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Drugs of Abuse

- **Drug abuse/ Substance abuse:** Using chemicals for nontherapeutic effects on the body or mind.

- Excessive use or misuse of drugs or alcohol for intoxicating or mind altering effects.

Examples on commonly abused substances:

- Amphetamines.
- Cocaine.
- MDMA
- Synthetic cathiones (Bath salts).
- LSD.
- Marijuana.
- Synthetic cannabinoids.
- Ethanol.
- Prescription drugs (particularly opioids).

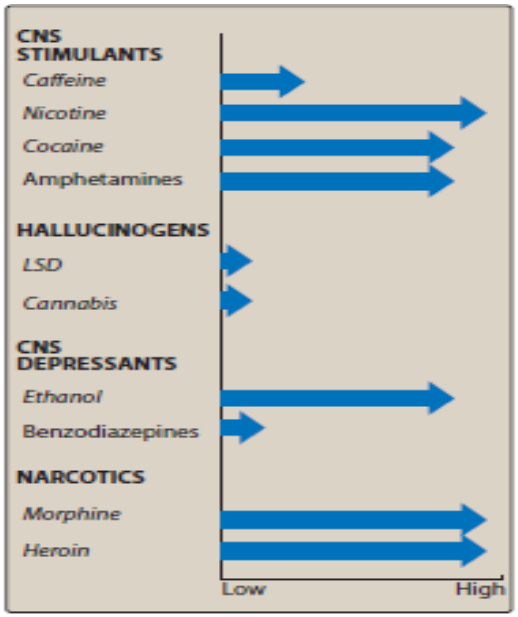


Figure 15.3
Relative potential for physical dependence of commonly abused substances.

Substances have become more potent, and their routes of administration have become increasingly effective, resulting in greater risks of addiction and toxicity.

Sympathomimetics

- **Amphetamines.**
- **Cocaine.**
- **Methylenedioxymethamphetamine (MDMA).**
- **Synthetic cathiones (Bath salts).**

Sympathomimetics

- Stimulants that mimic the sympathetic nervous system, producing “fight- or-flight” responses.
- Produce a relative increase of adrenergic neurotransmitters at their sites of action causing tachycardia, hypertension, hyperthermia, and tachypnea.
- Many have a remarkable ability to produce pleasure with high addictive potential.

Cocaine

- Derived from the erythroxylon coca shrub.

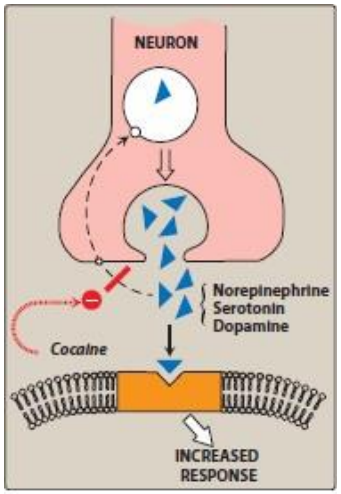


Figure 15.4
Mechanism of action of *cocaine*.

- Causes CNS stimulation by inhibiting the reuptake of NE.
- The profound ability of cocaine to stimulate the pleasure center of the human brain is thought to result from inhibition of reuptake of dopamine and serotonin.
- Minimal bioavailability when taken by the oral route.
- Cocaine hydrochloride powder is snorted, or solubilized and injected.
- Crack cocaine, an alkaloidal form, can be smoked.
- Smoking is an extremely effective route of administration, as the drug reaches the brain within seconds" that is followed rapidly by an intense dysphoria or "crash"
  - It is this immediate positive reinforcement, followed rapidly by the negative reinforcement, that makes the drug so addictive.

Cocaine

- Most drugs of abuse are usually adulterated.
- An example of a common adulterant of cocaine is levamisole, which causes agranulocytosis.
- Common reasons for cocaine users to come to the emergency department include psychiatric complaints (depression precipitated by cocaine dysphoria, agitation/paranoia), convulsions, hyperthermia, and chest pain.
- Hyperthermia is a major causes of cocaine fatalities.
- Commonly, cocaine is consumed with alcohol, which creates a cardiotoxic metabolite called cocaethylene.

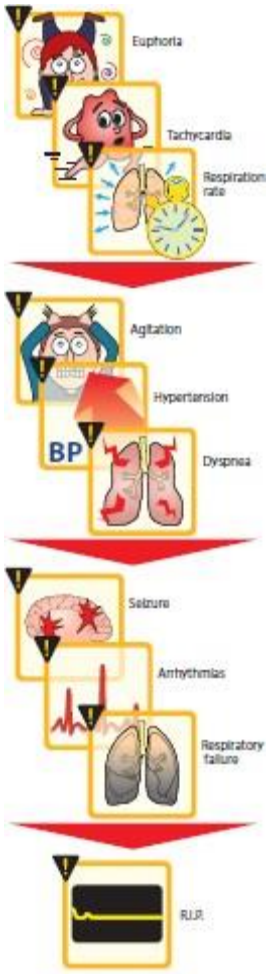


Figure 15.5
Major effects of cocaine use.

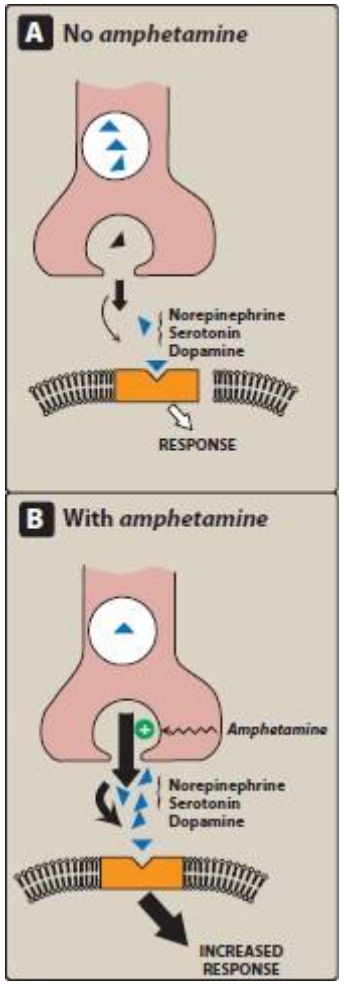
Cocaine

Cocaine toxicity management:

- Calming and cooling the patient.
- Benzodiazepines, such as lorazepam, help to calm the agitated patient, can treat and prevent convulsions.
- Short-acting antihypertensives.
- Anticonvulsants.
- Symptomatic supportive care.

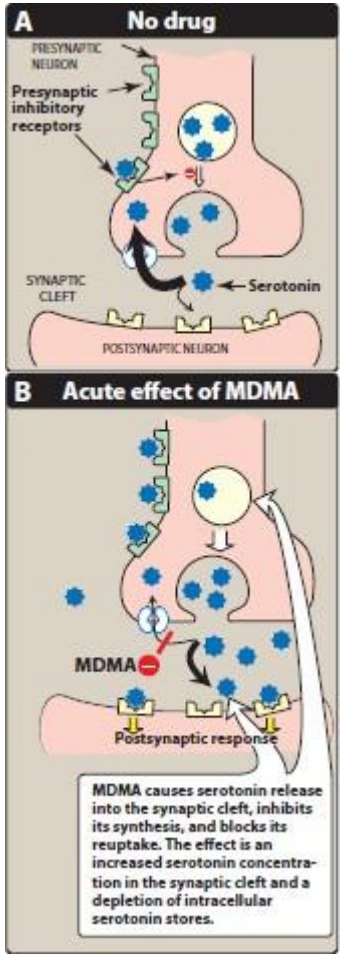
Amphetamines

- As methamphetamine.
- Clinical effects similar to cocaine.
- These effects may last longer with more stimulation and less euphoria compared to cocaine.
- Treatment of amphetamine toxicity is similar to that of cocaine toxicity.



MDMA

- Street names ecstasy or Molly.
- A hallucinogenic amphetamine with profound serotonin- releasing effects.
- Many users describe a sense of well-being and social interactivity.
- Some of the early deaths associated with MDMA toxicity involved dehydration and renal failure.
- MDMA abuse can cause profound hyperthermia, altered mental status, and movement disorders known as the serotonin syndrome.
- **Treatment for MDMA toxicity:**
  - Benzodiazepines help to calm and cool the patient.
  - Life-threatening hyperthermia has been treated with neuromuscular blockers and endotracheal intubation to control excessive movement and heat generation.
  - Cyproheptadine is a serotonin antagonist that has been used to treat serotonin syndrome.

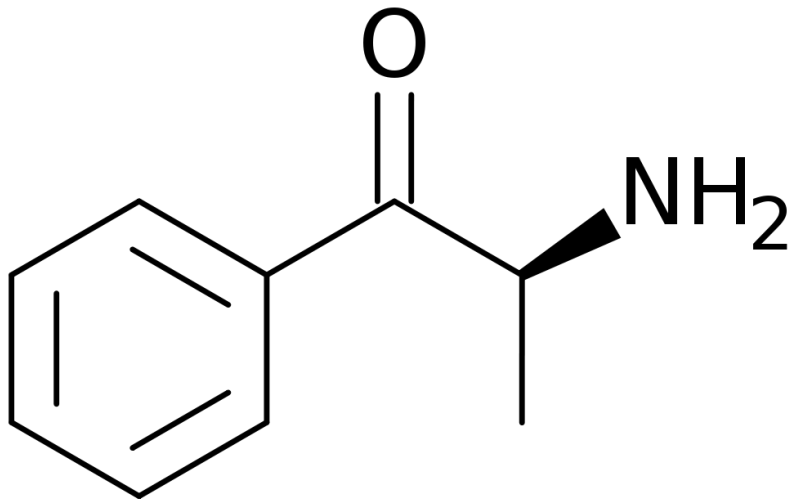


Synthetic Cathinones

- **Cathinone is the psychoactive component in an evergreen shrub called Khat.**
- **Synthetic cathinones, “bath salts,”.**
- **Synthetic cathinones are not easily detected on urine toxicology screens.**
- **These drugs increase the release and inhibit the reuptake of catecholamines (norepinephrine, epinephrine, and dopamine).**

Synthetic Cathinones

- **A rapid onset of amphetamine-like stimulation with psychotomimetic effects of variable duration is common.**
- **Bath salts are generally snorted or ingested but may also be injected.**
- **Treatment is similar to amphetamines and cocaine.**



Hallucinogens

- **LSD.**
- **Marijuana.**
- **Synthetic cannabinoids.**

LSD

- first created from ergot.
- Partial agonist at 5-HT2A receptors.
- Cery colorful hallucinations and mood alterations, sleep disturbances, and anxiety.
- Repeated use rapidly produces tolerance through down-regulation of the serotonin receptors
- Physical side effects are typically minimal, LSD may cause tachycardia, increased blood pressure and body temperature, dizziness, decreased appetite, and sweating.
- The most troubling side effects are the loss of judgment and impaired reasoning.
- After long-term use, withdrawal from LSD is considered more emotional than physical in nature.

Marijuana

- ***Cannabis sativa*** **is the plant most often used for its hallucinogenic properties.**
- **The main psychoactive alkaloid contained in marijuana is tetrahydrocannabinol (THC).**
- **Cannabinoid or CB1 receptors in the brain are found to be reactive to THC.**
- **When CB1 receptors are activated by marijuana, produced physical relaxation, hyperphagia, increased heart rate, decreased muscle coordination, conjunctivitis and minor pain control.**

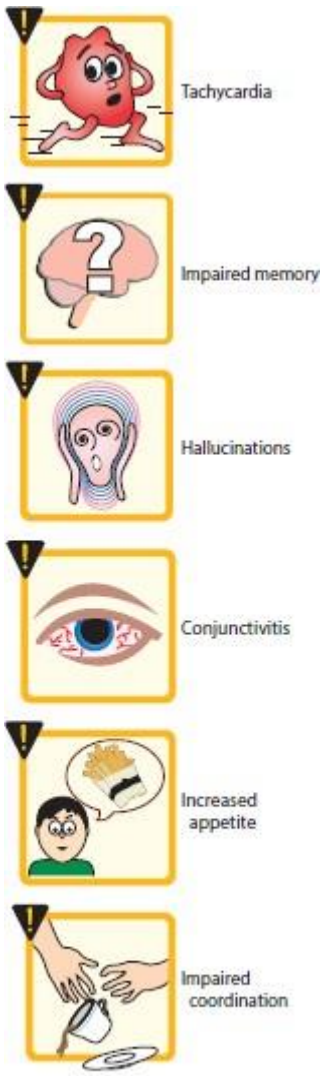


Figure 15.8
Effects of *tetrahydrocannabinol*.

- **Marijuana stimulates the amygdala, causing enhancement of sensory activity.**
- **Heavy users have a down-regulation in their CB1 receptors, leaving them with a feeling of boredom when not taking the drug.**
- **The effects of marijuana on GABA in the hippocampus diminish the capacity for short-term memory.**
- **THC decreases muscle strength and impairs highly skilled motor activity.**

Marijuana

- Long-term effects of use may include chronic bronchitis, COPD, increased progression of HIV and breast cancer, exacerbation of mental illness.
- Tolerance develops rapidly in users.
- Withdrawal may include depression, pain, irritability.
- Has been used to help in the treatment of chemotherapy-induced nausea and vomiting, cachexia secondary to cancer and AIDS, epilepsy, chronic pain, multiple sclerosis, glaucoma, anxiety.
- THC is available as the prescription product dronabinol for treatment of emesis and to stimulate the appetite,

Synthetic Cannabinoids

- **The molecular structure of synthetic cannabinoids is much different from the cannabinoids found in marijuana plants, users do not test positive for THC with traditional drug tests.**
- **The effects of these agents may be up to 800 times greater than with cannabis.**
- **Sympathomimetic effects may also be seen in users, including tachycardia and hypertension.**
- **Possibly the greatest danger includes extreme hallucinations.**

Ethanol (EtOH)

- Clear colorless hydroxylated hydrocarbon that is the product of fermentation of fruits, grains, or vegetables.
- It is a major cause of fatal automobile accidents, drownings, and fatal falls and is a related factor in many hospital admissions.
- Alcoholism decreases life expectancy by 10 to 15 years.
- It is thought that ethanol exerts its desired and toxic effects through several mechanisms:
  - Enhancing the effects of the inhibitory neurotransmitter GABA.
  - Inducing the release of endogenous opioids.
  - Altering levels of serotonin and dopamine.
- At high doses, it is a general CNS depressant, which can result in coma and respiratory depression.

- Drinking ethanol traditionally has been the most common route of administration, although recently the inhalation of aerosolized ethanol has gained popularity.
- Peak ethanol levels are generally achieved in 20 minutes to 1 hour of ingestion.
- Ethanol is metabolized by alcohol dehydrogenase to acetaldehyde and then by aldehyde dehydrogenase to acetate in the liver.
- Zero-order elimination.
- Breath sample can be used to determine blood alcohol levels.

Medical management of acute ethanol toxicity:

- Symptomatic supportive care.
- Administration of thiamine and folic acid to prevent/treat Wernicke encephalopathy and macrocytic anemia.
- Extremely high levels can be dialyzed (rarely necessary).

- Chronic ethanol abuse can cause profound hepatic, cardiovascular, pulmonary, hematologic, endocrine, metabolic, and CNS damage.
- Sudden cessation of ethanol ingestion in a heavy drinker can precipitate withdrawal manifested by tachycardia, sweating, tremor, anxiety, agitation, hallucinations, and convulsions.

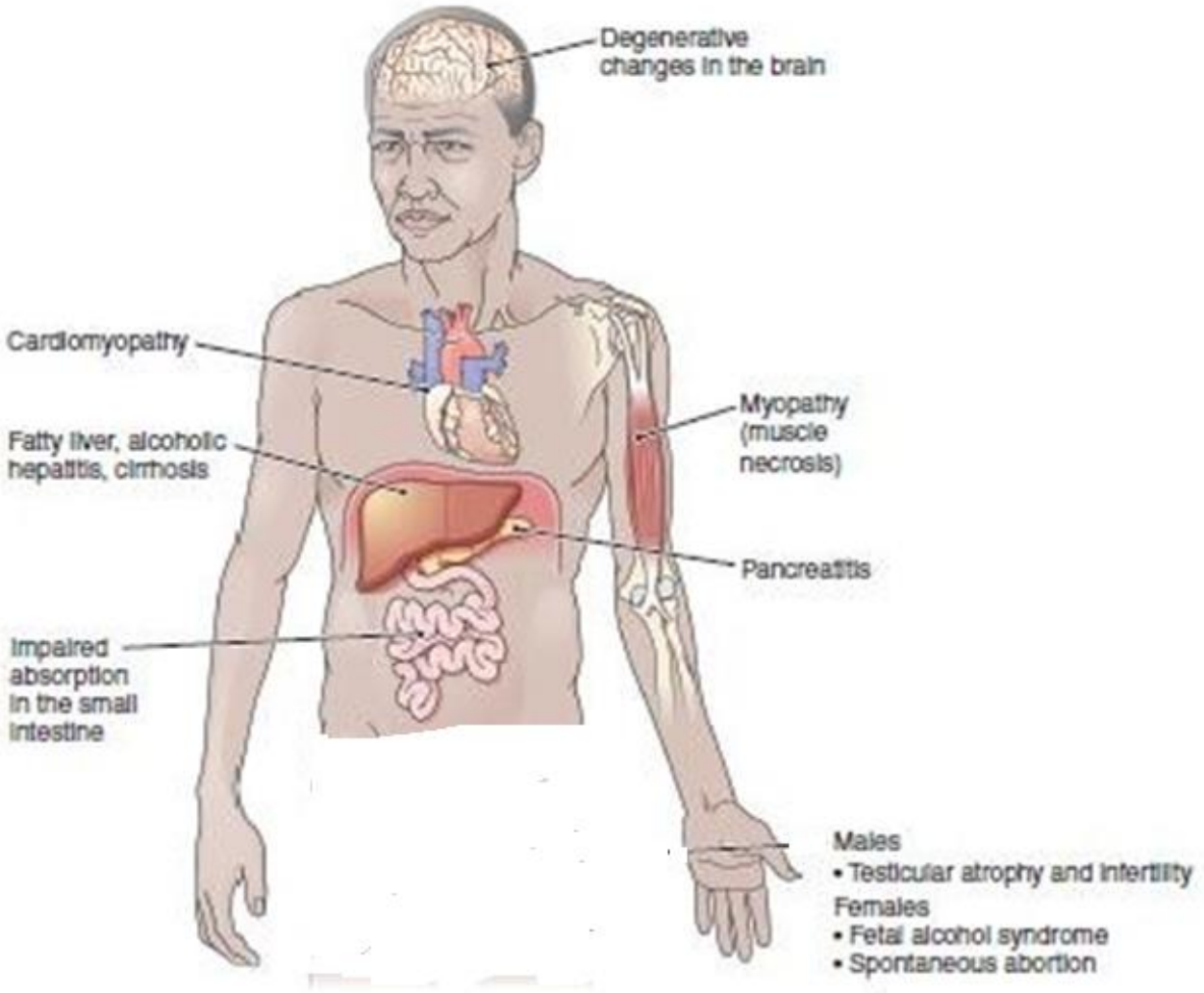


Figure 15.10
The effects of chronic alcohol abuse.

- **Alcohol withdrawal is a life-threatening situation that should be medically managed with symptomatic/supportive care, benzodiazepines, and long-term addiction treatment.**
- **Drugs used in the treatment of alcohol dependence:**
  - **Disulfiram.**
  - **Naltrexone.**
  - **Acamprosate (unknown mechanism).**
- **Supportive psychotherapy should also be available.**

Disulfiram:

- Blocks the oxidation of acetaldehyde to acetic acid by inhibiting aldehyde dehydrogenase.
- Acetaldehyde accumulates in the blood, causing flushing, tachycardia, hyperventilation, and nausea.
- Disulfiram has found some use in the patient seriously desiring to stop alcohol ingestion.
- A conditioned avoidance response is induced so that the patient abstains from alcohol to prevent the unpleasant effects of acetaldehyde accumulation.

Naltrexone is better than disulfiram, it does not produce aversive reaction.

Prescription drug abuse

- **Prescription drug abuse is becoming an epidemic in some parts of the world.**
- **Commonly abused prescription:**
  - **Opioids.**
  - **Benzodiazepines.**
  - **Barbiturates.**
- **There is an increase in prescribing of these medications especially opioids.**
- **Visits to the emergency department related to misuse of pharmaceuticals now exceed those related to illicit drug use.**
- **In the US prescription pain relievers account for more deaths than heroin and cocaine.**


اللهم عجل لوليك الفرج
صلواتك عليه وعلى آبائه في هذه الساعة وفي كل ساعة وليا
وحافظا وقائدا وناصرا ودليلا وعينا حتى تسكنه أرضك طوعا
وتمتعه فيها طويلا