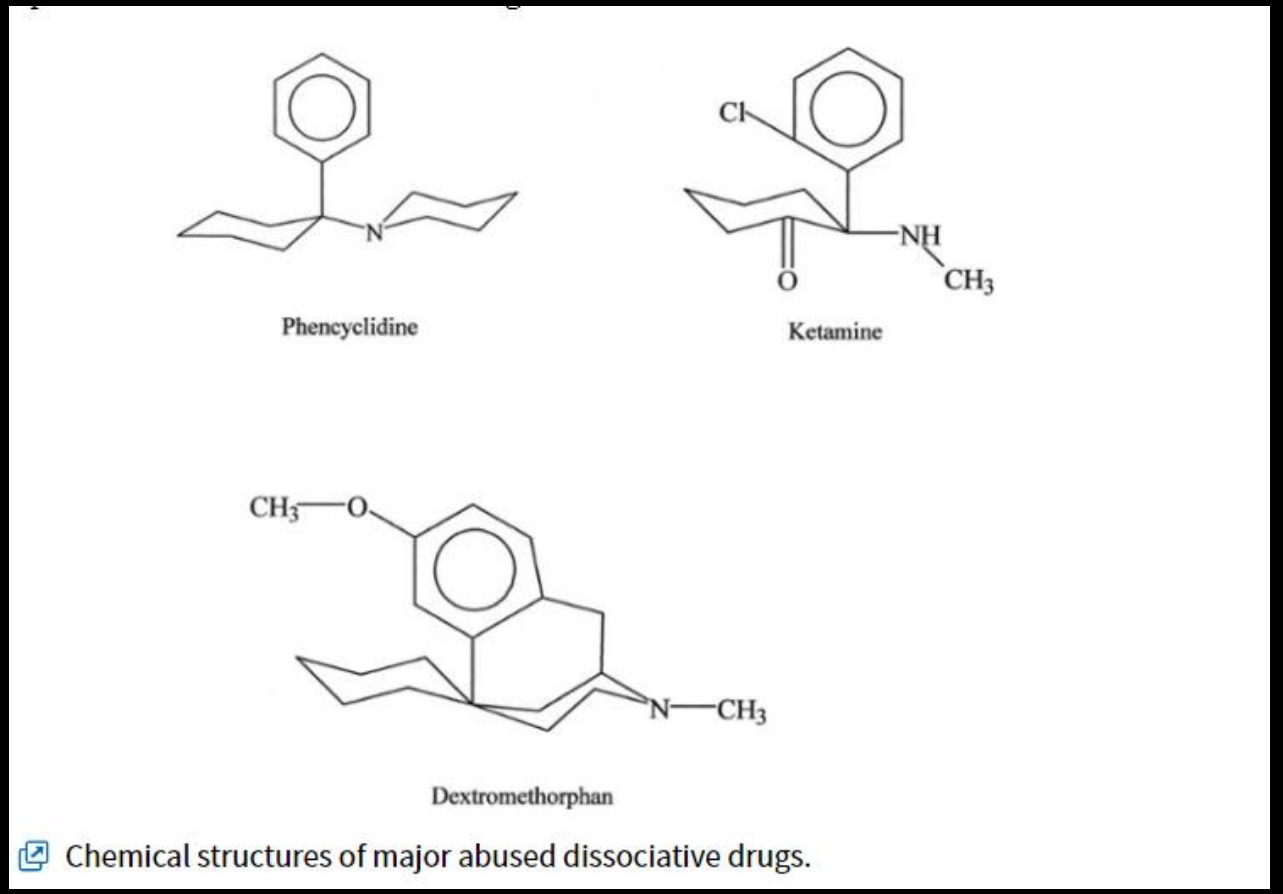
- Hallucinogens exert an activating effect on parts of the CNS due to their **agonist** properties at **serotonergic, adrenergic,** and **dopaminergic** neurotransmitter-modulated brain systems
- The serotonergic system appears to be especially affected
- The classical hallucinogens (like **LSD, psilocybin, DMT**, and **mescaline**) have high affinity for **5-HT receptors**
- **The 5-HT2A receptor** appears to be the primary site of action
- Daily administration of LSD and other hallucinogens selectively **decreases** 5-HT2 receptor density in rat brain by down-regulation
- Hallucinogens **enhance** glutamatergic transmission in the cortex

# Relative addiction liability…

- Use of hallucinogens very **rarely** meets the ICD-10 or DSM-5 criteria for a substance use disorder
- Studies in the United States suggest **that less than 3%** of past-year hallucinogen users develop dependence, with another **20% developing abuse**
- **MDMA** shares some pharmacologic properties with the amphetamines and, therefore, has some reinforcing efficacy but significantly less than methamphetamine and cocaine (this will be discussed more in Club Drugs)

# A brief word on the Dissociatives…

- Dissociatives are antagonists of **(NMDA)** receptor subtype of glutamate neurotransmitter system




Chemical structures of major abused dissociative drugs.

# Methods of use and abuse…

- **Ketamine (Schedule III):**

✓ Available as a sterile solution for use in general anesthesia in both animals and humans

✓ Schedule III substance

✓ In medical settings, it is injected intravenously or intramuscularly in doses of 0.1 to 1.0 mg/kg, depending on its clinical use

✓ Also effective when insufflated, smoked, or taken orally.

✓ It is abused by various routes in different doses. Doses of ketamine as large as 900 to 1,000 mg given intravenously or intramuscularly are lethal

- **Phencyclidine (PCP, Schedule II)**

✓ No longer available as a medical commercial preparation approved by the FDA

✓ Initially developed as a dissociative anesthetic but withdrawn because of emergence delirium

✓**Dextromethorphan**

✓ Legal DXM preparations are administered orally and are not controlled, but sales restriction may be age-related

✓ Capsules, tablets, lozenges, or solutions of DXM hydrobromide are available alone or in combination with many other substances as cough, cold, and flu relief preparations

✓ The usual antitussive dosage for adults is 10 to 20 mg every 4 hours or 30 mg every 6 to 8 hours, not to exceed 120 mg daily

# Addiction liability and toxicity …

- **Why these substances are reinforcing is difficult to understand (as they are not reported by users as eliciting a state of pure euphoria), except in the context of individuals who wish to experience the feelings of floating in space, dissociation, sensory isolation, mental distortions, and so forth that dissociatives provide**
- **Dissociatives are self-administered by animals under testing conditions:**

✓ Rhesus monkeys self-administer PCP, and social stimulation among monkeys in adjoining cages enhances reinforcing strength of PCP

- **NMDA antagonists have remarkable effects on brain neurons including toxicity**
- **Such neurotoxic changes are reduced by pretreatment with benzodiazepines**

# PCP, Ketamine, and DXM intoxication…

**TABLE 46-3 ACUTE PSYCHOLOGICAL AND BEHAVIORAL EFFECTS OF INTOXICATION WITH LSD, MARIJUANA, PCP, OR MDMA**

| EFFECTS | LSD | MARIJUANA | PHENCYCLIDINE | MDMA |
|---|---|---|---|---|
| "Abnormal" overall behavior and appearance | XX | X | XXX | X |
| Disoriented to person, place, time, or situation | XX | None | XX | None |
| Impaired memory | X | XX | XX | X |
| Inappropriate affect | XXX | X | XXX | XX |
| Depressed mood | XX | X | XX | X |
| Overly elated mood | XXX | XX | XX | XXX |
| Confused, disorganized thinking | XX | XX | XXX | X |
| Hallucinations | XXX | X | XXX | X |
| Delusions | X/XXX | XXX | XX | ? |
| Bizarre behavior | XXX | X | XXX | ? |
| Suicidal or danger to self | XX | XX | XX | ? |
| Homicidal or danger to others | XX | X | XXX | X |
| Poor judgment | X/XXX | XXX | XXX | XX |

# Psychological and behavioral effects of DXM intoxication…

**TABLE 46-5 PSYCHOLOGICAL AND BEHAVIORAL EFFECTS OF DXM INTOXICATION**

| PLATEAU | DOSE (mg) | BEHAVIORAL EFFECTS |
|---|---|---|
| First | 100–200 | Mild stimulation |
| Second | 200–400 | Euphoria and hallucinations<br>Distorted visual perceptions |
| Third | 300–600 | Loss of motor coordination<br>Disorientation |
| Fourth | 500–1,500 | Depersonalization<br>Dissociative sedation |
| Toxicity | Variable | Hyperexcitability, lethargy, ataxia, diaphoresis, hypertension, and nystagmus |

Adapted from Schwartz RH. Adolescent abuse of dextromethorphan. *Clin Pediatr* 2005;44(7):565–568.

# Management of intoxication…

- **3 stages of dissociative anesthetic intoxication:**

✓ **Stage I-** conscious with psychological effects but at most mild physiologic effects:

➢ May see nystagmus (especially horizontal) tachycardia, increased BP, ataxia, dysarthria, numbness, increased salivation, and hyperreflexia

✓ **Stage II**-stuporous or in a light coma, yet responsive to pain

✓ **Stage III**-comatose and unresponsive to pain

➢ Stage II and III associated with severe medical effects including hypertension, stroke, cardiac failure, seizures, rhabdomyolysis, acute renal failure, and death

- **Management of the psychological and behavioral effects of dissociative anesthetics is largely supportive and aimed at controlling or reversing specific signs and symptoms**

# Procedures for managing acute PCP intoxication…

**TABLE 46-6 PROCEDURES FOR MANAGING ACUTE PCP INTOXICATION**

| PROCEDURE | STAGE I | STAGE II | STAGE III |
|---|---|---|---|
| Monitor level of consciousness. | Yes | Yes | Yes |
| Monitor vital signs. | Yes | Yes | Yes |
| Collect blood and urine samples for toxicology. | Yes | Yes | Yes |
| Lower body temperature. | Loosen clothing | Sponging, ice packs | Sponging, ice packs |
| Catheterize urinary bladder. | No | Yes | Yes |
| Gastric lavage | No | Sometimes | Yes |
| Oral suctioning | Rarely | Gently, as needed | Yes |
| Tracheal suctioning | No | Sometimes | Yes |
| Insert nasogastric tube. | No | Sometimes | Yes |
| Neuromuscular blockade and mechanical ventilation | No | Sometimes | Sometimes |

# Inhalant intoxication…

- Inhalants are a chemically heterogeneous group of **volatile hydrocarbons**
- Found in **glue, fuel, paint, aerosol propellant**, and other products
- Inhalant intoxication produces initial euphoria or "rush" followed by lightheadedness excitability and perceptual changes
- Significant mood changes or cognitive impairment is rare
- Higher doses or more prolonged exposure may cause dizziness, slurred speech, and motor incoordination, followed by drowsiness and headache
- **Intoxicated users rarely seek medical attention** in part because exposure tends to be self-limited and the duration of effects from a single exposure is usually only a few minutes
- There is no specific treatment for inhalant intoxication→Initiate supportive care

# Club drugs…

- **Club drugs** are a pharmacologically heterogeneous group of drugs associated with the youth subculture that revolves around late night dance parties known as “raves” or “trances”
- Illicit use of these substances was popularized in this setting because of their perceived ability to enhance the sensory experience and allow for long periods of dancing to repetitive music
- **Common club drugs include:**

✓ MDMA (“Ecstasy”)

✓ GHB

✓ Flunitrazepam (Rohypnol, “roofies”, or “date rape drug”)

# MDMA: (3,4-Methylenedioxymethamphetamine)…

- **MDMA = stimulant + mild hallucinogen**
- Known as an **entactogen**

✓ Low-to-moderate oral doses of MDMA (50 to 150 mg) produce an **intense** initial effect lasting for 30 to 45 minutes, including:

✓ Increased wakefulness and energy

✓ Euphoria

✓ Increased sexual desire and satisfaction

✓ Heightened sensory perception

✓ Increased sociability, and empathy and sense of closeness to others

- This is followed by several hours of less intense experience
- Users start to “come down” 3 to 6 hours after ingestion

# MDMA…

- **Undesired effects with repeated use or higher dose include:**

✓ Hyperactivity

✓ Fatigue

✓ Insomnia

✓ Anxiety

✓ Agitation

✓ Impaired decision making

✓ Hallucinations

✓ Depersonalization and derealization

✓ Bizarre or reckless behavior

# MDMA intoxication treatment…

- **Initial treatment is the same as for hallucinogen intoxication:**

✓ Placement in a quiet, reassuring environment, with observation.

✓ Physical restraints are contraindicated.

✓ Severe or persisting symptoms may require benzodiazepines.

✓ **Antipsychotics should be avoided**

- **MDMA is not detected by routine drug screens, which may be positive for amphetamines (products of MDMA metabolism)**
- **Gastric lavage with activated charcoal may be helpful within the 1st hour after ingestion**
- **Induced emesis is not recommended because of the risk of CNS depression**

# Acute physical effects of MDMA...

- **At typical doses resemble those of a stimulant:**
- Jaw clenching
- Bruxism
- Restlessness
- Insomnia
- Ataxia
- Decreased appetite
- Dry mouth
- Dilated pupils

# More physical effects of MDMA…

- Increased heart rate and blood pressure noted
- Treatment involves close monitoring of serum creatinine kinase levels (to detect rhabdomyolysis) and reversal of hyperthermia
- **Benzodiazepines** are preferred to antipsychotics
- **Dantrolene** (1 mg/kg iv) may be helpful.
- Acute cardiovascular toxicity is treated with an adrenergic antagonist like **phentolamine** (Regitine), combined with a vasodilator if needed to control BP
- A pure *β*-adrenergic blocker should be avoided (due to risk of unopposed alpha)
- Acute toxicity can result from hyponatremia: Initial treatment is fluid restriction.
- Profound hyponatremia has been treated with hypertonic saline solution.
- There is no withdrawal syndrome that requires specific pharmacologic treatment.

# γ-HYDROXYBUTYRATE (GHB or “liquid Ecstasy”)

- **Naturally occurring metabolite of (GABA)**
- **Approved for the treatment of narcolepsy.**
- **Popular because:**

✓ Reputed aphrodisiac

✓ Disinhibitory and amnesic effects

✓ Short duration of action

✓ Absence of “hangover”

- **Nondetectability by standard drug screens**
- **GHB is taken orally as a liquid, is rapidly absorbed from the gastrointestinal tract, and readily crosses the blood–brain barrier**
- **Effects begin within 15 minutes of ingestion and last 2 to 4 hours**
- **Signs and symptoms resemble those of most CNS depressants**
- **GHB is not detected by routine drug toxicology assays, and there is no known antidote**

# More GHB effects…

- Increased heart rate and blood pressure.
- Doses >200 mg are associated with life-threatening toxicities
- Treatment involves close monitoring of serum creatinine kinase levels (to detect rhabdomyolysis) and reversal of hyperthermia
- Benzodiazepines are preferred to antipsychotics
- Dantrolene (1 mg/kg iv) may be helpful
- Acute cardiovascular toxicity is treated with an adrenergic antagonist, combined with a vasodilator if needed to control blood pressure
- A pure β-blocker is **contraindicated**
- Acute toxicity can result from hyponatremia
- Initial treatment is fluid restriction
- Profound hyponatremia has been treated with hypertonic saline solution.
- There is no withdrawal syndrome that requires specific pharmacologic treatment.

# GHB effects…

- **Low dose** GHB produces:

✓Relaxation

✓Euphoria

✓Sedation

✓Disinhibition

✓Sociability, and anterograde amnesia

- **Higher doses produce somnolence, confusion, and hallucinations**
- **Unintended overdose may occur because of GHB's very steep dose–response curve and the great variability in potency of street preparations**
- **Effects are prolonged and intensified when taken with other CNS depressants**

# More GHB effects…

- **Low-to-moderate oral doses cause:**

✓ Headache

✓ Dizziness

✓ Ataxia

✓ Hypotonia

✓ Vomiting

- **Moderate to higher doses:**

✓ Incontinence

✓ Myoclonic movements

✓ Bradycardia

✓ Hypotension

✓ Hypothermia

✓ Generalized tonic–clonic seizures

✓ Coma

# GHB withdrawal…

- **Cessation of chronic GHB use leads to a discrete withdrawal syndrome resembling that of severe sedative–hypnotic withdrawal:**

✓Anxiety,

✓Restlessness

✓Insomnia

✓Tremor

✓Nystagmus

✓Tachycardia

✓Hypertension

# Progression of GHB withdrawal…

- Withdrawal symptoms usually appear 2 to 12 hours after the last dose
- Mild symptoms usually resolve gradually over 1 to 2 weeks
- More severe withdrawal may cause:

✓ Delirium with hallucinations

✓ Psychosis

✓ Agitation

✓ Autonomic instability

✓ Death

✓ Withdrawal can usually be managed with benzodiazepines or baclofen

# Flunitrazepam…

- **AKA: Rohypnol or ‘roofies”**
- **Potent, fast-acting benzodiazepine difficult to detect with routine UDS**
- **Illegal in the United States because of association with date rape.**
- **Intoxication is characterized by:**

✓Sedation
✓Disinhibition
✓Anterograde amnesia
✓Confusion
✓Ataxia
✓Bradycardia
✓Hypotension
✓Respiratory depression

# More Flunitrazepam…

- Treatment is supportive: activated charcoal and gastric lavage may be helpful. Severe respiratory depression or circulatory compromise can be treated with flumazenil.
- Flumazenil precipitates acute withdrawal in patients who are physically dependent on benzodiazepines and lowers their seizure threshold
- Flumazenil has a short half-life, making repeated dosing necessary to avoid resedation.
- Symptoms of withdrawal include anxiety, restlessness, tremors, headache, insomnia, and paresthesias
- Treatment is similar to benzodiazepine OD

# The kitchen sink: “Bath salts”…

- Legal alternatives to classical illicit drugs like cocaine, methamphetamine, and 3,4-methylenedioxymethamphetamine (MDMA)
- Not detected by routine toxicology screens
- Initial dose enhances mood and increases alertness
- What you see in ED and EPS: agitation, combative behavior, psychosis, tachycardia, and hyperthermia
- Synthetic derivatives of **cathinone**, an amphetamine-like stimulant found in the **khat** plant ***Catha edulis***
- The three most popular bath salts constituents are 4-methylmethcathinone (**mephedrone**), 3,4-methylenedioxymethcathinone (**methylone**), and 3,4-methylenedioxypyrovalerone (**MDPV**)
- MDPV is the chief substance detected in blood and urine from patients hospitalized for bath salts overdose in the united states, while mephedrone is more commonly associated with adverse clinical outcomes in Europe
- Owing to public health risk, the governments of many countries have made mephedrone, methylone, and MDPV illegal, but are quickly replaced by other substituted cathinones
- **Mephedrone** and **methylone** exert amphetamine-like actions at transporters for NE, DA, 5-HT
- MDPV is structurally distinct from other cathinones and produces a cocaine-like blockade of transporters for DA and NE, thereby inhibiting the uptake of these transmitters.
- Treatment is primarily **supportive**, with benzodiazepines for agitation and excessive sympathetic stimulation, and aggressive cooling for severe hyperthermia.

# The kitchen sink: Kratom…

- Derived from ***Mitragyna speciosa****, a* tropical evergreen tree in the coffee family native to southea
- Used in traditional medicine since at least the 19th century
- Has opioid properties and some stimulant-like effects
- Use: managing chronic pain, treating opioid withdrawal, high abuse potential
- Onset of effects typically begins within 5 to 10 minutes and lasts 2 to 5 hours.
- Common minor side effects may include nausea, vomiting, and constipation
- More severe side effects may include respiratory depression, seizure, addiction, and psychosis
- Other side effects may include elevated HR and BP, trouble sleeping, and, rarely, liver toxicity
- When use is stopped, withdrawal symptoms may occur
- Deaths have occurred with kratom, both by itself and mixed with other substances
- Between 2011 and 2017, 44 kratom-related deaths occurred, with one involving kratom alone.
- Nine kratom-related deaths occurred in Sweden in 2011 and 2012, all involving a mixture of kratom with other opioids
- Treatment is supportive
- **Naloxone does NOT reverse kratom overdose**

# The kitchen sink: Flakka…

- α-Pyrrolidinopentiophenone (PVP), a Psychostimulant
- Acts as a norepinephrine-dopamine reuptake inhibitor
- Frequently seen in South Florida, name derived from Spanish word ***flaca,*** slang for a “thin, attractive young lady”
- Can cause hyperstimulation, paranoia, and hallucinations
- Flakka has been reported to be the cause, or a significant contributory cause, of death in suicides and overdoses caused by combinations of drugs
- Flakka has also been linked to at least one death with pulmonary edema and moderately advanced atherosclerotic coronary disease when it was combined with **pentedrone** (a cathinone stimulant)
- Treatment for acute intoxication similar to that of other stimulants

# Questions you may see again…


# What are the EEG patterns observed in cocaine abstinence?

- A. Epileptiform activity
- B. Lower amplitude in all phases
- C. Decreased delta and alpha
- D. Decreased delta and alpha and increased alpha and beta
- E. No significant changes present

# Answer: D. Decreased delta and alpha and increased alpha and beta

Delta and theta wave are low frequency and reflect a state of somnolence and drowsiness. Higher frequency waves in alpha and beta are associated with alertness and awareness. In contrast, during chronic cocaine use more than normal amounts of persistent beta activity is present and associated with agitation, tenseness and fear. Continued abstinence results in a gradual return to normal of all EEG activity. Epileptiform EEG activity or seizures are not commonly associated with cocaine or stimulant withdrawal.

# Which is the only medication FDA approved for use in the maintenance treatment in cocaine use disorder?

- A. Desipramine
- B. Fluoxetine
- C. Methylphenidate
- D. Gabapentin
- E. There are no medications  FDA approved

# ANSWER: E. There are no medications  FDA approved

- TCA’s have been studied, especially **desipramine**, but studies have yielded mixed results

In patients who abuse stimulants, what is the yearly percent of high schoolers who abuse methylphenidate on an annual basis?

- A. 1%
- B. 4%
- C.10%
- D.20%
- E. 30%

# B. 4%

- Most studies show a range of 2%-5%

Which of the following drugs when combined with cocaine makes it the most difficult for cocaine to be eliminated from the body?

- A. Marijuana
- B. Methamphetamine
- C. Nicotine
- D. Codeine
- E. Alcohol

# ANSWER: E. Alcohol

- Cocaine + alcohol → **cocaethylene** by transesterification
- **Cocaethylene:**

✓Less potent than cocaine

✓Longer half-life than cocaine

✓More severe and longer lasting toxic effects than cocaine

✓Risk of sudden death is 18 times greater when alcohol and cocaine are used together

In patients who abuse stimulants, which of the following age groups is most likely to abuse stimulants?

- A. Teenagers aged 13-17
- B. Young adults aged 18-25
- C. Middle-aged adults ages 26-35
- D. Older adults aged 36-40
- E. Elderly individuals older than age 55

# ANSWER:B. Young adults aged 18-25

- Of course!!!

A 19-year-old patient presents to the emergency department after "partying with friends" at a local nightclub. He admits to using LSD with his friends. The following are symptoms expected in hallucinogen-induced mental disorders EXCEPT?

- A. Visual distortions and frank hallucinations
- B. Panic attacks
- C. Dependence and withdrawal symptoms
- D. Flashbacks, and depression especially in chronic users
- E. A state of paranoia

# ANSWER:C. Dependence and withdrawal symptoms

- **Visual distortions and frank hallucinations are common with hallucinogen usage**
- **All hallucinogens are associated with drug-induced panic reactions that feature panic, paranoia, and even delusional states in addition to the hallucinations**
- **Hallucinogen use is NOT associated with dependence or withdrawal symptoms**
- **A few hallucinogen users experience chronic reactions, involving:**

✓ Prolonged psychotic reactions

✓ Depression, which can be life-threatening

✓ Flashbacks

✓ Exacerbations of pre-existing psychiatric illnesses

GHB is a club drug that is a member of the sedative hypnotic class. Which of the following characterizes the pharmacokinetic profile of GHP?

- A. High doses of GHB stimulate dopamine release
- B. GHB has a low overdose risk
- C. GHB acts on dopamine receptors in the brain
- D. GHB has a long half-life and can be detected in the urine for 2 to 3 days after use
- E. GHB is metabolized in the liver

# ANSWER: E. GHB is metabolized in the liver

- GHB acts at two receptor sites in the brain:

✓GABA-B receptor

✓Specific GHB receptors

- Low doses of GHB stimulate release of dopamine
- Higher doses of GHB inhibit release of dopamine
- GHB has a half-life of 30 to 60 minutes and only 5% is excreted by the kidneys
- 95% of GHB is metabolized in the liver


The End