Substance Abuse
CNS stimulants

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Stimulants

Stimulants are substances that induce a number of characteristic CNS effects include alertness with increased vigilance, a sense of well-being, and euphoria

- Examples include:
  - Amphetamines: Methamphetamine, Methylphenidate (Ritalin), MDMA (3,4-methylenedioxymethamphetamine) Ecstasy.
  - Cocaine
  - Caffeine
  - Nicotine

Clinical Presentation

- Elevated mood, increased alertness, increased energy, insomnia, and anorexia are all common symptoms
- Chest pain, tachypnea, nausea, abdominal pain, and headaches may also be associated with it
- Long-term stimulant use may result in tolerance, weight loss, and potential adverse psychiatric symptoms such as irritability, aggression, impulsivity, hallucinations, and delusion
- MDMA intoxication may include restlessness, anxiety, trismus, fever, and impaired memory

Physical Exam

- Increases in blood pressure, heart rate, and pupillary dilation
- Hyperthermia, hyponatremia, arrhythmias, myocardial infarction, and hemorrhagic stroke (from excessive dopaminergic discharge, dyskinesias)
- MDMA short-term effects include dehydration, hyperthermia, and heat stroke.
- Overdoses can simulate methamphetamine overdose.
- Rhabdomyolysis and acute renal failure have also been reported.

Mental Status

- Attitude - Tense, anxious, restless, agitated
- Psychomotor activity - Increased; dyskinesia
- Mood/affect - Good/euphoric or irritable and labile
- Speech - Talkative
- Thought processes - Flight of ideas; tangentially
- Thought content - Paranoia; auditory, visual, and tactile hallucinations; grandiosity; homicidal ideation
- Insight or judgment - Impaired
- Orientation - Confusion, delirium
- Memory - small doses may improve alertness and task performance, the heavy use associated with stimulant abuse can be detrimental to memory

Withdrawal

- Behavior - Sedated
- Psychomotor activity - Decreased
- Mood or affect - Depressed or irritable
- Speech - Decreased production
- Thought processes or content - Linear, at times with suicidal ideation and drug craving. Homicidal ideation; paranoia
- Insight or judgment - Variable
- Orientation - May be normal or close to normal
- Memory - Likely impaired due to sleep deprivation, associated fatigue, decreased attention and irritability

Method of Abuse

- Methamphetamine is swallowed, snorted, injected, or smoked.
- Smokable form of methamphetamine, is a large, usually clear crystal of high purity that is smoked, like crack, in a glass pipe.
- Amphetamines and methylphenidate are usually swallowed in pill form.

Cocaine

- Cocaine is a tropane ester alkaloid found in leaves of the *Erythroxylum coca* plant, a bush that grows in South America.
- Use is most prevalent in North America, Central and South America and in Western and Central Europe
- Cocaine users are at high risk for developing a cocaine use disorder.

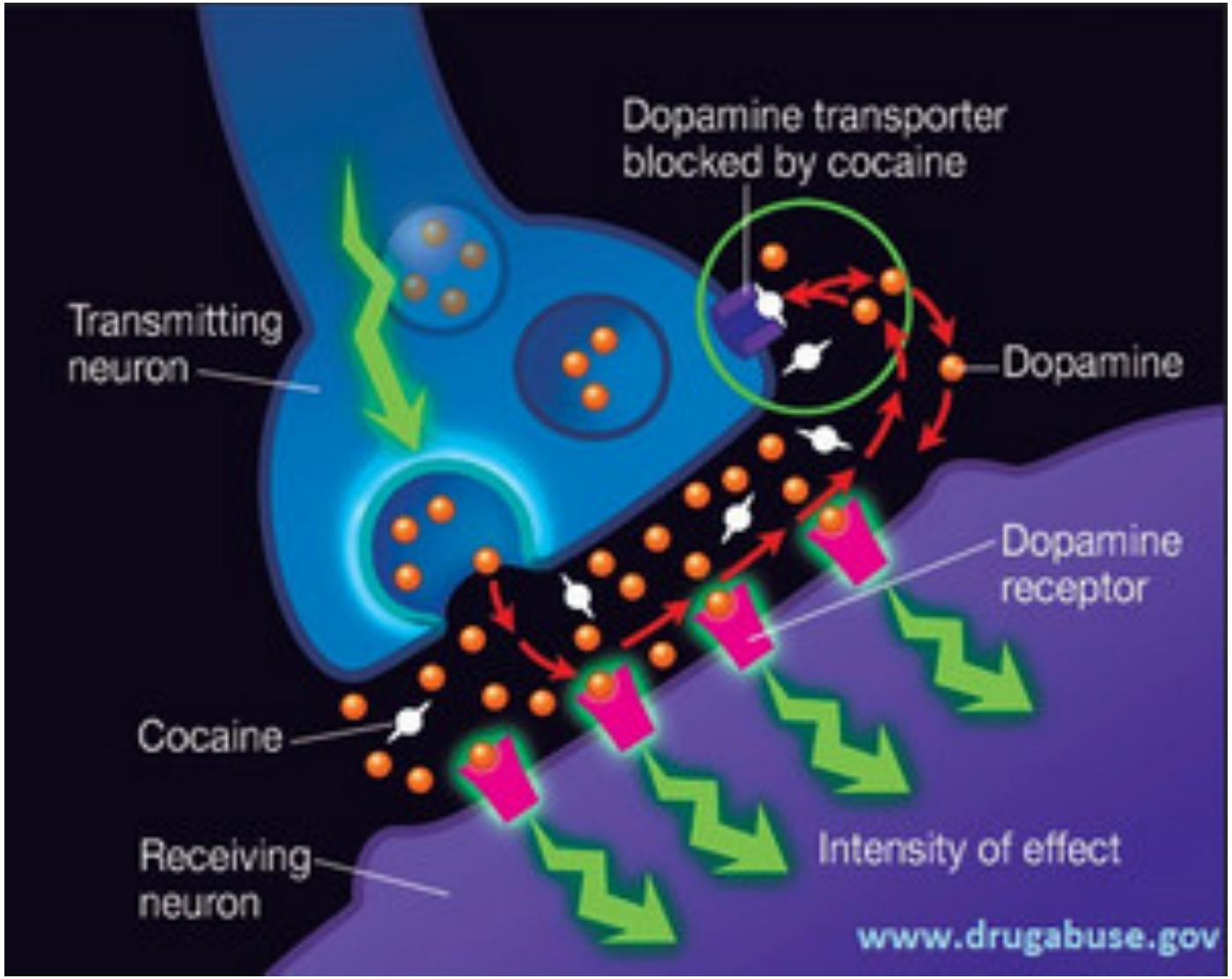
Cocaine

- Cocaine forms: same molecule and exert same pharmacological actions. Differ in physical properties.

1. **Cocaine base ("crack," "freebase")** can be smoked, has a relatively low melting point (98ºC) and vaporizes before substantial pyrolytic destruction. Difficult to dissolve for injection, relatively insoluble in water.
2. **Cocaine salt**, cannot be smoked, it melts at 195ºC, with substantial breakdown of cocaine molecule before vaporization. Readily injected or insufflated ("snorted") through the nose; highly water soluble, easy to dissolve for injection purposes and facilitates absorption across mucus membranes.

Mechanism of Action

- Cocaine enhances monoamine neurotransmitter (dopamine, norepinephrine, and serotonin) activity in the CNS and peripheral nervous systems by blocking the presynaptic reuptake pumps for these neurotransmitters .
- Cocaine's positive psychological effects and abuse liability are considered to be due to its enhancement of brain **dopamine** activity, especially in the corticomesolimbic dopamine reward circuit.
- Cocaine is unique among stimulant drugs in having a second action of blocking voltage-gated membrane sodium ion channels. This action accounts for **its local anesthetic effect**, and may contribute to cardiac arrhythmias


Dopamine transporter
blocked by cocaine
Transmitting
neuron
Dopamine
Dopamine
receptor
Cocaine
Receiving
neuron
Intensity of effect
www.drugabuse.gov

Routes of Admnisitration

Route	Onset	Peak Effect (min)	Duration (min)	Half-Life (min)
Inhalation	7 s	1-5	20	40-60
Intravenous	15 s	3-5	20-30	40-60
Nasal	3 min	15	45-90	60-90
Oral	10 min	60	60	60-90

Street dealers generally dilute cocaine with other substances (such as cornstarch, talcum powder, or sugar), with active drugs (such as procaine, a chemical that produces local anesthesia), or with other stimulants (such as amphetamines).

Cocaine

- **Distribution** — rapidly taken up into most body organs; heart, kidney, adrenal glands, and liver. Cocaine (and its metabolites) appears in blood, urine, hair , sweat, saliva, and breast milk and placenta
- **Metabolism** — 95 percent metabolized by hydrolysis to benzoylecgonine and to ecgonine methylester in the liver, plasma, brain, lung, and other tissues
- **Elimination** —Cocaine is largely eliminated in the urine. Benzoylecgonine is the metabolite found in highest concentration in urine. That is measured in urine drug tests for cocaine

Cocaine Intoxication

- **CVS** :arterial vasoconstriction and enhanced thrombus formation, tachycardia, hypertension, coronary vasoconstriction in a dose-dependent fashion, cardiac ischemia. At high blood concentrations, cocaine's negative inotropic effects may cause acute depression of left ventricular function and heart failure. Most common CVS presentation: Chest pain.
- **CNS**: psychomotor agitation, seizures, coma, headache, intracranial hemorrhage, stroke, and focal neurologic symptoms. euphoria is associated with transient increases in EEG activity followed by longer-lasting increases in activity .

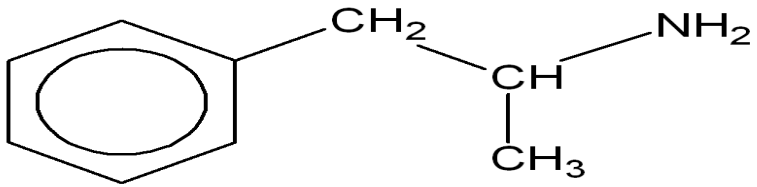
- **Respiratory**: Angioedema and pharyngeal burns (smoked) Injury to the upper and lower airway occurs primarily from inhalation. Pneumothorax, pneumomediastinum, and pneumopericardium (inhalational use/ intranasal), exacerbations of reversible airway disease and bronchospasm, shortness of breath, hemoptysis, wheezing,
- **Gastrointestinal system:** reduces salivary secretions, gastric motility and delays gastric emptying. Induced vasoconstriction and ischemia may result in gastrointestinal ulceration, infarction, perforation, and ischemic colitis
- **Skin:** Cocaine use is associated pseudovasculitic lesions that may mimic rheumatologic syndromes such as Wegener's granulomatosis, necrotizing vasculitis.

Cocaine

- Management:
  - Supportive care: ABC of Medicine
  - Care for cardiac complications, arrhythmia, hypertension, hyperthermia, convulsion, agitation, irritability, nutritional status
  - No definitive role for antidotes

Amphetamines

- Phenethylamines' (including amphetamines) Stimulation of alpha and beta adrenergic receptors is primarily responsible for the acute effects of amphetamines, which include hyper-alertness, hypertension, tachycardia, mydriasis, and diaphoresis (sympathomimetic toxic syndrome)



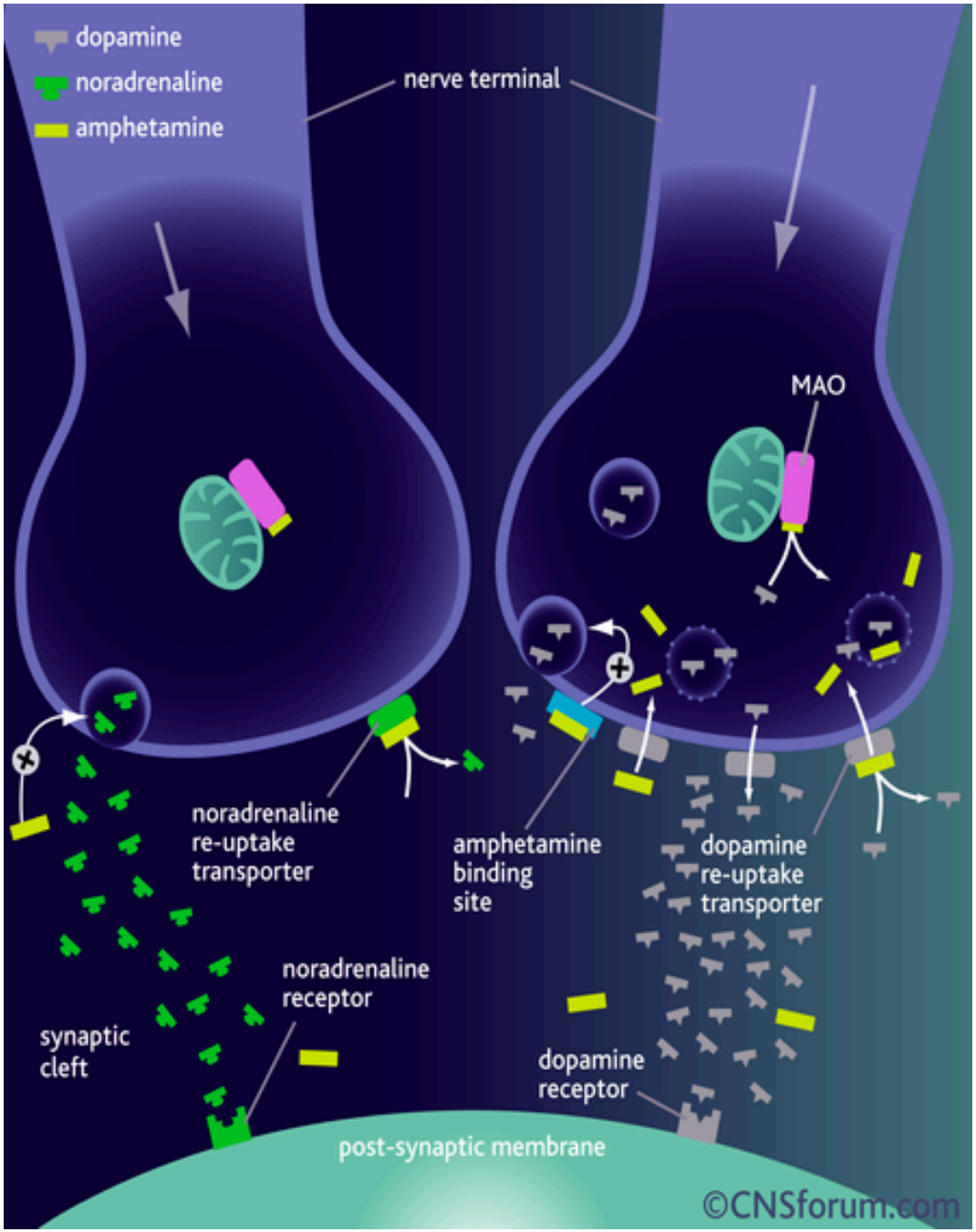
- <u>Target organs</u>:
  - CNS → stimulation 'euphoria, agitation, convulsion, tremor
  - CVS → tachycardia, HTN, arrhythmia, collapse
  - Other systems to be affected: endocrine, GI, skin, genitourinary
  - Pregnancy → Spontaneous Abortion, Teratogenic

Methamphetamine (Crystal Meth)

- Methamphetamine is a **sympathomimetic amine** that belongs to a class of compounds, the phenethylamines, with a variety of stimulant, anorexia, euphoric, and hallucinogenic effects.
- Methamphetamine is used clinically for treatment of attention deficit disorder with hyperactivity (ADHD), and adult narcolepsy.
- After cannabis, it is **the most widely abused drug worldwide**.

Methamphetamine

- Methamphetamine lacks direct adrenergic effects, but is instead an indirect neurotransmitter.
- Methamphetamine is incorporated into cytoplasmic vesicles where it displaces epinephrine, norepinephrine, dopamine, and serotonin into the cytosol.
- As cytosolic concentrations rise, neurotransmitters diffuse out of the neuron and into the synapse where they activate postsynaptic receptors.
- Methamphetamine also inactivates neurotransmitter reuptake transporter systems.


dopamine
noradrenaline
amphetamine
nerve terminal
MAO
noradrenaline re-uptake transporter
amphetamine binding site
dopamine re-uptake transporter
noradrenaline receptor
synaptic cleft
dopamine receptor
post-synaptic membrane
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Acute Clinical Presentation

- Increased energy and alertness
- Decreased need for sleep
- Euphoria
- Sweating
- Disrupted sleep patterns
- Tightened jaw muscles
- Grinding teeth
- Loss of appetite, contributing to weight loss with chronic use
- Disorganized thinking
- Itching
- GI symptoms such as nausea, vomiting, or diarrhea
- Dry mouth leading to serious tooth decay with chronic use
- Changes in mood consisting of irritability, anxiety, aggression, or panic

Management

- **General approach:** Control of agitation and other signs of sympathetic excess
  - Supportive care: ABC of Medicine
  - Care for cardiac complications, arrhythmia, hypertension, hyperthermia, convulsion, agitation, irritability, nutritional status
  - No definitive role for antidotes
- Assess the hydration and nutritional status.