

Northwest Community Healthcare  
Paramedic Education Program  
**TOXICOLOGY EMERGENCIES**  
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**Reading assignment:** Aehlert Vol. 1; pp. 1098-1124; 1132-1138 (great charts & tables in book)  
SOP: Drug Overdose / Poisoning; Alcohol intoxication/ withdrawal

**KNOWLEDGE OBJECTIVES:**

Upon completing the assigned readings, class, and homework questions, each participant will independently do the following with at least an 80% degree of accuracy with no critical errors:

1. Describe the incidence, morbidity and mortality of toxic and drug abuse emergencies.
2. Identify the risk factors most predisposing to toxic emergencies.
3. Discuss the anatomy and physiology of the organs and structures related to toxic emergencies.
4. Describe the routes of entry of toxic substances into the body.
5. Discuss the role of the poison control centers in the U.S.
6. Discuss the pathophysiology, assessment findings, need for rapid intervention and transport and management of toxic emergencies.
7. List the most common poisonings, pathophysiology, assessment findings, and management of poisoning by ingestion, inhalation, absorption, injections, and overdose.
8. Define the following terms:
  - Substance or drug abuse
  - Substance or drug dependence
  - Tolerance
  - Withdrawal
  - Addiction
9. List the most commonly abused drugs (both by chemical name and by street names).
10. Describe the pathophysiology, assessment findings, and management of commonly used drugs.
11. Explain the clinical uses, street names, pharmacology, assessment findings and management for patients who have taken, abused, and or been exposed to the following substances:
  - Alcohols
  - Amphetamines and amphetamine-like drugs
  - Barbiturates
  - Benzodiazepines
  - Bath salts
  - Carbon monoxide
  - Caustics
  - Cocaine
  - Common household substances
  - Cyanide
  - Hydrocarbons
  - Lithium
  - MAO inhibitors Drugs abused for sexual purposes/sexual gratification
  - Marijuana and cannabis compounds
  - Metals
  - Narcotics/opiates
  - Non-prescription pain medications: NSAIDS, salicylates and Acetaminophen
  - Plants and mushrooms
  - Sedative-hypnotics
  - Tricyclic antidepressants (TCAs)
  - Serotonin reuptake inhibitors (SSRIs) and serotonin syndromes
  - Theophylline

# NCH Paramedic Education Program Toxicology Emergencies

## I. Introduction

- A. **Toxicology:** Study of **toxins** (drugs and poisons) and antidotes and their effects on living organisms.
- B. The American Association of Poison Control Centers estimate that there are over 4 million poisonings every year. Poisoning deaths include those resulting from drug overdose, those resulting from other misuse of drugs, and those associated with solid or liquid biologic substances, gases or vapors, or other substances such as pesticides or unspecified chemicals.
- C. Children under the age of 6 years account for over 70% of all poisoning cases, but only 5% of deaths. More serious cases in children may involve intentional poisoning by parents or caretakers.
- D. Adults account for most hospitalizations. Most deaths (95%) occur in adults and adolescents. Most are intentional due to illicit drug use, alcohol abuse, attempted suicide and "suicidal gesturing".
- E. A child who has experienced an accidental ingestion has a 2.5% chance of another, similar ingestion within one year

### F. Forms of toxic exposure

Biological Nuclear Irritants Chemical Nerve agents Blister agents Blood agents	Farm chemicals Cleaning agents Petroleum products & by-products Medicine/drugs Inert gases Explosion hazards
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### G. Largest number of deaths

Opiates Analgesics Antidepressants (TCAs) Sedatives (benzodiazepines) Stimulants (cocaine) CV agents ( $\beta$ /Ca blockers) Alcohols Gases, fumes	Auto products (ethylene glycol) Chemicals Hydrocarbons Antihistamines (diphenhydramine) Cleaning substances (caustics) Asthma meds (theophylline)
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#### Most frequent exposures

- |                        |                              |
|------------------------|------------------------------|
| 1. Cleaning substances | 9. Hydrocarbons              |
| 2. Analgesics          | 10. Foreign bodies           |
| 3. Cosmetics           | 11. Antimicrobials           |
| 4. Cough/cold remedies | 12. Sedatives/antipsychotics |
| 5. Plants              | 13. Chemicals                |
| 6. Bites/envenomations | 14. Food                     |
| 7. Pesticides          | 15. Alcohols                 |
| 8. Topical agents      | 16. Vitamins                 |

### H. Poison control centers

- 1. Set up across the U.S. and Canada to assist in the treatment of poison victims and to provide information on new products and new treatment recommendations. Staffed by physicians (toxicologists), pharmacists, nurses or paramedics with special training in toxicology.

**Toxicology emergencies**

2. Available 24/7
3. **Poison control center for Illinois:** [www.mchc.org/ipc](http://www.mchc.org/ipc)

**II. Classifications**

- A. **Poisoning:** Exposure to non-pharmacological substances
  1. 75% less than 5 years of age
  2. Majority are caused by household products
  3. Increasingly, they are due to exposure to chemical and toxins on the farm or in the industrial workplace.
  4. More rarely, intentional poisonings are from homicidal intent or chemical warfare.
- B. **Misuse:** The use of prescription drugs in a manner other than as directed
- C. **Abuse:** Continued use of illicit or prescription drugs despite problems from drug use with relationships, work, school, health or safety. People often experience loss of control and take drugs in larger amounts or for longer than they intended.
- D. **Overdose:** When a drug is swallowed, inhaled, injected, or absorbed through the skin in excessive amounts and injures the body.
  1. **Intentional**
    - a. Prescription drugs and ETOH
    - b. Suicide: 80% of all *attempted* suicides involve a drug overdose
  2. **Unintentional**
    - a. Iatrogenic: Giving patients the wrong medication
    - b. Drug errors when taking medications
    - c. Combination of Rx
  3. Miscalculation
  4. Change in strength
- E. **Abuse:** Technically a form of poisoning
  1. May involve therapeutic prescriptions and recreational drugs
  2. **Risk factors for substance abuse**
    - a. Family history
    - b. Stress at work and home
    - c. Emotional problems otherwise
    - d. Untreated psychiatric condition
    - e. Sensation seeking behaviors
  3. Drugs activate brain circuits that produce feelings of pleasure and reward. Euphoria propels users to consume drugs again and again.
  4. **Do we have a problem?** Increased recreational drug use: Some 13 million people abuse drugs on a regular basis because drugs activate circuits in the brain that produce feelings of pleasure and reward. This euphoria propels users to consume drugs again and again.  
**Defined by 3 criteria**
    - a. Pattern of pathological use
    - b. Impairment of social/work functions
    - c. Duration greater than 1 month
  5. **Stages of drug use**
    - a. Stage 1: **Experimenting with drugs:** A person tries a drug in search of "fun". There is often strong peer pressure to enter this stage. There is usually no change of behavior, except for secret activities meant to hide the drug use.

**Toxicology emergencies**

- b. Stage 2: **Actively seeking drugs:** In this stage, a person needs more drugs to get the same feelings (Tolerance). A person may use drugs daily to get "high" and escape reality.

**Tolerance:** Increasing resistance to usual effects of a drug resulting from continued use. Characterized by needed increases in amount and frequency of use to achieve same effect

- c. Stage 3: **Preoccupation with drugs:** Significant loss of control over drug use. The user may become angry or isolated without them. Heavy drug use is costly and user may lie/steal from family or friends to pay for them.

Physical and psychologic state of an individual in which the usual or increasing amount of a drug are required to gain wanted effect  
Dependency does not always imply addiction. If no withdrawal symptoms occur when the drug is stopped, addiction does not exist

- d. Stage 4: **Addiction.** Characterized by overwhelming desire or need (craving) to continue using substance and obtain it by any means. Addict must use every day, all day to feel "normal". Cannot function without the substance and will experience withdrawal S&S if substance is withheld.

6. **Common factors in abuse**

- a. Self-administered
- b. No medical control or indication for use
- c. No preparation of sterile access
- d. Legal and illegal procurement of agents
- e. Indiscriminant use of medical and non-medical agents for supposed effects

F. **Dependence**

1. More severe than simple abuse
2. **Tolerance** - decreased response to drug, increased dose needed
3. Withdrawal symptoms from abrupt discontinuation of the drug
4. **Addiction:** Psychological or physical need to take the drug

III. **Mechanisms of entry** (routes of toxic exposure)

A. **Ingestion**

1. Most common: 75% of exposures; 78% of fatalities
  - a. Household products
  - b. Petroleum-based agents (gasoline, paint)
  - c. Cleaning agents: alkalis, soaps
  - d. Cosmetics
  - e. Plants
  - f. Meds: Prescription, non-prescription, illicit. The range between curative and toxic doses of a medication is called the **therapeutic index**. Patients who have overdosed on medications have blood levels in the toxic range.
  - g. Foods
2. **Effects**
  - a. **Immediate:** Caustics - strong acids or alkalis: Burns to the lips, tongue, throat and esophagus.
  - b. **Delayed**
    - (1) Depends on GI tract absorption
    - (2) Stomach absorbs only small amount
    - (3) Most absorbed from small intestine
    - (4) May remain in stomach for hours: Ex. aspirin - the tablets may bind together to form a large bolus that is difficult to remove or break down.

3. **One mouthful may hold variable volume by age and size**
  - a. Adults = 30 mL
  - b. Child over 2 years = 15 mL
  - c. Child less than 2 years = 5 mL
- B. **Injection (IV, Sub-q)**
  1. Injection of a toxic agent under the skin, into muscle or into a blood vessel
  2. Immediate and delayed reactions
    - a. Immediate: localized to site of injection. Appears as red, irritated and edematous skin
    - b. Delayed: Systemic reaction, occasional anaphylaxis
      - (1) Infection: Local (cellulitis) or systemic (hepatitis, AIDS)
      - (2) Cut with substances: Lung and brain infarcts
    - c. Examples: Insects and animal bites; intentional injection of illicit drugs
- C. **Surface absorption (Dermal and ocular)**
  1. Entry through the skin or mucous membranes
  2. Examples: Contact with poisonous plants, caustics, organophosphates; **Intranasally** (Cocaine, bath salts): Absorbed through nasal mucosa and vessels
  3. Effects - immediate and delayed, local and systemic
- D. **Body packing**
  1. "Body packing" refers to the smuggling of illicit drugs by concealing them internally within the body. The drug is transported in the form of packets that are ingested orally, often with a constipating agent, or they are inserted rectally into the colon. Packets have also been found in the vagina. The first reported case of body packing was in 1973, when a body packer had developed a small bowel obstruction nearly 2 weeks after swallowing a condom filled with hashish. The patient underwent surgical removal.<sup>[1]</sup> Cocaine, heroin, amphetamines, 3,4-methylenedioxymethamphetamine ("Ecstasy"), marijuana, and hashish are the drugs that are usually smuggled in this manner.<sup>[2]</sup>
  2. Body packers usually carry about 2.2 lb (1 kg) of drugs divided into 50-100 packets of 0.29-0.35 oz (8-10 g) each; however, persons carrying more than 200 packets have been reported.<sup>[2]</sup> The packets are usually well-designed and constructed, possibly with the help of machines, so as to make them resistant to rupture.<sup>[4]</sup> The drug is first packed into a balloon or condom, followed by additional layers of latex and, finally, sealed with wax.<sup>[2]</sup> If a packet ruptures, however, it releases a high dose of drug into the gastrointestinal tract that can lead to drastic consequences. The acute drug intoxication that can result is associated with high mortality rates.<sup>[4]</sup>
  3. Body packing should be suspected in anyone exhibiting signs of drug-induced toxic effects after a recent arrival on an international flight, or when there is no history of recreational drug use.<sup>[2]</sup> When a suspected body packer presents, a detailed history should be obtained, followed by a thorough physical examination. Information should be gathered on the type of drug, the number of packets, the nature of the wrapping, and the presence of any GI symptoms. Assessment of the vital signs, mental status, pupil size, bowel sounds, and skin findings can provide useful clues to the nature of the drug. Physicians will do a gentle rectal and vaginal examination to disclose the possible presence of packets.<sup>[2]</sup>
  4. Body packers may present with clinical toxidromes if a packet ruptures. They may also present with symptoms of intestinal obstruction or other complications, such as gastrointestinal hemorrhage or perforation.<sup>[2,5]</sup>

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5. Paramedics should be aware of this potentially fatal form of drug smuggling and its various presentations, in order to make a prompt diagnosis and begin the appropriate management.

**E. Inhalation**

1. Rapid absorption through the alveoli-capillary membrane into the bloodstream, then they are quickly distributed to the brain and other organs.
2. Can irritate pulmonary passages causing extensive edema and destroy tissues
3. Absorption can cause systemic effects
4. Caustic agents can be in the form of gasses, vapors, fumes or aerosols. Examples: Gases - CO, NH<sub>4</sub> (ammonia), chlorine, freon, carbon tetrachloride, methyl chloride, tear gas, mustard gas, nitrous oxide; spray paint (particularly metallics); household chemicals like cooking spray, furniture polish, correction fluid, propane, mineral spirits, nail polish remover, aerosol propellants, glue, oven cleaners, lighter fluid, and gasoline.
5. Inhalants are attractive to students because they are legal, easily accessible, and affordable. They are often gateway drugs.
6. **Abuse mechanisms seen in children/adolescents**
  - a. **Sniffing:** Abuser inhales directly from an open container or from a surface upon which the substance has been applied.
  - b. **Huffing:** Inhaling the volatile substance from a piece of cloth that is placed next to or over the mouth or the nose.
  - c. **Bagging:** Substances is placed in a plastic or paper bag and the vapors are inhaled with an open mouth. Once inhaled these substances produce a high that lasts from 15-45 minutes, if not sudden death.
7. Done to get high. Abuser experiences alcohol-like effects that can often include slurred speech, ataxic movements, euphoria, dizziness and hallucinations. Signs and symptoms may also include a bad headache, nausea/vomiting, syncope, mood changes, short-term memory loss, diminished hearing, muscle spasms, brain damage, non-cardiogenic pulmonary edema, and dysrhythmias.
8. Sniffing volatile solvents can affect the nervous system, liver, kidneys, blood, bone marrow and can cause severe damage to the brain. Sniffers can suffer from "sudden sniffing death" from a single session of inhalant use.
9. Look for discoloration, spots or sores around the mouth, nausea, anorexia, chemical breath odor and drunken appearance.

**IV. Patient assessment****A. Scene size up**

1. Assure your own safety –meth labs are dangerous!
2. Suicidal patients may be violent
3. Intoxicated or chemically impaired persons will not be rationale and may not be cooperative
4. Look for signs of overdose or drug paraphernalia
5. Do not put your hand blindly into patient's pockets. They may contain needles.
6. If a chemical spill or hazardous gas situation, wear appropriate protective equipment prior to entering the scene.

**B. Primary assessment**

1. Form a general impression; quickly assess mental status. **Uncooperative behavior may be due to intoxication/poisoning; do not get distracted from assessment of underlying pathology**
2. Anticipate hypoxia, respiratory arrest, seizure activity, dysrhythmias, and/or vomiting

3. **Assess, secure, and maintain ABC's** - top priority
4. **Airway**
  - a. Assess for hoarseness, stridor
  - b. Protect C-spine if any risk of injury (assoc. trauma common)
  - c. Open and maintain patency: BLS to ALS
  - d. **Prevent aspiration:** Frequent complication due to altered mental status and decreased gag reflex - primary concern of management.
  - e. Assess need for advanced airway if GCS  $\leq$  8, aspiration risk, or airway compromised unless otherwise specified

**Adjuncts as needed:** Suction, OPA, NPA, ETI; King

  - (1) May need DAI if teeth are clenched or patient is responsive but vomiting. Better decision may be to insert one or two NPAs, ventilate with BVM and rapidly transport to hospital for RSI if intubation would be difficult or contraindicated
  - (2) **DAI not** indicated for Club drugs (Ecstasy, GHB, Ketamine, and Rohypnol) unless an aspiration risk – See SOP
5. **Breathing; gas exchange**
  - a. Assess general rate, depth and pattern of ventilations
  - b. Assess for dyspnea, retractions, chest pain or tightness
  - c. SpO<sub>2</sub> capnography
  - d. Support ventilations w/ 15L O<sub>2</sub>/BVM if respiratory depression, hypercarbic ventilatory failure
6. **Circulation; ECG**
  - a. Skin color, temperature, moisture
  - b. General rate, strength and rhythmicity of peripheral pulses
  - c. Cardiac monitor
  - d. IV NS - rate depends on patient's status
7. **Disability/drugs**
  - a. Protect from harm to self and others, consider need for physical and/or chemical restraint
  - b. Assess LOC (Glasgow Coma Scale), motor and sensory function
  - c. Decreased LOC = increased risk aspiration if vomiting; position on side if ventilations are adequate and no suspicion of spine injury to protect airway
  - d. Decreased LOC = Assess glucose
    - (1) If glucose < 60: Dextrose 10% (250 mL = 25 Gm) IVP/IO
    - (2) If glucose level 60-70: Dextrose 10% (125 mL = 12.5 Gm) IVP/IO
  - e. If AMS + RR < 12 and substance unknown (pupils may be small): **NALOXONE** 0.4 mg IVP/IN/IO/IM. May repeat to total of 2 mg IVP/IN/IO/IM if initial response is inadequate until ventilations increase (EMT can give IN). **GIVE AND DOCUMENT THE CORRECT DOSE.**
    - (1) Competitively binds to narcotic sites
    - (2) Duration of effect up to 60 min.
    - (3) Use diagnostically (decreased LOC, decreased RR)
    - (4) Caution if chronic drug abuser
      - (a) Will cause acute withdrawal; patient may be violently combative and dangerous. Restrain first - titrate dose.
      - (b) May cause flash pulmonary edema; assess carefully

- (c) May try to refuse transport once they wake up; BAD IDEA; need hospital evaluation regardless to assess for suicidal ideation
    - f. If convulsive activity, excited delirium, severe anxiety/agitation, serotonin syndrome: MIDAZOLAM 2 mg increments IVP/IO q. 30-60 sec (0.2 mg/kg IN) up to 10 mg prn titrated to stop seizure activity. If IV unable and IN contraindicated: IM dose 5-10 mg (0.1-0.2 mg/kg) max 10 mg single dose. All routes: May repeat prn to a total of 20 mg if SBP  $\geq$  90 (MAP  $\geq$  65) unless contraindicated.
  - 8. **Expose and examine** - Undress patient for detailed assessment; maintain patient modesty and keep warm
  - 9. **Transport decision**
- C. **Secondary Assessment**
  - 1. **History** - May obtain while completing primary assessment
    - a. May be difficult to obtain, but careful history may be very helpful
    - b. Talk to patient, family and significant others
      - (1) Who Description of patient - peds, elderly
      - (2) What: Exactly what was taken (look at container, contents; anything else?
      - (3) When: Time of exposure; how long ago taken
      - (4) Where: What route of exposure?
      - (5) Why: Suicide attempt or accidental?
      - (6) How much: Swallow or just a taste; look at date prescription filled and amount remaining to get an estimate of amount missing
      - (7) Rx : Antidote given? Vomiting occurred or induced? Save vomitus if possible and bring to hospital.
    - c. A common error is obtaining an inadequate or misinterpreted history. One study of tox patients showed in only 20% of cases did lab confirm history, 25% found drug(s) totally unsuspected.
    - d. **General past medical history**
      - (1) **Allergies**
      - (2) **Medications**
      - (3) **PMH** - psych, previous suicide attempt, precipitating personal crisis, drug abuse
      - (4) **Last oral intake**
      - (5) **Events surrounding incident** - Suspect when
        - (a) Sudden onset, unexplained signs/symptoms
        - (b) CNS changes - altered LOC – seizures
        - (c) GI complaints - particularly in a child
        - (d) Psych presentation - bizarre behavior
        - (e) Trauma
        - (f) Young person with dysrhythmias
        - (g) Numerous medications
        - (h) Pulmonary edema - young person
  - 2. **Vital sign changes**

	Decreased	Increased
<b>Temperature</b>	Narcotics, barbiturates, ethanol, sedatives-hypnotics, clonidine, phenothiazines, hypoglycemia	Salicylate (ASA), stimulants/amphetamines, phencyclidine, anticholinergics, seizures due to any cause
<b>Pulse</b>	Beta/Ca blockers, Dig, organophosphates, cyanide, opiates	Theophylline, cocaine, PCP, amphetamines, stimulants
<b>Respiration</b>	ETOH, opiates	Salicylates or other agents causing metabolic acidosis, stimulants
<b>BP</b>	Sedative-hypnotics, narcotics, antihypertensives, theophylline, clonidine, beta-blockers, TCAs, theophylline, opiates	Amphetamines, phencyclidine, phenylpropanolamine, anticholinergics, cocaine, nicotine

3. **Review of Systems**

a. **Eyes**

- (1) **Pupils** - Size, shape, equality, and movement - Ocular signs:
  - (a) **Miosis** (pinpoint): Narcotics, clonidine, organophosphate, phenothiazines, deep sedative-hypnotic overdose, pilocarpine
  - (b) **Mydriasis** (dilated): ETOH, amphetamines, cocaine, anticholinergics, TCA, LSD, glutethimide
- (2) **Nystagmus**: Phenytoin, phencyclidine (especially vertical nystagmus), alcohol, and many sedative-hypnotics
- (3) Ophthalmoplegia: Botulism, sedative-hypnotics
- (4) Oculogyric crisis: Haloperidol, other antipsychotics
- (5) Optic neuritis: Methanol
- (6) Visual disturbances
- (7) Coloration of vision

b. **Mouth**: S&S of caustic ingestion, huffing or bagging (paint on upper or lower lips; amount of salivation, presence of vomitus)

c. **Gag reflex**: Tap between the eyebrows and check for a blink reflex

d. **Breath odor**

- (1) Smoke: Fire-associated toxins
- (2) Fruity/acetone: DKA, Isopropanol
- (3) Bitter almond: Cyanide
- (4) Garlic: Arsenic, arsine gas, organophosphate
- (5) Wintergreen: Methylsalicylate
- (6) Pear-like: Chloral hydrate
- (7) Rotten eggs: Hydrogen sulfide
- (8) Moth balls: Camphor
- (9) Gasoline: Hydrocarbons
- (10) Typical odors of: ethanol, ammonia, tobacco, disinfectants, glue, paraldehyde

e. **Chest/thorax**

- (1) Cough, dyspnea
- (2) **Lung sounds**: Crackles/wheezing; consider incidence of aspiration, pneumonia, noncardiogenic pulmonary edema

(3) **ECG** - Electrocardiographic manifestations of poisoning

<u>Signs</u>	<u>Possible cause</u>
AV blocks	Beta/Calcium blockers, digitalis, aminoglycosides, TCAs, type I antiarrhythmic agents
Prolonged QRS	Phenothiazines (selected), TCAs, Type I antiarrhythmic agents
Prolonged QT interval	Arsenic, hypocalcemia (ethylene glycol), phenothiazines, TCAs, Type I antiarrhythmic agents
V-tachyarrhythmias	Amphetamines, cocaine, digitalis glycosides, theophylline, TCAs, Type I antiarrhythmic agents
Ischemic pattern	Cellular asphyxiants (cyanide, CO), hypoxemia (pneumonia)

f. **Abdomen:** Abdominal pain may result from poisoning from salicylates, methyl alcohol, caustics or botulism toxin, or bowel obstruction

g. **Back and extremities**

- (1) Sensory (sensation & reflexes)
- (2) Motor (ROM & muscle tone)

<u>Altered muscle tone</u>	<u>Possible cause</u>
Increased	Amphetamines, phencyclidine, antipsychotics
Flaccid	Sedative-hypnotics, narcotics, clonidine
Fasciculations	Organophosphate, lithium
Rigidity	Haloperidol, phencyclidine, strychnine
Dystonic posturing	Antipsychotics, phencyclidine
Tremor	Lithium, nicotine, stimulant, alcohol-sedative withdrawal
Asterixis (flapping tremor)	Agents causing liver encephalopathy
Seizures	TCAs, theophylline, amphetamines, cocaine, phencyclidine, phenothiazines, isoniazid, lindane, other chlorinated hydrocarbons and pesticides

h. **Skin**

- (1) Cyanosis: Ergotamine, hypoxemia, hypotension, methemoglobinemia
- (2) Flushed, red: Carbon monoxide (rare), cyanide (rare), anticholinergics, boric acid
- (3) Greenish tint: Whickie sticks - Marijuana dipped in embalming solution
- (4) Acne rash: Bromides, chlorinated aromatic hydrocarbons
- (5) Bullae: Nonspecific for sedative-hypnotic overdose, CO
- (6) Staining: Chronic exposure to mercuric chloride, bromine or similar chemicals
- (7) Needle marks/tracks?
- (8) Itching? Intense itching may indicate an opiate OD as many cause the body to release histamine

D. **Rule-out other causes**

1. Head trauma / stroke
2. Metabolic / endocrine / hypoxia

3. Hemorrhage / shock
4. Infection
5. Electrolyte imbalance
6. Hypothermia

V. **Planning & implementing appropriate interventions**

A. **Priorities:** Most patients require supportive care rather than a specific antidote

1. ABCs – Suction; prevent aspiration
2. Prevent absorption
3. Enhance elimination
4. Provide appropriate antidotes
5. Provide psychological support

Common toxidromes			
<b>Opiates:</b>	Constricted pupils Decreased RR, P, BP, T	<b>Cholinergic:</b>	Constricted pupils "SLUDGE" reaction
<b>Stimulants:</b>	Dilated pupils Increased RR, P, BP, T	<b>Anticholinergic:</b>	Dilated pupils Skin hot, dry, flushed

B. **Substance identification based on clinical presentation (toxidrome)**

1. Is patient presentation consistent with history?
2. Sedatives, barbiturates, tranquilizers, ETOH: Lethargy, slurred speech, nystagmus, ataxia
3. Opiates: Coma, hypoventilation, small pupils
4. Stimulants: Agitation, belligerence, tremors, headache, dry mouth, dilated pupils
5. Hallucinogens & atropine: hallucinations, agitation, dilated pupils, dry & flushed skin, fever
6. Phenothiazines: Dystonia, oculogyric crisis, ataxia, hypotension
7. Tricyclic antidepressants: Agitation, coma, seizures, hypotension, dysrhythmias
8. Salicylates, acetaminophen: Hyperventilation, fever, vomiting

C. **Prevent absorption - decontamination:** Process of minimizing toxicity by reducing the amount of toxin absorbed into the body.

1. **Reduce intake of surface-absorbed toxins**
  - a. Remove from environment where they are inhaling toxic fumes
  - b. Remove a stinger or sac from someone stung by a bee
  - c. Remove clothing and clean the skin with soap and water for a patient who is exposed to a toxic chemical or gas
2. **Reduce absorption of toxin once in the body**
  - a. Usually applies to ingested toxins
  - b. **Syrup of Ipecac** is no longer used. Vomiting limits usefulness of antidotes that must be given P.O. like activated charcoal or N-Acetylcysteine. Also an increased risk of aspiration with vomiting.
  - c. **Gastric lavage:** "Pumping the stomach". Also has a limited use at the hospital.
  - d. Some EMS systems (not NWC EMSS) carry **activated charcoal** that binds with and inactivates an ingested poison. It can prevent the absorption of some toxins into the bloodstream but not all. Dose: Adults 60-100 g; children 30-60 g

3. **Enhanced elimination of the toxin**
  - a. **Cathartics:** Sorbitol (often mixed with charcoal) increase gastric motility. Contraindicated in pediatric patients due to potential to cause electrolyte imbalances.
  - b. **Whole bowel irrigation:** Administration of polyethylene glycol continuously at 1-2 L/hr through a nasogastric tube until the effluent is clear or objects are recovered. Not an EMS intervention.
4. **Antidotes:** Any agent that will neutralize a specific toxin or counteract its effect on the body. These are mostly administered at the hospital.
  - a. Acetaminophen (Tylenol): N-Acetylcysteine (Mucomyst) 140 mg/kg
  - b. Benzodiazepines: Flumazenil 0.2 mg q. 1 min to a total of 1-3 mg
  - c. Cyanide: **AMYL NITRITE** inhalants **OR HYDROXOCOBALAMIN**
  - d. Ethylene glycol: Fomepizole 15 mg/kg IVP or methyl alcohol
  - e. Iron: Deferoxamine 10-15 mg/kg/hr IV
  - f. Lead: Edetate calcium disodium 1 amp/250 mL D5W over 1 hr or Dimercaptrosuccinic acid (DMSA) 250 mg PO
  - g. Mercury, arsenic, gold: BAL (British anti-Lewisite) 5 mg/kg IM or DMSA 250 mg PO
  - h. Methyl alcohol: Ethyl alcohol +/- dialysis
  - i. **Narcotics or synthetic narcotics: naloxone**
  - j. Nitrates: Methylene blue 0.2 mL/kg of 1% sol. IV over 5 min.
  - k. **Organophosphates: atropine 2-5 mg IVP or IM**  
**Or WMD gasses pralidoxime (Protopam): Initial 1 Gm IV or IM**

D. **Withdrawal syndromes**

Potentially fatal withdrawal syndromes may occur for alcohol, benzodiazepines, and other depressants. The body responds to the depressants by increasing the level of endogenous stimulation. When the depressants are no longer present...whomp. Narcotics and barbiturate withdrawal are uncomfortable, but rarely fatal (Bledsoe, 2006).

## **TRICYCLIC ANTIDEPRESSANT (TCA) OVERDOSES**

**Use:** TCAs had been popular for the treatment of depression caused by a chemical imbalance in the brain that produces the typical signs and symptoms. They have a very narrow therapeutic index. Relatively small increases in dose can quickly lead to toxic effects. The patients who need this drug to treat their depression are the most likely to take an overdose. TCAs are still used to treat chronic pain or migraine headaches.

**Morbidity:** TCAs used to be the **#1 cause of death from drug ingestion**. Deaths have dropped significantly due to the advent of safer drugs to treat depression. Fatalities have occurred after minimal ingestions. Mortality is approximately 10%. (Am. Assoc. of Poison Control Centers)

**Action:** **Binds alpha receptors on the blood vessels and blocks sodium channels in the heart**

### **Signs & symptoms**

**VS:** **Tachycardia, hypotension**

**HEENT:** Dilated pupils, blurred vision, nystagmus, dry mouth

**CV:** **Tachycardia - ST, SVT**

**Conduction disturbances - Widened QRS, prolonged PR, heart blocks** due to sodium channel blockade - QRS > 0.10 s considered a significant indication of severity and risk of sudden death - should be aggressively treated

**Ventricular dysrhythmias - PVC's, VT, VF, torsades de pointes**

**Hypotension** - Results from depletion of norepinephrine due to inhibition of neuronal uptake of this catecholamine (alpha blockade) - initially hypertension may be seen

**Resp:** **Respiratory depression - may occur rapidly**

**Neuro:** Confusion, hallucinations, CNS depression, lethargy, **seizures - may occur abruptly**

**GU/GI:** Urinary retention, decreased GI motility, constipation

**Skin:** Late: hyperthermia

### **GENERIC AND TRADE NAMES**

Adapin, Sinequan (doxepin)	Desyrel Elavil (amitriptyline)	Mianserin Norpramine	Surmontil (trimipramine) Tofranil (imipramine)
Amatid	Endep	nortriptyline	trazodone
Amitril	Janimine	Pamelor	Triavil
Ascendin (amoxapine)	Limbitrol	perphenazine	Vivactil
Anafranil	Loxapine	Pertofrane	Vivalan
Aventyl	Loxitane	Presamine	Zimelidine
Clomipramine	Ludiomil	protriptyline	
desipramine	maprotiline	SK-Pramine	

### **Treatment**

- **Monitor vital signs and ECG for at least 6-24 hours in asymptomatic patients**
- **Ventricular arrhythmias:** Conduction defects may respond to alkalinization and loading of the sodium channels.  
**If hypotensive: IV/IO NS wide open up to 1 L (to offset alpha receptor blockade)**  
**If wide QRS: SODIUM BICARB 1 mEq/kg IVP. Repeat dose if ↓ BP, deterioration of mental status, wide QRS, or dysrhythmias.**  
Alkalinization to pH above physiologic may be necessary to reverse arrhythmias.  
Alkalinization of the blood works by affecting plasma protein binding of TCAs.
- **Hypotension: Dopamine may not be effective as a pressor agent due to alpha blockade**
- **Seizures: Administer midazolam per SOP**

## **MONOAMINE OXIDASE INHIBITORS (MAO Inhibitors)**

**Use:** Sometimes used to treat depression. Used recently to treat obsessive-compulsive disorders. MAO inhibitors have a narrow therapeutic window, multiple drug interactions, serious interactions with foods containing tyramine (red wine and cheese) and high morbidity and mortality when taken in overdose (Bledsoe, 446). Symptoms of OD may not appear for six hours. Newer MAOs are less toxic.

**Action:** Inhibit the breakdown of neurotransmitters such as norepinephrine and dopamine while increasing the availability of the components needed to make more neurotransmitters.

### **Signs & symptoms**

**VS:** Severe hypertension, tachycardia, palpitations, hyperthermia

Late: Bradycardia, hypotension

**HEENT:** Headache

**CV:**

**Resp:**

**Neuro:** Agitation, restlessness, tremor, coma

**GU/GI:** Nausea

**Skin:**

### **GENERIC AND TRADE NAMES**

Nardil	Parnate	Eldepryl
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### **Treatment**

- Monitor vital signs and ECG - supportive care
- Seizures and hyperthermia: Midazolam

## **SEROTONIN REUPTAKE INHIBITORS (SSRIs)**

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**Use:** Agents to treat depression; have almost totally replaced TCAs.

**Action:** Prevent the reuptake of serotonin, increasing the levels in the brain.  
Generally very safe.

### **Signs & symptoms**

VS: Sinus tachycardia

HEENT:

CV:

Resp:

Neuro: Drowsiness, tremor

GU/GI: Nausea, vomiting

Skin:

**S&S of Serotonin Syndrome** - Occurs when patients on SSRIs are given a second drug such as Demerol, codeine, dextromethorphan or other antidepressants. This can be life-threatening.

- Agitation, anxiety, confusion, insomnia
- Headache, drowsiness, coma
- Nausea, salivation, diarrhea, abdominal cramps
- Hyperthermia, tachycardia
- Rigidity, shivering, incoordination, myoclonic jerks

### **TRADE NAMES**

Prozac	Luvox	Paxil	Zoloft
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### **Treatment**

- Monitor vital signs and ECG - supportive care
- **Midazolam** may be used to improve patient comfort, but rarely given in field



# ORGANOPHOSPHATE – Cholinergics

**Examples:** Insecticides, bug bombs, flea collars, fly paper

**Action:** Entry through surface absorption. Allow accumulation of acetylcholine at neuroreceptor sites and results in excessive stimulation of the parasympathetic nervous system (cholinergic crisis)

**Ext. toxic** Cause more than 50% of poisoning deaths in children

## **Signs and symptoms: SLUDGE Reaction**

HEENT	Lacrimation, constricted pupils, blurred vision
NEURO	Headache, ataxia, dizziness, seizures, decreased LOC
RESP	Pulmonary edema, bronchoconstriction, dyspnea, crackles
CV	Bradycardia, hypotension, chest pain, dysrhythmias
GI	Salivation (drooling), nausea, vomiting, diarrhea, abdominal pain
SKIN	Diaphoresis, hyperthermia may be seen

## **Treatment**

- Wear gloves and protective clothing
- Remove from exposure, move to fresh air
- Establish airway, adequate ventilation, suctioning
- **ATROPINE** - blocks excessive acetylcholine at receptor sites - 2 mg IVP q 5 min until secretions dry  
Most common cause of treatment failure is inadequate atropine  
May experience respiratory arrest - atropine won't help
- Flush and wash X 3 with soap and water
- Emesis is contraindicated because risk of respiratory depression and seizures
- Gastric lavage, with airway protected, may be indicated
- Charcoal effective

September 9, 2010. The US Food and Drug Administration (FDA) has approved the pediatric use of pralidoxime chloride (*Protopam Chloride*; Baxter Healthcare), a drug used to treat poisoning by organophosphates, including neurotoxins. The drug can be administered to children either IV or IM. "We know this drug has been widely used for many years to treat poisoning in pediatric patients in emergency situations," said Russell Katz, MD, director of the Division of Neurology Products in the FDA's Center for Drug Evaluation and Research, in an agency release. "Improving the drug's label with new dosing information for children will give health care professionals better guidance on how to use this drug safely and effectively."

"It can be difficult to use IV drugs in children, particularly in emergency situations, so having the new option of [intramuscular] injection may help healthcare professionals use this medicine quickly and accurately," added Dianne Murphy, MD, director of the FDA's Office of Pediatric Therapeutics.

Pralidoxime chloride was approved by the FDA in 1964 to treat various types of pesticide and chemical poisoning in adults. The drug works as an antidote to organophosphate poisoning by inhibiting attachment of the chemical to neuroreceptors.

Organophosphates are used most often in pesticides by farmers and professional exterminators. Symptoms of poisoning include runny nose, teary eyes, blurred vision, double vision, dizziness, headache, drowsiness, vomiting, difficulty breathing, weakness, increased heart rate, increased blood pressure, and convulsions.

Immediate medical attention is indicated when chemical poisoning is suspected. More information is available on the [MedLine Plus: Poisoning](#) and the [Poison Control Centers](#) Web sites or by calling 800-222-1222.

# HYDROCARBONS

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Organic compounds composed mostly of carbon and hydrogen

## Examples

Petroleum distillates: Oils, wax, polish, gasoline, kerosene, pine oil, turpentine, naphtha, propane  
Halogenated: Carbon tetrachloride, trichloromethane  
Aromatic: Toluene, benzene, xylene  
Found in lighter fluid, paint, glue, lubricants, solvents and aerosol propellants

**Routes of entry:** Ingestion, inhalation or surface absorption

**Morbidity:** **Most deaths are from pulmonary effects of aspiration pneumonia**

Toxicity is related to the viscosity - Determines likelihood of entry into lung

- High viscosity = Low toxicity (vaseline, motor oil)
- Low viscosity = High toxicity (camphor, phenol)

Hydrocarbons are a leading cause of poisoning deaths. Many cases of teenagers abusing inhalants.

## Signs and Symptoms

NEURO	Malaise, headache, dizziness, slurred speech, CNS depression or excitement, ataxia, dulled reflexes (obtundation), seizures, coma
RESP	Coughing, choking, tachypnea, dyspnea, cyanosis, retractions, hypoxia, crackles, wheezing, hemoptysis, pulmonary edema, aspiration pneumonia - most serious side effect
CV	Pulse increased, dysrhythmias
GI	Nausea, vomiting, abdominal pain, diarrhea
MS	Foot and wrist drop with numbness and tingling
SKIN	Burns due to local contact; fever may be seen

## Treatment

- Symptomatic care
- VS stabilization, oxygen administration
- Consider DAI to protect airway
- Charcoal is ineffective, they will not bind hydrocarbons. May be a case where gastric lavage is useful.

# CARDIAC DRUGS

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## Beta blocking agents

<b>Examples:</b>	Betagan (levobunolol)	Corgard (nadolol)	Sectral (acebutolol)
	Betopic (betaxolol)	Inderal (propranolol)	Tenormin (atenolol)
	Blocadren (timolol)	Lopressor (metoprolol)	Timoptic (timolol)
	Brevibloc (esmolol)	Normodyne (labetalol)	Trandate (labetalol)
			Visken (pindolol)

## Signs and symptoms

HEENT	Diplopia
NEURO	Fatigue, sleepiness, headache, sedation, dizziness, confusion, seizure, coma
RESP	Bronchospasm, resp depression, cyanosis, pulmonary edema (esp. beta blockers)
CV	Bradycardia, heart block, hypotension (sometimes profound)
GI	Nausea, vomiting, diarrhea

## Treatment

- Monitor ECG and VS
- Emesis with ipecac is contraindicated
- Bradycardia, conduction defects, hypotension should respond to IVF, If no response to atropine, dopamine, and pacing: **GLUCAGON**  
Glucagon stimulates an increase in cellular cAMP just like a sympathomimetic, by acting on the same type of receptor/receptor complex (S-type G protein). Thus, causing an increase in heart rate and contractility that is not dependent on beta stimulation.  
Adult 1 mg IVP/IN/IO over 1 min; may need initial dose of 3 mg

## Calcium channel blockers (Calcium antagonists)

<b>Examples</b>	Cardizem (diltiazem)	Procardia, Adalat (nifedipine)
	Calan, Isoptin (verapamil)	Cardene (nicardipene)

## Signs and symptoms

NEURO	Drowsiness, Confusion, Seizures
RESP	Pulmonary edema
CV	Hypotension, bradycardia, dysrhythmias, tachycardia may be seen
GI	Nausea, vomiting

## Treatment

- Supportive care
- Emesis with Ipecac contraindicated due to potential for seizures, may cause vagal stimuli
- At hospital: Calcium chloride 10% 10-20 mL over 5-10 minutes IV - may improve BP

## Digging Deeper

Toxicity due to calcium-channel blockers (CCBs) or  $\beta$ -blockers results in significant morbidity and mortality.<sup>[9]</sup> The manifestations of toxicity are generally extensions of the drugs' pharmacologic and therapeutic effects and often include hypotension, bradycardia, conduction block, and myocardial depression.<sup>[28,29]</sup> Depending on the amount of the offending drug ingested and the patient's underlying cardiovascular health, the patient could remain asymptomatic or progress to cardiovascular collapse.

Subtleties in presenting symptoms can help differentiate CCB and  $\beta$ -blocker poisoning. Patients experiencing a CCB overdose tend to remain awake and alert, even in the event of profound hypotension and bradycardia, while patients with  $\beta$ -blocker poisoning are more likely to have an altered mental status and respiratory depression.<sup>[29]</sup> The more severe the CCB overdose, the more likely the patient is to exhibit

## Toxicology emergencies

hyperglycemia, because CCBs also inhibit the release of insulin from pancreatic  $\beta$ -cells via a calcium-dependent pathway.<sup>[30]</sup> Children experiencing a  $\beta$ -blocker overdose may develop hypoglycemia, an uncommon symptom in adults. Dihydropyridine CCBs such as nifedipine are more potent peripheral vasodilators than nondihydropyridine CCBs; they have limited effects on cardiac rhythm and are more likely to cause hypotension with reflex tachycardia. Propranolol, a  $\beta$ -blocker with high lipophilicity and sodium-channel-blocking effects, is more likely than other  $\beta$ -blockers to cause patients to have a seizure and to exhibit a widened QRS complex on electrocardiography.<sup>[28,29]</sup> Toxicity resulting from the ingestion of the combination of a  $\beta$ -blocker and a CCB can be particularly serious and life-threatening. Even at therapeutic doses, the ingestion of more CCB or  $\beta$ -blocker medication than is prescribed can be life-threatening in a patient with a tenuous cardiac history.

Because of the pathophysiologic similarities of CCB toxicity and  $\beta$ -blocker toxicity, their management is similar. The [treatment](#) of patients with bradycardia and hypotension begins with fluids and atropine, but patients who are more than mildly poisoned typically do not have an adequate response to these therapies. Other treatment modalities include calcium, glucagon, hyperinsulinemia–euglycemia therapy (HIET), vasopressors, cardiac pacing, i.v. 20% fatty acid emulsion, extracorporeal circulatory support, and intra-aortic balloon pump therapy.

### Calcium

Calcium plays an integral role in myocardial function and is necessary for automaticity, conduction, contraction, and vascular tone. In theory, the administration of exogenous calcium to patients with CCB toxicity should competitively increase calcium [entry](#) into the myocardium via nonblocked channels. Calcium has also been used to treat  $\beta$ -blocker toxicity.<sup>[28]</sup>

Along with atropine, calcium is considered a first-line therapy for CCB or  $\beta$ -blocker toxicity. Patients with mild toxicity seem to have an adequate response to calcium therapy; those with severe toxicity usually require additional therapies.

Calcium is available as either calcium chloride or calcium gluconate. Because of differences in the molecular weights of the chloride and gluconate components, 30 mL of 10% calcium gluconate is equivalent to 10 mL of 10% calcium chloride. Extravasation of calcium must be avoided. In particular, calcium chloride is extremely damaging to tissue should extravasation occur. For this reason, it is recommended that calcium chloride be administered through a central line or only with good peripheral venous access. Care should also be taken not to extravasate calcium gluconate, but the consequences are less severe, so the administration of calcium gluconate through a peripheral vein is more appropriate.

A reasonable starting dose in adults is 30 mL of calcium gluconate or 10 mL of calcium chloride, with additional doses administered in 15–20 minutes. After three doses, careful monitoring of ionized calcium is necessary to avoid dangerous hypercalcemia. Calcium is administered to improve hemodynamics.

Hypercalcemia may lead to an ileus, myocardial depression, hyporeflexia, and an altered mental status. The administration of calcium to a patient with cardioactive-steroid (e.g., digoxin) toxicity may lead to asystole and should be avoided.

**Implications for the Pharmacist** To avoid hypercalcemia and its associated risks, close monitoring of the serum ionized calcium level is required, especially in patients receiving multiple doses of exogenous calcium. The use of calcium should be avoided in a patient with known or suspected digoxin toxicity.

### Glucagon

It is glucagon's ability to increase cardiac cyclic adenosine monophosphate (cAMP) directly and independently of the  $\beta$ -adrenergic receptor that has established its role in the management of  $\beta$ -blocker overdoses.<sup>[29]</sup> The increase in cardiac cAMP enhances inotropy and chronotropy and may improve conduction.

**Glucagon causes dose-dependent and rate-related nausea and vomiting with a risk of aspiration;** thus, antiemetics such as metoclopramide and serotonin antagonists are often used in patients receiving the drug.<sup>[29]</sup> Other adverse effects of glucagon can include hyperglycemia, followed by hypoglycemia in rare cases; gastrointestinal (GI) smooth-muscle relaxation and diarrhea; hypokalemia; and, rarely, allergic reactions. Tachyphylaxis with continued administration of glucagon is a theoretical concern.

**Implications for the practitioner:** The doses of glucagon necessary for the management of  $\beta$ -blocker toxicity are much higher than those typically used to induce hyperglycemic or antispasmodic effects. The

## Toxicology emergencies

endpoints for discontinuing glucagon infusions are not clear; however, it is reasonable that once a patient is hemodynamically stable for a minimum of 6 hours, a slow taper of a single agent at a time can be employed. Anecdotal evidence and clinical experience suggest that once therapy is discontinued, close observation is necessary for a minimum of 12 hours.

### HIET

The management and outcomes of patients severely poisoned by CCBs or  $\beta$ -blockers have improved substantially since the advent of HIET.<sup>[31,32]</sup> High-dose insulin has long been reported to be an inotrope.<sup>[33]</sup> It was only in the late 1990s that HIET was demonstrated to be effective in treating patients severely poisoned with CCBs or  $\beta$ -blockers.<sup>[32]</sup> The mechanism of HIET's effectiveness has not been clearly delineated; the available data suggest it enhances carbohydrate use and energy production by myocardial cells, resulting in improved contractility.<sup>[34-37]</sup> Because of the alterations in myocardial cell metabolism, it is not surprising that the beneficial effects of HIET in patients with CCB or  $\beta$ -blocker toxicity are delayed, generally occurring after 15–60 minutes.<sup>[37-39]</sup> Therefore, HIET should be started early in the course of management. If a patient remains hypotensive and bradycardic after receiving fluids, atropine, calcium, and glucagon, HIET should be administered. As HIET is particularly effective in improving myocardial contractility, the early administration of HIET may avoid the need for vasopressors or allow the use of lower doses, thereby reducing the potential for ischemic consequences.<sup>[39]</sup>

The major adverse effects associated with HIET are hypoglycemia and hypokalemia. The sicker the patient is from a CCB overdose, the more likely it is that hyperglycemia will develop before HIET is instituted; as the patient recovers, the need for supplemental glucose increases.<sup>[30]</sup> Insulin causes an intracellular shift of serum potassium, and potassium supplementation should be considered when the serum potassium concentration is  $<3$  mEq/L.

HIET should begin with an IV loading dose of 1 unit/kg of regular insulin followed by an infusion of 0.5–1 unit/kg/hr.<sup>[39]</sup> The infusion dosage can be increased every 20–30 minutes. Doses of 2.5–3 units/kg/hr have been used depending on the response. Experimental studies have used even higher doses.<sup>[40]</sup> Serum glucose should be maintained at a concentration of  $>100$  mg/dL during HIET. A maximum insulin dose has not been established. If the initial blood glucose concentration is  $<400$  mg/dL, an i.v. loading dose of 0.5 g/kg dextrose should be administered with the insulin and followed by an infusion of 0.5 g/kg/hr of dextrose, with meticulous and frequent monitoring of serum glucose and potassium concentrations.<sup>[39]</sup> This dose of dextrose can be administered in a concentrated form (e.g., a 20–25% concentration) through a central line to avoid problems with fluid overload and venous irritation. The recommended goal is to maintain a serum glucose concentration of 100–250 mg/dL. A patient with a falling glucose concentration should be treated by increasing the amount of supplemental glucose (not by decreasing the insulin infusion) until the patient is hemodynamically stable.

**Implications for the hospitals:** The use of HIET has resulted in a decline in mortality among patients with severe CCB or  $\beta$ -blocker toxicity. There is a delay in the benefits of HIET, so it should be started early. A general rule of thumb is to initiate HIET when it is apparent that calcium and glucagon are ineffective or as soon as the decision is made to initiate a vasopressor.

Marraffa, J. M., Cohen, V., and Howland, M.A., (2012). Antidotes for toxicological emergencies: A practical review. *American Journal of Health-System Pharmacy*; 69(3), 199-212. [On-line] Posted: 02/14/2012.

# DIGOXIN

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**Examples:** Lanoxin, Lanoxicaps, digitoxin

**Toxicity** Adult 10 mg, Child 4 mg  
Death has been reported after ingestion of 23 mg

## Signs and symptoms

Onset (30 min) and peak manifestations (3-12 hrs) following acute poisoning  
Activates the parasympathetic nervous system

**HEENT** Visual disturbances, photophobia, aberrations of color (see yellow halos around lights)  
**NEURO** Drowsiness, fatigue, weakness, lethargy, headache,  
Psych complaints, abnormal dreams

**CV** Dysrhythmias - PAT with AV Block. In the largest case series of digoxin toxicity (Circulation Vol 81, No 6, June 1990, p. 1750), only 10 of 69 cases had a K > 6.4. When there is hyperkalemia from dig toxicity, the ECG shows accelerated junctional rhythm, ventricular dysrhythmias). It does not manifest the typical peaked T waves of hyperK.

**GI** Nausea, appetite loss, abdominal pain, vomiting, diarrhea

**Elect.** Hyperkalemia is common - The problem with Dig is that it is primarily renally excreted (about 85%; with the rest hepatically metabolized). In an otherwise healthy middle-aged adult with normal renal function - the half-life of Dig is ~36 hours. In renal failure, the half-life increases up to 5 days - so it is usually the renal dysfunction that predisposes the patient to develop Dig toxicity (rather than the other way around). As noted from the AHA update,- if you see hyperkalemia in severe Dig toxicity that is a very poor prognostic sign.

## Treatment

Supportive Management  
Hyperkalemia - Sodium bicarbonate or albuterol 10 – 20 mg / HHN  
Dysrhythmias - Treat per SOP

Digitoxin Specific Antibody Fragments (Digibind or Digifab) can be given at hospital for truly life-threatening Dig toxic arrhythmias. Once AB are given, can no longer follow the Dig level

Indicated for ingestions of 10 mg or more in adults, 4 mg child  
One vial contains 40 mg which will neutralize 0.6 mg of digoxin

## Digging Deeper

### Digoxin-specific Antibody Fragments

Digoxin-specific antibody fragments (Fab) are lifesaving agents in the management of toxicity associated with the use of digoxin and other cardioactive steroids, including digitoxin and those derived from oleander, fox glove, lily of the valley, and toad venom.<sup>[63]</sup> They are safe and effective in both adults and children with acute or chronic toxicity.<sup>[64-69]</sup>

Digitalis, the most widely used cardioactive steroid, has a narrow therapeutic index.<sup>[64,68]</sup> Cardioactive steroids act on the heart to enhance contractility, act on the conduction system of the heart to produce a variety of effects, and also act on the autonomic nervous system. The agents' toxicity is related to an exaggeration of those effects and often involves an increase in intracellular calcium. Electrocardiographic changes secondary to digoxin toxicity can be marked and highly variable.

In patients with acute digoxin poisoning, empiric treatment with digoxin-specific Fab should be considered in any patient exhibiting consequential rhythm or conduction disturbances, including symptomatic bradycardia or progressive heart block unresponsive to atropine; ventricular arrhythmias such as

**Toxicology emergencies**

ventricular tachycardia or fibrillation; or a serum potassium concentration of  $>5.0$  meq/L in the absence of another identifiable cause.<sup>[70,71]</sup> Significant nausea and vomiting after an acute digoxin overdose might also warrant the use of digoxin-specific Fab, since conduction disturbances are likely to follow. This form of therapy also should be considered if there is firm evidence of ingestion of  $>4$  mg of digoxin by a child or  $>10$  mg by an adult, as those total body loads of digoxin will almost certainly cause significant cardiac toxicity as the digoxin moves from the blood compartment to the heart.

The indications for digoxin-specific Fab therapy in cases of chronic digoxin poisoning are less clear but similar to those for cases of acute poisoning. Treatment with digoxin-specific Fab should be considered in any patient with a life-threatening or potentially life-threatening dysrhythmia, including severe sinus bradycardia or heart block unresponsive to atropine, as well as ventricular ectopy, tachycardia, or fibrillation.<sup>[71-73]</sup> GI complaints are less common in the context of chronic digoxin poisoning, but confusion and an altered mental status are more frequent in the elderly and might suggest the need for digoxin-specific Fab in a patient with a chronically elevated serum digoxin concentration ( $>2.5$  ng/mL). Patients at risk for chronic digoxin toxicity include elderly patients with declining renal function, patients who have received inappropriate dosages of digoxin, patients with electrolyte abnormalities, and patients administered drugs known to inhibit the elimination of digoxin.

Digoxin-specific Fab is generally well tolerated. The adverse-effect profile includes the potential for hypokalemia, worsening of heart failure, a rapidly conducted ventricular rate, and, rarely, allergic reactions.<sup>[64]</sup>

The dosage calculation for digoxin-specific Fab can be made according to the known ingested digoxin dose, according to the serum digoxin concentration, or empirically. The empiric dosing for acute toxicity is 10–20 vials (each 38- or 40-mg vial binds 0.5 mg of digoxin); the empiric dosing for chronic toxicity is 3–5 vials for adults and 1–2 vials for children.<sup>[73]</sup> To calculate a dosage using a known serum digoxin concentration, the concentration (in nanograms per milliliter) is multiplied by the patient's weight (in kilograms) and divided by 100; the result is rounded up to the nearest integer to arrive at the required number of vials.

**Implications for the practitioner** The goal of treatment with digoxin-specific Fab is to reverse digoxin-induced cardiotoxicity. Monitoring should include electrocardiography and serum potassium determinations. Once digoxin-specific Fab has been administered, serum digoxin concentrations are no longer useful in dosage calculation, as there is a resultant increase in the total digoxin concentration; therefore, repeat digoxin concentrations should not be obtained for 24 hours.<sup>[74,75]</sup>

Marraffa, J. M., Cohen, V., and Howland, M.A., (2012). Antidotes for toxicological emergencies: A practical review. *American Journal of Health-System Pharmacy*; 69(3), 199-212. [On-line] Posted: 02/14/2012.

# SALICYLATES

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Decreasing incidence with packaging improvements and increased use of APAP (Acetaminophen)

**Examples** Alka-Seltzer, Anacin, Ascriptin, Bayer, Bufferin, Disalcid, Doan's Pills, Easprin, Ecotrin, Emprin, Mono-Gesic Tablets, P-A-C, Trilisate, Zorprin  
Combination products - Fiorinal, Percodan, Pepto-Bismol

## Types of Ingestion

Acute	Accidental - often child
Intentional	Frequently suicide attempt
Chronic	Causing ulcers, GI bleeding and renal damage

## Signs and symptoms

HEENT	Tinnitus (ringing in the ears), visual complaints
NEURO	Lethargy, confusion, disoriented, seizures, coma (indicator of poor prognosis: However, in one study of salicylate fatalities, 45% were alert upon presentation to hospital, McGuigan, 1987)
RESP	Tachypnea, non-cardiogenic pulmonary edema common
Acid/base	Acidosis stimulates respiratory center causing hyperventilation, initial respiratory alkalosis is followed by metabolic acidosis
CV	Dysrhythmias due to electrolyte abnormalities
GI	Nausea, vomiting, abdominal pain, hemorrhage, dehydration (caused by hypothermia, hyperventilation, diaphoresis)
SKIN	Hyperthermia common (treat with external cooling, no ASA or APAP)
Toxic:	150-200 mg/kg
Lethal:	500 mg/kg (10-30 Gm)

## Treatment

- Routine toxicology management (charcoal effective)
- IV fluid replacement
- IV bicarbonate may be used to alkalinize urine - Correct pH to 7.4  
Acid urine excretes only 10% - half-life 200 hours  
Alkaline urine excretes 85% - half-life 4 hours

# ACETAMINOPHEN (APAP)

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**Examples** Tylenol, Anacin-3, Apacet, Datriil, Excedrine, Genapap, Halenol, Liquiprin, Panadol, Tempra. Found in numerous cough, cold, pain medications either alone or in combination with other drugs. Widespread availability - high incidence of OD

Acute APAP ingestion is defined as a toxic amount of the drug taken over a maximum time period of eight hours. Time of ingestion should be listed as when the patient *started* ingesting APAP.

## Life threatening due to delayed hepatic toxicity

**Toxicity**

Adult	=	150 mg/kg (30 tabs)
Child	=	140 mg/kg

**Signs and symptoms** appear in 4 stages:

< 24 hrs	GI symptoms often mild, malaise, weakness, fatigue, anorexia, N/V, diaphoresis
24-48 hrs	RUQ abdominal pain, elevated liver enzymes, decreased urine
72-96 hrs	Jaundice, liver disruption
4-14 days	Gradual recovery or progressive liver failure

## Treatment

- Routine toxicology management
- Charcoal - some advocate removal (by lavage) if given less than 1 hr before Mucomyst
- Antidote at hospital: Mucomyst (*N*-acetylcysteine, "NAC") PO
- Administer if toxic level on nomogram or toxic dose (7.5 grams) ingested within 24 hrs
- Best if therapy initiated within 8 hours, most effective if administered within 16 hrs, but has statistical efficacy when given up to 24 hrs post-ingestion
- Load 140 mg/kg, then q.4h 70 mg/kg X 17 doses PO over 72 hours
- Has foul smell, like rotten eggs. Mix with juice or soda. May have to give via NGT
- acetylcysteine (Acetadote) for IV injection over 20 hours. Most effective when administered within eight to 10 hours after overdose. Caution in patients with bronchospasm or asthma.

## Digging Deeper

### ***N*-acetylcysteine**

*N*-acetylcysteine (NAC) is a lifesaving therapy in the management of acetaminophen poisoning.<sup>[102-109]</sup> While acetaminophen is still present in the plasma, NAC acts as an antidote, primarily by replenishing glutathione stores. Secondly, it acts as a glutathione substitute and replenishes sulfate. These mechanisms of action all serve to either limit the formation of the toxic metabolite or to detoxify it; in this way, if NAC is administered in a timely fashion, acetaminophen toxicity can be prevented.<sup>[108,109]</sup>

The Rumack-Matthew<sup>[106]</sup> nomogram is used to predict whether patients will develop hepatotoxicity, defined as a serum AST concentration of >1000 units/L, based on an initial plasma acetaminophen concentration obtained four or more hours after a single acute ingestion of acetaminophen. Indications for the initiation of NAC include a serum acetaminophen level on or above the Rumack-Matthew nomogram; situations in which a serum acetaminophen level is not available within eight hours of a potentially toxic ingestion; and hepatotoxicity, as defined by clinical symptoms or liver enzyme elevations above baseline.

Once fulminant hepatic failure has occurred, whether it is acetaminophen related or not, and even when all of the acetaminophen has already been metabolized, i.v. NAC therapy is still beneficial and may be life saving. In patients with acetaminophen-induced fulminant hepatic failure, i.v. NAC decreased mortality by 50% relative to use of a placebo.<sup>[110]</sup> NAC is believed to work through antioxidant and antiinflammatory effects, some related to glutathione formation, to improve oxygen delivery and utilization. Intravenous NAC

**Toxicology emergencies**

improves cerebral, cardiac, and renal blood flow, resulting in the improved function of extrahepatic organs. NAC may also be beneficial in preventing or treating the hepatotoxicity associated with carbon tetrachloride,<sup>[111,112]</sup> *Amanita phalloides*,<sup>[113]</sup> and other toxins.<sup>[114,115]</sup>

Although no head-to-head studies comparing i.v. and oral NAC have been published, both routes are believed to be equally efficacious when NAC is administered within eight hours of an acetaminophen overdose.<sup>[116]</sup> NAC is effective and beneficial when given later, although the rate of hepatotoxicity increases. However, only i.v. NAC is demonstrated to be beneficial in patients with fulminant hepatic failure.<sup>[110,117]</sup> Theoretically, oral administration should provide a higher concentration of NAC to the liver due to the high extraction ratio, and i.v. dosing should provide a higher serum NAC concentration that may be more beneficial at extrahepatic sites.

The FDA-approved dosing of IV NAC is a loading dose of 150 mg/kg infused over 1 hour followed by a *total* of 50 mg/kg over four hours, followed by a *total* of 100 mg/kg given over the next 16 hours. Anaphylactoid reactions can occur, particularly with the loading dose, which is a concern in the ED; the manufacturer recommends that the loading dose be given over 60 minutes to minimize this risk.<sup>[118]</sup> In the event of an anaphylactoid reaction, discontinuing the infusion is the first step, to be followed by supportive therapy. Once the reaction abates, i.v. NAC therapy can be restarted at a much slower infusion rate or oral NAC can be administered. In patients with severe reactive airway disease, oral NAC (which rarely produces an anaphylactoid reaction) might be preferred to i.v. NAC. Improper dilution or dosing has resulted in overdoses of NAC, leading to hyponatremia, cerebral edema, and death.<sup>[105,110,117,119]</sup>

The FDA-approved dosing of oral NAC is 140 mg/kg as a loading dose followed by 70 mg/kg every four hours for a total of 17 doses. The oral dose must be repeated if emesis occurs within one hour. Although oral NAC is rarely associated with anaphylactoid reactions, nausea and vomiting occur frequently, may delay the time to administration of an effective dose, and often require the administration of an antiemetic.<sup>[120,121]</sup>

The benefits of NAC outweigh the risks in pregnant patients with acetaminophen toxicity who meet the criteria for NAC administration. Although there are conflicting data, i.v. NAC is often recommended with the belief that i.v. NAC more readily crosses the placenta.<sup>[122,123]</sup>

NAC should not be discontinued until the acetaminophen concentration is undetectable or lower than the level of sensitivity; the AST concentration is normal or significantly improved; the synthetic function of the liver has improved, as evidenced by an International Normalized Ratio of <2; and there is no evidence of an altered mental status due to hepatic encephalopathy.<sup>[124]</sup>

**Implications for the Practitioner** The decision to treat with NAC must be made quickly and based on multiple factors, including the determination of a toxic acetaminophen level and the time since overdose. NAC is nearly 100% hepatoprotective if given within the first eight hours of an overdose, and its efficacy decreases every hour after that.<sup>[108]</sup> Although most effective if given early, NAC has a clear role in late therapy and has been shown to decrease mortality.<sup>[117,125]</sup>

NAC therapy should be continued until acetaminophen is undetectable, the AST concentration is improving, and evidence of hepatic failure is no longer present. If treatment is necessary beyond the standard 21-hour dosing regimen for i.v. NAC, the third part of the protocol (6.25 mg/kg/hr) should be continued. Unusually high or prolonged serum acetaminophen concentrations may require a change in the NAC protocol; consultation with a poison center is critical.

Marraffa, J. M., Cohen, V., and Howland, M.A., (2012). Antidotes for toxicological emergencies: A practical review. *American Journal of Health-System Pharmacy*; 69(3), 199-212. [On-line] Posted: 02/14/2012.

# IBUPROFEN

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**Examples** Motrin, Advil, Nuprin

## Signs and symptoms

Majority of cases are asymptomatic

HEENT	Nystagmus, diplopia, H/A, tinnitus
NEURO	Lethargy, drowsiness, coma
RESP	Apnea has been reported
CV	Hypotension, bradycardia
GI	Abdominal pain, nausea, vomiting
ACID/BASE	Metabolic acidosis may result

## Treatment

- Routine Toxicology Management
- Treat acidosis with sodium bicarbonate

# ALCOHOLS

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**Methanol** (Methyl alcohol, wood alcohol): Paint and removers, varnish, solvent, liquid canned fuel

Potent inhibitor of alcohol dehydrogenase. Highly toxic, **produces metabolic acidosis, blindness, and death** due to high levels of formic acid (> 20 mmol/L). Ingestion of as little as 4 mL (absolute methanol) has caused **blindness**, and 15 mL (40% methanol) has caused death.

May have latent period of 18-24 hrs between ingestion and symptoms

## Signs and symptoms

HEENT	Blurred or double vision, constricted visual fields, whiteness of or spots in visual fields, decreased visual acuity, nystagmus, pupils non-reactive
NEURO	Intoxication similar to ETOH, coma, seizures
RESP	Breathlessness, tachypnea, respiratory failure
CV	Pulse may be slow
GI	Abdominal pain, anorexia, nausea, vomiting

Transport ASAP. Patient can receive fomepizole and dialysis at the hospital that may reverse the effects.

## Ethylene Glycol

**Examples:** Antifreeze, hydraulic brake fluid, solvent  
Sweet taste - ETOH substitute for destitute

**Morbidity:** Death has occurred after ingestion of 60 mL  
Toxicity is from breakdown products and acidosis

## Signs and symptoms

Phase I	30 min to 12 hrs after ingestion ETOH-like inebriation, minor ataxia, slurred speech, seizures, coma, metabolic acidosis, tachypnea, hematuria
Phase II	12-36 hr post ingestion Tachypnea, cyanosis, pulmonary edema, cardiomegaly
Phase III	2-3 days post ingestion Renal failure - dialysis candidate 3rd and 7th CN palsies

## Treatment

Symptomatic care: Manage acidosis with bicarbonate

Ethanol therapy at hospital - partially inhibits formation of toxic metabolites

1 gm/kg 100 proof liquor = 50% alcohol or 50 g/100 mL

Smirnoff Blue vodka is 100 proof

Aim at achieving and maintaining blood level of 100-130 mg/dl

Hospitals may use an alcohol dehydrogenase inhibitor agent like fomepizole (Antizol). Metabolizes ethanol causing excretion of the ethylene glycol unchanged in the urine. Loading dose costs \$1000, two days of therapy is \$4000 but does not cause nearly as many side effects as alcohol therapy.

## Isopropyl Alcohol (Isopropanol)

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**Examples:** Disinfectants, cleaning agents, hair sprays, skin lotions, most rubbing alcohol contains 70% isopropanol alcohol

**Toxicity:** Toxic by oral, dermal, and inhalation exposures  
More toxic than ethanol, but less toxic than methanol

### Signs and Symptoms

HEENT Characteristic rubbing alcohol smell (no retinal toxicity like methanol)  
NEURO Rapid onset of deep coma, areflexia, CNS depression, sleepiness, lethargy  
RESP Respiratory failure may occur  
CV Tachycardia common, hypotension may occur, cardiomyopathy, Dysrhythmias  
GI Vomiting, gastritis, dehydration  
Hypothermia may occur

### Treatment

- Symptomatic and supportive treatment
- Emesis not recommended as CNS depression occurs rapidly
- Dermal exposure - wash thoroughly with soap and water
- Eye exposure - irrigate copiously, eye referral

## Ethanol (ETOH)

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Excessive consumption of alcohol was responsible for 88,000 deaths and millions of shortened lifespans between 2006 and 2010, making it the fourth-leading cause of preventable death in the United States, according to recent findings published in **CDC's** Morbidity and Mortality Weekly Report (3-15).

The report, which examined data from 11 U.S. states, placed the median alcohol-related death rate at 28.5 per 100,000 people, with the highest death rate at 50.9 per 100,000 in New Mexico and the lowest at 22.4 per 100,000 in Utah. About 70% of the preventable deaths involved working-age adults.

It found that, although the percentage of individuals who consume alcohol has not changed much over the past 10 years, binge drinking and heavy drinking have become more prevalent. Heavy drinking is defined as drinking more than two drinks daily for men and more than one drink daily for women, while binge drinking involves consuming five drinks in one occasion for men and four drinks in one occasion for women.

### "Smoking Alcohol"- Coming To An ED Near You?

Robert Glatter, MD, Emergency Medicine, 08:19PM Jun 7, 2013

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A new and concerning trend to get drunk without gaining weight referred to as "smoking alcohol" or "drunkorexia" has been gaining popularity recently among teens and college age individuals. People vaporize the alcohol using a number of methods with bicycle pumps or poured over dry ice.

The alcohol vapors go straight to the brain from the lungs after being inhaled, creating an exceedingly high alcohol level quite rapidly -- it is achieved by bypassing the stomach and liver and any metabolism -- and as a result, no calories. In most cases, when people drink alcohol, they vomit from the gastric irritation when they become more intoxicated. However, when alcohol is vaporized and inhaled, this is unlikely to occur, and alcohol levels may dangerously rise without any warning. This is not only dangerous and can lead to alcohol intoxication quickly, but can be irritating to the bronchioles and alveoli, leading to drying of the mucosa and increased susceptibility to lung injury and infection.

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### Signs and Symptoms

HEENT Impaired eye movements, nystagmus  
NEURO Mental confusion, ataxia, lethargy, coma, exaggerated emotional states, Seizures, Disturbances in sensation and perception  
RESP Respiratory failure  
CV Tachycardia common, hypertension may be seen

**Toxicology emergencies**

GI                    Nausea, vomiting, abdominal pain  
                         Hypoglycemia

**Treatment**

- Routine toxicology management
- Position patient to avoid aspiration, patient will often vomit
- Check blood sugar, administer glucose if less than 60 mg/dl, preceded by thiamine 100 mg to prevent Wernicke-Korsakoff syndrome
- Charcoal not effective
- Midazolam for DTs and seizures
- Consider need for magnesium
- Treat alcohol withdrawal - DTs have a high mortality

**Digging Deeper - Antidotes for Toxic-alcohol Poisoning**

The use of ethanol or, preferably, fomepizole for alcohol dehydrogenase (ADH) inhibition is a mainstay in the management of toxicity due to ingestion of methanol, ethylene glycol, or diethylene glycol.<sup>[6-8]</sup>

The toxicity of methanol and of ethylene glycol is well described, and each year in the United States there are about 5000 exposures that require [treatment](#) and 20–30 associated deaths reported to poison centers.<sup>[2,9,10]</sup> Methanol and ethylene glycol, as parent compounds, are relatively nontoxic. However, they are metabolized by ADH to toxic metabolites that can cause end-organ damage and death. Methanol is metabolized via ADH to formic acid, which results in anion-gap metabolic acidosis and ocular toxicity. Retinal toxicity secondary to methanol poisoning is usually irreversible.<sup>[6,11]</sup> Ethylene glycol is metabolized via ADH to [glycolic acid](#), which results in anion-gap metabolic acidosis, and oxalic acid, which results primarily in renal toxicity due to the formation of calcium oxalate crystals.<sup>[7,12]</sup> Both can produce irreversible CNS toxicity.

Poisoning by diethylene glycol (historically and tragically used as a glycerin substitute and also in household products such as wallpaper stripper and Serno brand heating fuel<sup>[13,14]</sup>) is less common but associated with very high morbidity and mortality.<sup>[15,16]</sup> Diethylene glycol is metabolized via ADH to hydroxy-ethoxyacetic acid and diglycolic acid and causes anion-gap metabolic acidosis, bilateral cortical necrosis, and sensorimotor polyneuropathy.<sup>[16-20]</sup>

**Ethanol**

For many years, ethanol has been used to inhibit ADH and limit the metabolism of methanol and ethylene glycol to their respective metabolites.<sup>[21]</sup> The dose of ethanol needed to competitively inhibit ADH depends on the comparative affinity of the specific toxic alcohol for ADH. Most authorities recommend using a dose of ethanol sufficient to achieve and maintain a serum ethanol concentration of 100–150 mg/dL. In the presence of ethanol, the half-lives of ethylene glycol (in patients with normal renal function) and methanol are approximately 17.5 and 45 hours, respectively.<sup>[6,7]</sup>

Ethanol can be administered intravenously or orally. However, a commercial IV preparation of ethanol is no longer available, and extemporaneous preparation is too time-consuming to be considered satisfactory. A loading dose is necessary to quickly achieve the desired serum concentration of 100–150 mg/dL; then a maintenance dose is administered, using serum ethanol concentrations to maintain the desired [target](#). Repeat evaluations of the serum ethanol concentration are required to ensure that the target level is achieved and maintained. Individual differences in ethanol metabolism occur due to pharmacogenetics and whether the patient is induced or becomes induced secondary to chronic ethanol exposure.<sup>[6,7]</sup>

The risks associated with ethanol administration include central nervous system (CNS) depression, hypoglycemia (due to decreased gluconeogenesis), nausea, and vomiting. Intravenous administration of ethanol poses an additional risk of phlebitis and hypertonicity with hyponatremia. Frequent assessment of the serum ethanol concentration and monitoring of venous [blood glucose](#) are required.

**Fomepizole**

Fomepizole competitively inhibits ADH and is an effective and safe antidote for both ethylene glycol and methanol toxicity.<sup>[6,7]</sup> In the presence of fomepizole, the half-lives of ethylene glycol (in patients with normal renal function) and methanol are 14.5 and 40 hours, respectively.<sup>[22]</sup>

The Food and Drug Administration (FDA)-approved regimen of fomepizole is an IV. loading dose of 15

### Toxicology emergencies

mg/kg over 30 minutes followed by a dose of 10 mg/kg every 12 hours, with the frequency of dosing increased to every 4 hours during hemodialysis.<sup>[23]</sup> Fomepizole induces its own metabolism, presumably through the cytochrome P-450 2E1 isoenzyme; therefore, after 48 hours of drug administration, the fomepizole dose should be increased to 15 mg/kg every 12 hours.

Fomepizole is generally well tolerated. Adverse events reported with the use of fomepizole include mild irritation at the IV infusion site, headache, nausea, dizziness, drowsiness, and a bad or metallic taste in the mouth.

Although there are no head-to-head comparisons of fomepizole versus ethanol for the management of toxic-alcohol poisoning, the former's ease of administration and relative lack of serious adverse effects have elevated it to preferred status. The clinical advantages of fomepizole over ethanol are a much higher potency of ADH inhibition ( $K_i = 0.1 \mu\text{mol/L}$ , a 1000-fold higher affinity than that of ethanol), better maintenance of therapeutic blood concentrations, and fewer adverse effects; moreover, the administration of fomepizole is less labor-intensive.<sup>[12]</sup>

### Additional and Supportive Therapy

In addition to antidote administration, hemodialysis should be considered in all toxic-alcohol exposures in which toxic metabolites have already formed, as evidenced by anion-gap metabolic acidosis or end-organ damage, and for patients with toxic serum methanol or ethylene glycol concentrations whose elimination of parent or toxic metabolites is expected to be inordinately prolonged (e.g., cases involving significant methanol exposure or ethylene glycol ingestion by a patient with renal impairment). Empiric hemodialysis is recommended if the serum methanol concentration is  $>25 \text{ mg/dL}$  and if the serum ethylene glycol concentration is  $>50 \text{ mg/dL}$  with renal insufficiency.<sup>[6,7]</sup> Hemodialysis also should be considered in cases of severe isopropyl alcohol poisoning in patients with hemodynamic instability.

Intravenous administration of 50 mg of folic acid every six hours enhances methanol elimination and has been shown to prevent retinal toxicity in animal models.<sup>[8,24,25]</sup> Also, urinary alkalization (i.e., a urine pH of  $>8$ ) with IV sodium bicarbonate enhances formate elimination and may reduce the distribution of formic acid to the eye.

Theoretically, the use of IV thiamine hydrochloride 100 mg and IV pyridoxine hydrochloride 50 mg every six hours should shunt the metabolism of ethylene glycol away from production of oxalic acid to production of less toxic metabolites<sup>[26,27]</sup> though there are no data from studies of humans to support this practice, these agents are well tolerated and the potential benefits outweigh any risks.

**Implications for the Pharmacist** Methanol or ethylene glycol toxicity should be suspected in a patient with anion-gap metabolic acidosis in whom laboratory testing reveals a low (or no) ethanol concentration, no ketones, and a normal lactic acid concentration (clinicians need to be aware that some test results can be skewed by glycolic acid, the toxic metabolite of ethylene glycol). Fomepizole and adjuvants that act as cofactors should be used as soon as toxic alcohols are included in the differential diagnosis. Fomepizole should be continued until the patient is no longer acidemic and the toxic-alcohol serum concentration is presumed or confirmed to be  $<25 \text{ mg/dL}$ . The availability of testing for toxic alcohols is limited.

Marraffa, J. M., Cohen, V., and Howland, M.A., (2012). Antidotes for toxicological emergencies: A practical review. *American Journal of Health-System Pharmacy*; 69(3), 199-212. [On-line] Posted: 02/14/2012.

# OPIATES

**Opioid pain relievers and benzodiazepines: Daily US stat:** 114 people die as a result of OD 6,748 are treated in the ED. Deaths from prescription painkillers have reached epidemic proportions. The number of overdose deaths is now greater than those of deaths from heroin and cocaine combined. **2010 stat:** Enough prescription painkillers were prescribed to medicate every American adult around the clock for a month!

COMMON PRESCRIPTION OPIOIDS	
CHEMICAL NAME	SELECTED BRAND NAMES
Oxycodone	Oxycontin, Percodan, Percocet
Propoxyphene	Darvon, Darvocet
Hydrocodone	Vicodin, Norco, Lortab, Lorcet
Hydromorphone	Dilaudid, Exalgo, Opana ER
Morphine	MS Contin, Kadian, Roxanol, Morphine Sulfate ER
Fentanyl	Duragesic, Sublimaze, Actiq
Methadone	Dolophine, Methadose, Diskets

Figure 2 MCHC Prescription Drug Abuse (12/13) p. 5

*Additional opiates: Codeine, heroin, meperidine (Demerol), diphenoxylate/atropine (Lomotil), Krokodil (desomorphine), Talwin, tramadol (Ultram), Tylox, Wygesic*

**Common street names for these drugs include: hillbilly heroin, oxy, OC, oxycotton, percs, vikes, happy pills.**

Routes	PO, IV, sub-q injection, intranasal, inhalation (smoking), body packing
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Note: Since 2010, OxyContin (controlled-release oxycodone) has been available in a formulation that prevents it from being chewed, crushed, or dissolved. A crush-resistant formulation of hydromorphone (Opana ER) was approved in September 2012.

## Signs and Symptoms

**Early:** Euphoria, drowsiness, nodding, nausea, **constricted pupils**; however, if hypoxic may be midrange or dilated

**Late:** **Respiratory depression** - major sign and cause of death  
**CNS depression** - seizures  
 BP decreased  
 GI stasis and constipation  
 Relative bradycardia  
 Relative hyperthermia

**Withdrawal:** Piloerection (gooseflesh), yawning, myalgia, lacrimation, rhinorrhea, increased oral secretions, sweating, nasal congestion, vomiting, abdominal cramping, diarrhea

The only heroin overdoses that may be problematic when reversed are those who have been using poly-drugs. If they have done speedballs (heroin and amphetamines), getting rid of the opiate will wake them going 100 mph.

**Treatment** Methods of street resuscitation by peers may include packing victim in ice or injecting milk

- Routine toxicology management – ABCs
- In an opioid-dependent patient, an inappropriate dose of naloxone has the potential to precipitate opioid withdrawal and to produce or worsen acute lung injury. It is advisable to start with a dose of 0.04 mg in all patients and adjust the dose upward in

## Toxicology emergencies

increments of 0.04 mg. That dose can safely reverse respiratory depression without producing unwanted and potentially dangerous withdrawal.

- If AMS + RR < 12 and substance unknown (pupils may be small): Naloxone standard dose for adults
- Peds dose – **NALOXONE (Narcan) 0.1 mg/kg** to a max single dose of 0.4 mg **IVP/IN/IO/IM**. May repeat prn in small doses (0.01-0.03 mg/kg) up to 2 mg if needed titrated to maintain ventilations.

Administer cautiously/slow for a known heroin OD - may need to restrain in advance  
Be prepared to deal with a potentially unstable airway; increased airway secretions (mainly nasal); tachycardia and hyperarousal; chest pain; SOB; diarrhea; agitation and violent behavior; and **emesis**.

- Patients may experience intense pain during withdrawal
- Fighters are usually concomitantly intoxicated. on crack, or on methamphetamines

The slower the course of reversal the easier it is to handle the side-effects.

Ventilate the patient to maximize oxygenation.

Increased dose needed for synthetic opiates like Darvon.

Hospitals may give Haldol 5 mg and Ativan 2 mg IM (B52) for extreme agitation.

Assess for hypothermia, cerebral, cardio/pulmonary complications

## Digging Deeper - Naloxone

The most commonly used antidote in the ED setting,<sup>[2]</sup> naloxone is a competitive antagonist at all opioid receptors, including the  $\mu$ -opioid receptor.<sup>[126,127]</sup> It is a well-established antidote for respiratory depression secondary to opioid toxicity. The efficacy and safety of naloxone are dose dependent. In a previously opioid-naïve patient experiencing an opioid overdose, even high doses of naloxone can be given safely.<sup>[128]</sup> However, **Opioid withdrawal with abrupt catecholamine release, especially in an apneic patient, is likely to induce vomiting and aspiration or acute lung injury.**

Although case reports have suggested that naloxone may be useful in reversing toxicity due to clonidine,<sup>[129,130]</sup> ibuprofen,<sup>[131]</sup> valproic acid,<sup>[132,133]</sup> and captopril,<sup>[134]</sup> the reported effects were quite variable, often minor, and usually inadequate.

Buprenorphine is a partial  $\mu$ -agonist whose toxic effects cannot be easily reversed with naloxone. Buprenorphine has a very high affinity for the  $\mu$ -receptor and most likely affects  $\mu$ -receptor subtypes in a dose-dependent and variable manner; this makes reversal with naloxone tricky, and a bell-shaped dose-response curve has been described, indicating that a dose too low or too high will be ineffective. In one experimental model, adults required an i.v. naloxone loading dose of 2–3 mg followed by a continuous infusion of 4 mg/hr for one hour before the respiratory depressant effects of buprenorphine were reversed;<sup>[135–139]</sup> dosages greater than 4 mg/hr were actually ineffective, consistent with a bell-shaped dose-response relationship.

The IV route of naloxone administration is preferred due to a predictable, quick, and titratable onset of action. Oral or sublingual administration result in poor absorption and limited effects.<sup>[140]</sup> Although naloxone is well absorbed with other parenteral routes of administration (intralingual, endotracheal, intranasal, subcutaneous, and intramuscular), a delayed onset of action or difficulty in titrating the dose makes those routes less desirable.

An initial naloxone dose of 0.04–0.05 mg IV in both opioid-dependent and opioid-naïve adult patients is recommended.<sup>[140]</sup> Increasing the dose until reversal of respiratory depression maximizes the benefits while minimizing the potential for significant opioid withdrawal. Titration can be accomplished by doubling the dose every one to two minutes or escalating the dose from 0.05 mg to 0.1 mg to 0.4 mg to 2 mg to 10 mg. During dose titration, bag-valve mask ventilation should be used as necessary. Although there is not a consensus on the initial dose, starting with a lower dose of naloxone (0.04–0.05 mg) rather than the "standard" 2-mg dose is considered best practice. A lack of sufficient patient response to treatment with 10 mg of naloxone should call into question a diagnosis of isolated opioid toxicity. Patients experiencing an overdose of synthetic opioids (e.g., buprenorphine, fentanyl, methadone) often require higher doses of naloxone but generally respond to doses of 10 mg.

Due to the relatively short half-life of naloxone, the duration of its clinical effect is generally 30–90 minutes.

## Toxicology emergencies

This relatively brief duration of effect is critical to clinicians because the duration of effect of the opioid is frequently much longer than that of naloxone and, therefore, respiratory depression may recur. Repeat doses or a continuous infusion at an hourly dose equal to two thirds of the initial dose of naloxone may be necessary, so close monitoring of the patient is required in the ED. It is recommended that the naloxone infusion be started at two thirds of the hourly dose that was effective in reversing the respiratory depression. This is based on a pharmacokinetic study done in the 1980s.<sup>[140]</sup>

Marraffa, J. M., Cohen, V., and Howland, M.A., (2012). Antidotes for toxicological emergencies: A practical review. *American Journal of Health-System Pharmacy*; 69(3), 199-212. [On-line] Posted: 02/14/2012.

## Heroin Toxicity

Rania Habal, MD; Chief Editor: Michael R Pinsky, MD, CM, FCCP, FCCM

Updated: Apr 15, 2011

<http://emedicine.medscape.com/article/166464-overview> Accessed 1-12-13

### Background

Heroin (diacetylmorphine) is a semisynthetic narcotic that was first synthesized in 1874. It was originally marketed as a safer, nonaddictive substitute to morphine. Soon after its introduction, heroin was realized to be clearly as addictive as morphine, prompting the US government to institute measures to control its use. By 1914, the Harrison Narcotics Act prohibited the use of heroin without a prescription. In 1920, the Dangerous Drugs Act prohibited the use of heroin altogether, thus driving it underground. In the United States, heroin remains one of the most frequently abused narcotics.

In its pure form, heroin is a white powder with a bitter taste. Street heroin samples are frequently mixed with other substances so dealers may maximize their profits. Because of these impurities and additives, street heroin may appear in various hues and colors, ranging from white to dark brown. Heroin is occasionally sold as a black, tarry substance, especially when crude processing methods are used to manufacture it.

The presence of impurities and additives also limits heroin absorption through mucous membranes, thus limiting its "rush" and "high" when it is sniffed or snorted. In patients who are dependent on heroin, intravenous injection ("mainlining") becomes the only effective method of heroin use. During the 1990s, the purity of US street heroin increased significantly, and its price sharply dropped. In 1980, for example, the average street sample (100-mg bag) contained 3.6% heroin (3.6 mg of heroin) and cost \$3.90, compared with 1999, when the average street sample contained 38.2% heroin and cost \$0.80.

Samples from South America appeared to have the highest purity, reaching the 90% range. Not surprisingly, this dramatic increase in heroin purity, coupled with the well-publicized dangers of intravenous drug use, led to a change in the pattern of use. Snorting and smoking became the methods of choice and were especially favored by the younger users and new users. Recent samples, however, have demonstrated a rise in impurities. Analysis of heroin powder seized by the US Food and Drug Administration (FDA) in 2005 revealed a heroin content that ranged from 7.3-75%.

Heroin poisoning occurs when an individual accidentally or intentionally overdoses on the drug or when an ingested heroin packet ruptures in the GI tract of a "body packer" or "body stuffer."

### Pathophysiology

Heroin is a highly addictive semisynthetic opioid that is derived from morphine. When used intravenously, it is 3-5 times more potent than its parent compound and is able to modulate pain perception and cause euphoria. Similar to morphine, heroin and its metabolites have mu, kappa, and delta receptor activity. In general, stimulation of the mu receptors results in analgesia, euphoria, CNS depression, respiratory depression, and miosis. Stimulation of the delta and kappa receptors also results in analgesia, but the kappa receptors are mostly involved in spinal analgesia.

Heroin, like morphine and other narcotics, reduces the brain's responsiveness to changes in PCO<sub>2</sub> and hypoxia, thus resulting in respiratory depression. It also reduces peripheral vascular resistance (resulting in mild hypotension), causes mild vasodilation of the cutaneous blood vessels (resulting in flushing), and stimulates histamine release (resulting in [pruritus](#)).

## **Toxicology emergencies**

Heroin's inhibitory effects on baroreceptor reflexes results in bradycardia, even in the face of hypotension.

Finally, heroin decreases gastric motility, inhibits the effect of acetylcholine on the small intestine, and diminishes the colonic propulsive waves, resulting in gastric-emptying time that is prolonged by as much as 12 hours and constipation.

The onset of action, peak effects, and duration of action vary with the different methods of use. Patients experience heroin's effect within 1-2 minutes when injected intravenously and within 15-30 minutes when injected intramuscularly. Heroin's peak therapeutic and toxic effects are generally reached within 10 minutes when injected intravenously, within 30 minutes when injected intramuscularly or when snorted, and within 90 minutes when injected subcutaneously. Analgesic effects generally last 3-5 hours.

Intravenously injected heroin creates a "rush" or a sensation of intense pleasure that begins within one minute of the injection and lasts from one to a few minutes. This "rush" is followed by a period of sedation that lasts about an hour. The initial "rush" is likely due to heroin's high lipid solubility and rapid penetration to the brain. The half-life of heroin is 15-30 minutes.

Heroin is rapidly converted to 6-monoacetylmorphine (6-MAM) by the liver, brain, heart, and kidney and may not be detected in the blood at the time of blood draw. 6-MAM is then converted to morphine. Morphine is metabolized by the liver and excreted as a glucuronide product or in its free form by the kidneys. Morphine's half-life is considerably longer than heroin's, ie, 2-3 hours. A small amount of unchanged 6-MAM is excreted in the urine for up to 24 hours after heroin use. Because 6-MAM can originate only from heroin, its detection in the urine can mean only that the patient used either heroin or 6-MAM.

## **Epidemiology**

### **Frequency**

#### **United States**

The true prevalence of heroin use is probably much higher than reported in surveys because surveys depend on self-reporting and may not reach some of the persons who use heroin the heaviest. Results from the [SAMHSA](#)'s 2008 National Survey on Drug Use and Health (NSDUH) revealed that the number of current heroin users increased from 136,000 in 2005 to 338,000 and then decreased to 213,000 in 2008 before increasing to 339,000 in 2009. In 2009, 180,000 persons aged 12 or older had used heroin for the first time within the past 12 months. The average age at first use among recent initiates aged 12-49 years was 25.5 years in 2009.<sup>[1]</sup>

Additionally, for 2009 the [Drug Abuse Warning Network \(DAWN\)](#) estimated that heroin was involved in 200,666 ED patient visits.

### **Mortality/Morbidity**

According to the American Association of Poison Control Centers' National Poison Data System annual report in 2009, 1919 case mentions of heroin exposure were documented. Nine deaths were reported.<sup>[4]</sup>

About 3-7% of patients treated for heroin overdose require hospital admission because of complications such as pneumonia, noncardiogenic pulmonary edema (NCPE), and infectious complications.

Most fatalities from heroin overdose occur in long-term users, usually early in their third decade of life. Fatality rates are higher in patients who use alcohol and other drugs such as benzodiazepines and cocaine. Death is most commonly due to respiratory failure or asphyxiation.

### **Race**

Although heroin addiction has traditionally been viewed as a disease of the economically disadvantaged population, addiction among the affluent is grossly underreported. According to the [National Institute on Drug Addiction \(NIDA\)](#), little difference exists in lifetime heroin use among races and ethnic backgrounds.<sup>[5]</sup>

### **Sex**

Although heroin addiction has traditionally been viewed as a disease of males, addiction among females is grossly underreported. According to NIDA, males were more likely than females to report heroin use during their lifetime.<sup>[5]</sup>

## History

In general, when it is the sole agent used, the clinical presentation of heroin poisoning and its diagnosis hold little challenge for the experienced health care practitioner. The diagnosis of heroin poisoning should be suspected in all comatose patients, especially in the presence of respiratory depression and miosis.

Symptoms generally develop within 10 minutes of intravenous heroin injection. Patients who survive heroin poisoning commonly admit to having used more than their usual dose, having used heroin again after a prolonged period of abstinence, or having used a more concentrated street sample.

Heroin toxicity shares common clinical characteristics with other medical or toxicologic conditions. For example, clonidine administration in a patient with pontine hemorrhage may cause coma, respiratory depression, and miosis similar to opioid intoxication. Phencyclidine, certain phenothiazines, and organophosphates may also cause miosis with altered mental status.

The clinical presentation of heroin poisoning may be altered by a number of the following factors:

- **Concomitant conditions:** The presence of CNS disease, traumatic injuries, hypoxia, hypoglycemia, hypovolemia, acidosis, or metabolic disease may alter the clinical presentation of heroin poisoning.
- **Co-ingestions:** The most commonly co-ingested substance is alcohol, followed by benzodiazepines, cocaine, and amphetamines.
- **Contaminants:** Street heroin samples are often contaminated with agents that have their own toxicity profile, eg, sedative hypnotics, amphetamines, local anesthetics, anticholinergic agents, quinine, strychnine, arsenic, and, most recently, clenbuterol<sup>[6]</sup>.

## Physical

Coma, respiratory depression, and miosis are the hallmarks of opioid overdose. According to Hoffman and colleagues, the presence of these hallmarks (ie, coma, respiratory depression, miosis) has a 92% sensitivity and 76% specificity for heroin overdose.

The clinical presentation and depth of coma may be altered in patients with co-ingestions and in the presence of concomitant medical conditions such as hypoxia, [trauma](#), hypoglycemia, and shock or with concomitant ingestion of other toxins such as amphetamines, cocaine, and anticholinergics. In these circumstances, patients may exhibit delirium, tachypnea, and mydriasis. Delirium may also be noted in overdoses with prescription narcotics such as dextromethorphan, meperidine, and codeine. Convulsions occur with overdoses of meperidine, fentanyl, pentazocine, or propoxyphene.

Mild hypotension and mild bradycardia are commonly observed with heroin use. These are attributable to peripheral vasodilation, reduced peripheral resistance and histamine release, and inhibition of baroreceptor reflexes. In the setting of heroin poisoning, hypotension remains mild. The presence of severe hypotension should prompt a search for other causes of hypotension, such as hemorrhage, hypovolemia, [sepsis](#), pulmonary emboli and other causes of shock.

Respiratory depression, due to heroin's effect on the brain's respiratory centers is a hallmark. However, the presence of tachypnea should prompt the search for complications of heroin use such as pneumonia, pulmonary edema, pneumothorax; or an alternative diagnosis such as shock, acidosis or CNS injury. Tachypnea may also be seen in overdoses of pentazocine or meperidine.

Examination of the skin may also reveal patterns of heroin use such as track marks (shown in the image below), fresh puncture wounds, and "skin-popping" marks.



Track marks in a heroin intravenous drug user

## Causes

The most common scenarios for a significant heroin overdose are the use of a higher dose, the accidental injection of highly concentrated solution in the unsuspecting user, or the use of heroin after a prolonged period of abstinence. Intentional (ie, suicidal) overdoses are rare. Other scenarios include body packing and body stuffing.

## Toxicology emergencies

"Body packers," also called "mules," are people who pack their GI tract with bags of heroin in order to smuggle the illegal drug from one country to another. In these persons, the drugs are carefully packaged for safe passage. Persons may become symptomatic when a heroin-containing package ruptures or when the packages cause GI obstruction or rupture. Body packing should be suspected in persons who are found unconscious at airports, during international flights, or soon after a trip to endemic countries.

"Body stuffers," on the other hand, are people who ingest all the drugs in their possession in order to conceal the evidence from the police. Because these packages are typically not designed for safe GI transport, they easily rupture and frequently cause poisoning. The clinical presentation is often atypical because multiple substances may have been ingested.

### Medical Care

The direct effects of heroin on the CNS are quickly reversible with naloxone. Naloxone may be given intravenously, intramuscularly, subcutaneously, or through the endotracheal tube. A response should be expected within 5 minutes. The effects from naloxone generally last 20-40 minutes. Resedation occurs when large doses of heroin are used, when continuous absorption from a ruptured transport bag occurs, or in the presence of a long-acting narcotic agent. The absence of a response to naloxone should prompt a search for another cause of the clinical presentation, such as hypoglycemia. Respiratory support should be instituted early, when necessary.

Gastric lavage in the setting of oral heroin overdose is generally not recommended because it has no documented value. Furthermore, gastric lavage is contraindicated in "body packers" and "body stuffers" because the procedure may rupture a package.

Activated charcoal, which is indicated for orally ingested narcotics, especially those with large enterohepatic circulation (eg, propoxyphene, diphenoxylate) is of no value in pure heroin overdose.

"Body packers" and "body stuffers" also generally require whole-bowel irrigation, except in the presence of intestinal obstruction or perforation. Whole-bowel irrigation may be accomplished with an oral polyethylene glycol (GoLytely) solution at a rate of 2 L/h until stools are watery and clear.

Admission to the hospital is rarely necessary and generally limited to complications of heroin overdose and intravenous drug use. Admission to the intensive care unit is also rarely required and is indicated for patients who require respiratory support and those with life-threatening arrhythmias, shock, and recurrent convulsions, as well as those who require continuous naloxone infusions (rebound coma, respiratory depression).

### Pulmonary edema

- NCPE affects 0.3-2.4% of heroin overdoses and generally becomes clinically apparent within 2-4 hours of the overdose. NCPE is heralded by the onset of hypoxia, increased respiratory rate, and a cough that produces frothy pink sputum. Chest radiography generally reveals bilateral infiltrates. Heroin-related NCPE generally lasts 24-48 hours and responds to supportive care. In most instances, hypoxia improves with mask oxygen ventilation only, but NIPPV and endotracheal intubation may be required. Endotracheal intubation is indicated for airway protection, severe hypoxia, acidosis, and cardiovascular instability.
- While the cause of NCPE remains uncertain, hypoxia-induced lung damage is likely to play a major role in the development of pulmonary edema. Other causes that have been suggested include acute anaphylaxis, neurogenic effects, humoral effects, immune-complex deposition, and depressed myocardial contractility.

### Convulsions

- The presence of recurrent convulsions in a patient with heroin overdose should prompt a search for causes of seizures, such as hypoxia, CNS injury, adulterants, or co-ingestions (eg, tricyclic antidepressants, cocaine, amphetamines).
- Some narcotics, such as meperidine (Demerol), pentazocine (Talwin), diphenoxylate, and fentanyl (Actiq), may cause seizures. Seizures caused by these narcotics, excluding diphenoxylate and atropine (Lomotil), are usually of short duration and do not progress to status epilepticus.
- Heroin and narcotic-related convulsions respond to conventional benzodiazepine therapy.

**Toxicology emergencies****Rhabdomyolysis**

- Prolonged coma and convulsions may contribute to the development of rhabdomyolysis, which is treated conventionally, with large amounts of crystalloid solutions, alkalization of the urine, and forced diuresis.
- Infusion of large amounts of crystalloids in patients with narcotic overdose may require close monitoring of hemodynamic parameters because these patients are also at risk for pulmonary edema.

# **SEDATIVES / HYPNOTICS / TRANQUILIZERS**

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**Examples:** Benzodiazepines: Valium (diazepam), Versed (midazolam), Ativan (lorazepam), Librium, **Rohypnol** (flunitrazepam) Relatively non-toxic except when combined with other CNS depressants (ETOH). Rohypnol is about 10 times more powerful than an equivalent dose of diazepam. Used as one of the "date-rape" drugs.

Legally manufactured by Roche pharmaceuticals in Europe and Latin America. Used outside of the U.S. as a sleep aid and presurgical sedative. Listed as a Schedule IV drug under the Controlled Substances Act due to international treaty obligations. Schedule IV drugs are considered to have a lower abuse potential but can lead to physical or psychological dependence.

It is not approved for humans here, so it is illegal to possess, prescribe, or manufacture in our country. The penalties associated with the possession, trafficking, and distribution of Rohypnol are equivalent to those of a Schedule I substance (Schedule I substances include heroin, marijuana, and MDMA).<sup>1</sup>

**Street names:** Forget me drug, roches, roofies, ruffles; la roche, Rope, R2, rib, roach, roofenol, rope, rophies, the forget pill, getting roached, lunch money drug, Mexican Valium, pingus, Reynolds, Robutal, wolfies.

**Dose:** The drug is usually colorless and odorless when slipped into food or drink. Roche has reformulated Rohypnol so that the tablet dissolves more slowly and releases a blue dye that discolors a drink it is dropped into.

**Onset:** Ranges from 15-30 minutes after administration, peaks within two hours and lasts ~four to six hours. Some residual effects can be found 12 hours or more after administration.

**Side note:** Rohypnol is used by heroin addicts in combinations with low-grade heroin to boost the high and also following a cocaine binge to blunt the edge of the "crash" known as "parachuting". The drug is also commonly mixed with Ecstasy, which contributes to its label as a "club drug". Rohypnol can create drug dependence with withdrawal effects such as seizures, hypertension, tremulousness and diaphoresis.

## **Signs and Symptoms**

HEENT	Pupils dilated, visual disturbances
NEURO	CNS depression, impaired judgment, disinhibition, ataxia, slurred speech, LOC decreased, sedation, coma, seizures All produce amnesia to a certain degree. Rohypnol prevents the user from remembering any of the events occurring while under the influence of the drug.
RESP	Respiratory depression (VS most often affected) to apnea
CV	BP may be decreased P may be increased - palpitations, dysrhythmias
GI	Anorexia, nausea, vomiting, diarrhea
GU	Urinary retention
MS	Muscle relaxation and impairment of motor skills

## **Treatment of OD**

- Routine toxicology management
- Antagonist flumazenil (Mazicon, Romazicon) not typically used any more – see below

## Digging Deeper

### Flumazenil

The intentional ingestion of benzodiazepines is a common cause of overdoses.<sup>[2]</sup> Flumazenil is a competitive antagonist at the benzodiazepine-receptor binding site on  $\gamma$ -aminobutyric acid-A. Typically, when benzodiazepines are ingested in overdose, the patient exhibits a *toxidrome*, or toxic syndrome, of CNS depression with relatively normal vital signs. Deaths attributed solely to the oral ingestion of benzodiazepines are rare.

While the idea of using flumazenil to reverse benzodiazepine toxicity may be tempting, the risks usually outweigh the benefits.<sup>[76,77]</sup> In a benzodiazepine-dependent patient, flumazenil can precipitate symptoms of benzodiazepine withdrawal, including seizures.<sup>[77-80]</sup> Additionally, in cases of multiple-drug ingestion, flumazenil may remove the protective effect of the benzodiazepine and unmask cardiac arrhythmias and seizures.<sup>[76,77,80]</sup> Therefore, the use of flumazenil in overdose patients is discouraged unless it can be determined with certainty that only a benzodiazepine was ingested and that the patient is not benzodiazepine dependent and has no history of seizure.

Flumazenil also may serve a role in the treatment of children who present with altered mental status in whom possible ingestion of a benzodiazepine is suspected as the sole toxic exposure. In this scenario, invasive diagnostic techniques such as computed tomography of the head and lumbar puncture may be avoided. In such cases, flumazenil therapy will not reduce the required ED observation time; but if the child improves clinically, flumazenil can help confirm the diagnosis of benzodiazepine toxicity.

Flumazenil can also be used to reverse CNS depression associated with benzodiazepine administration during procedural sedation if the patient is known not to be benzodiazepine dependent. The initial dosage of flumazenil is 0.2 mg/min administered via a slow i.v. infusion. In the context of conscious sedation, many patients respond to total doses of 0.4 mg while some patients may require a total dose of up to 1 mg.<sup>[81]</sup> The reversal of benzodiazepine toxicity occurs rapidly after flumazenil administration; if re sedation occurs, doses can be repeated at intervals of no less than 20 minutes. Resedation after flumazenil therapy is most likely to develop if >10 mg of midazolam or a longer-acting benzodiazepine is used for conscious sedation. No more than 3 mg of flumazenil should be given in one hour. In general, if re sedation is not observed within two hours of the administration of a 1-mg dose of flumazenil, subsequent serious re sedation is unlikely.<sup>[81,82]</sup>

**Implications for the practitioner** Due to the associated risk–benefit ratio, flumazenil is rarely indicated in the management of acutely poisoned patients.<sup>[76]</sup> These patients often have an unclear history, which makes the administration of flumazenil potentially dangerous. Flumazenil does not consistently reverse hypoventilation secondary to benzodiazepine use.<sup>[80]</sup> In the rare instances when flumazenil may be considered, it is important to ascertain that the patient is not taking benzodiazepines chronically, has a normal electrocardiogram, and is not experiencing toxicity due to a polydrug ingestion. In the context of reversal of conscious sedation, it is important to ensure that the patient has no contraindications to flumazenil, as described above.

Marraffa, J. M., Cohen, V., and Howland, M.A., (2012). Antidotes for toxicological emergencies: A practical review. *American Journal of Health-System Pharmacy*; 69(3), 199-212. [On-line] Posted: 02/14/2012.

# BARBITURATES

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**Examples:** Phenobarbital, Seconal (secobarbital)  
Not frequently seen, but very serious, potentially lethal OD

**Street names:** Reds, yellow jackets, downers, ludes

**Uses:** Used to come down from the effects of stimulant drugs. Withdrawal from heavy use of barbs can be lethal. These drugs are often used to commit suicide.

## Signs and Symptoms

OD mimics that of ETOH intoxication

HEENT	Nystagmus, slurred speech
NEURO	Lethargy, drowsiness, emotional lability, impaired thinking, incoordination, flaccid muscle tone, slurred speech, unsteady gait, impaired judgment, poor impulse control, coma
RESP	Respiratory depression
CV	Hypotension; hypothermia is common

## Treatment

- Excellent supportive care (ETI usually required)
- Routine toxicology management (charcoal effective)

## **Gamma Hydroxybutyric Acid (GHB)**

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**Classification:** GHB is a central nervous system (**CNS**) **depressant** that was first synthesized in the 1960s as an aid to surgery for its ability to induce sleep and reversible coma. However, it had little analgesic effect, and the onset of coma was often associated with seizure activity. This made GHB impractical in a clinical setting. In the late 1980s, it resurfaced as a growth-hormone stimulant to help body builders gain and retain muscle mass. In 1991, the FDA banned GHB in nutritional products following a series of reports of adverse reactions. It is approved as an anesthetic in some countries (France, Netherlands, Germany), and is sold under the brand names of Gamma-OH and Somsanit. In March 2000, GHB was placed in Schedule I of the Controlled Substances Act. It is not approved for use in the US, with the exception of investigational research (for treatment of narcolepsy, cataplexy, sleep paralysis, and hypnologic hallucinations). Will produce normal REM sleep.

**Street names:** In the US, GHB has been produced illegally by mixing sodium hydroxide and butyryl lactone, with varying degrees of purity. It has been sold as a liquid or a powder, under the names: "Cherry meth", Easy Lay, GHB, GBH, G-Riffic, Grievous Body Harm, Liquid Ecstasy, Liquid "X", Liquid E, Organic Quaalude, Sodium Oxybate, Salty Water, Scoop, Soap, Goop and Somatomax.

It has been promoted illegally as a growth hormone stimulant, anabolic steroid, diet aid, hypnotic and euphoriant. GHB use has been seen primarily in party and nightclub attendees and body builders. It is one of several agents characterized as a "date rape" drug, although it does not produce amnesia like Rohypnol.

GHB comes as a white or tan powder which is mixed in a liquid for consumption, usually in a bottle cap with water or a sports drink. When it is mixed with Ketamine and alcohol, the cocktail is called a "Special-K Lude" because its effects mimic those of the more-difficult-to-obtain Quaalude. When in solution, GHB is colorless and difficult to detect.

**Effects:** GHB is found naturally in brain tissue. It is similar in structure to gamma-hydroxy butyric acid (GABA), an inhibitory neurotransmitter. GHB is rapidly absorbed and quickly crosses the blood-brain barrier. In the CNS, GHB binds to specific receptors in the basal ganglia and other cerebral tissues. These receptors stimulate growth hormone, blood central dopamine release (required for normal alertness and mood), increase the production of proenkephalines (precursors of endogenous opiates) and induce sleep.

The primary effect of GHB is dose-related psychological and physical relaxation similar to alcohol intoxication, somnolence, drowsiness, hypnosis, dizziness, euphoria (20-30 mg/kg), coma, bradycardia, bradypnea, nausea, and vomiting (50-70 mg/kg). The difference between the dose required to produce sleep and the dose required to produce coma or death is usually less than one gram. In a small person, 2 grams may be enough to produce coma.

Rapid return to normal with no hangover.

**HEENT:** Nystagmus may be seen  
Gag reflex intact; less effect than other CNS depressants  
These people will be hard to intubate - don't try

**CV:** Bradycardia and hypotension may be seen but are not common

**Resp:** **Respiratory depression**, Cheyne-Stokes pattern, apnea

**CNS:** **Coma (should be expected)**, hypotonia, somnolence, drowsiness, dizziness, euphoria, delusions, hallucinations, headache, confusion, ataxia, shaking, seizures. Unlike other sedatives and hypnotics, the obtundation is interrupted by episodes of extreme agitation and combativeness.

**GI/GU:** Vomiting is common. Urinary incontinence or urgency may occur.

**MS:** Random myoclonic "jerking" or "twitching" activity of the face and extremities is common; seizures may occur

**Toxicology emergencies**

Labs: Metabolic acidosis occasionally occurs. Potassium may drop. Sodium may increase; glucose may increase

Onset: IV 2-15 minutes; PO 15-30 minutes

Duration: 1-2 hours, with full recovery by 8 hours

Treatment: The majority of OD patients recover with supportive care in six to eight hours  
Half wake up during intubation attempt; don't intubate  
Monitor VS, especially RR, depth and SpO<sub>2</sub>  
If not intubated, position on side to prevent aspiration  
No known antidote. In animal studies, **naloxone** has reversed some effects but is not consistently effective.  
Because of the rapid absorption and onset of CNS depression, gastric lavage (after airway is protected) is preferred over emesis.  
Anticipate violent behavior that frequently accompanies GHB-induced comas

## **ECSTASY** [3.4 Methylene-dioxy-N-methamphetamine (MDMA)]

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**Action:** An hallucinogenic amphetamine, MDMA was originally synthesized and later patented in Germany by Merck in 1914 as an appetite suppressant for their soldiers in WWI. Merck never finished clinical trials and the drug was abandoned. Although it was never brought to market, rumor has it that during the 1950s, the US Army briefly investigated its use for possible military application as part of its chemical warfare program. MDMA gained popularity in the field of psychotherapy through the influence of Alexander Shulgin in the early 1970s due to its therapeutic properties to lessen inhibition, which helped patients explore topics that might have been difficult to discuss. It resurfaced in the 1980s as a designer drug known on the street as "Ecstasy, XTC, Disco Biscuit, Cristal or X". In 1985, the DEA made MDMA an illegal Schedule I controlled substances (same class as heroin and cocaine) due to its abuse potential as a modified methamphetamine. Ecstasy acts as a stimulant and a hallucinogen but also has effects not seen with either hallucinogens or methamphetamine. These are known as empathogenic properties (increased sociability and empathy) and account for the drug's popularity. Used as a "sex" drug as it causes euphoria and loss of inhibition.

When used in combination with particular styles of music known as techno, jungle, or drum and bass, thousands of young adults are enticed to all-night parties called "**raves**". The drug can be taken as a tablet, but it also comes in capsules, powders and suppositories and can be taken orally, smoked, or injected. The typical dose is about 80-150 mg with the primary effects lasting up to four hours. Unfortunately, a capsule may contain anywhere from 16 to 100 mg of MDMA which contributes to unexpected toxic and fatal overdoses. Ecstasy users sometimes combine the pills with alcohol, Rohypnol, LSD, Viagra, cocaine, benzodiazepines, cough syrup, and opioids other than heroin.

In [Monitoring the Future](#), a report on drug use released in 2012, 5.8 percent of college students reported having used ecstasy, a 1.6 percentage point increase from 2011. Among 12th-grade students, annual prevalence of ecstasy use had decreased from 5.3 percent in 2011 to 3.8 percent in 2012. The majority of young adults who are likely to try Molly at some point have already done so by the time they reach college,

**Street name:** Molly (a more pure form of Ecstasy, but may be another similar drug substituted for MDMA).

**S&S:** Euphoria (reported in 94% of users)  
Increased self-esteem, sense of spirituality, empathy and need for intimacy  
Increased sensory perception. Playing with everyday objects is a pleasurable experience.  
Heightens visual perception and sense of smell. They may be sucking on glow sticks, wearing brightly colored items or putting Vicks VapoRub under their nose.  
Pupil dilation (CNS stimulant effects)  
Dehydration - users are warned about this so they often drink copious amounts of water that cause severe electrolyte imbalances (hyponatremia)  
Tachycardia, hypertension; cardiac dysrhythmias  
Nausea/vomiting  
Bitemporal headache; dizziness  
**Jaw clenching, bruxism**  
Hallucinogenic effects without as many amphetamine effects like HTN and tachycardia  
Bizarre interest in light  
Agitation and seizures  
Severe cases: Hyperthermia, kidney or liver failure, uncontrolled bleeding, coma or possible death

**Hints:** Look for the patient to be **holding or wearing a pacifier** which is used to keep them from grinding their teeth (bruxism) as the drug can cause jaw clenching. Allergy masks are used in combination with Vicks Vapor rub to intensify the euphoria one gets while under the influence of Ecstasy.

The Vicks inhaler has perforations. A raver covers these openings with the mouth and simultaneously blows vapors released from the container into the receiving raver's eyes. The receiver stares into space for about half a minute and then regains his or her thoughts.

**Complications:**

Rhabdomyolysis (destruction of muscle causing renal sludging)  
DIC  
Death

**Complications cont.** May cause memory damage or **depression** for days or weeks after use due to damaged serotonergic neurons. As more research is done, there is greater evidence to support possibly permanent brain damage in users, including short-term memory problems, cognitive difficulties, insomnia and anxiety.

Adverse reactions can occur in patients who are also taking monoamine oxidase (MAO) inhibitors which include Nardil, Parnate, Eldepryl and protease inhibitors such as Ritonavir.

Combining MDMA with selective serotonin reuptake inhibitors (SSRIs) such as Prozac, Zoloft, Paxil or Luvoc can cause "serotonin syndrome", a potentially fatal condition that presents with hyperthermia, tremors, hyperreflexia, ataxia and altered mental status.

**Treatment:**

There is no antidote  
Supportive; if dehydrated, IV fluids. DO NOT INTUBATE  
If hyperthermia is evident, begin cooling measures.  
Control seizures with midazolam or other benzodiazepine

# STIMULANTS - "Uppers"

## Sympathomimetics

**Amphetamines:** Benzedrine, Dexedrine, Ritalin, Methamphetamine (crystal, ice), 3, 4 methylenedioxymethamphetamine (MDMA, Ecstasy)

Use: Act primarily to induce a euphoric feeling. Some take them to lose weight, reduce fatigue, or counteract the effects of depressants.

Effects: Hyperactivity, anxiety, insomnia, hypertension, tachycardia

Overdose: Can cause seizures and death.

## Cocaine:

Local anesthetic and sympathomimetic CNS stimulant

- Remains highly prevalent and accessible in the general population and continues to represent one of the most commonly reported substances in drug-related presentations to EDs, and is frequently implicated in drug-related deaths. Estimated 1.6 million current cocaine users aged 12 years and older, with 1.1 million classified as having substance dependence or abuse. An average of 1700 Americans use the drug for the first time every day. Cocaine abuse is a worldwide problem. The number of consumers is on the rise and they are appearing at younger ages.
- A huge variety of ECG manifestations can occur including rhythm disturbances (special attention should be given to atrial fibrillation and ventricular arrhythmias, the latter usually life-threatening), conduction disturbances, repolarization abnormalities (QT prolongation) and induction of dangerous ECG patterns, such as Brugada-like manifestations.
- Early recognition of the possible multiple patterns may help to initiate treatment and extend monitoring, as some of the ECG manifestations could occur several hours after last consumption.

Routes: IV, intranasally, smoked, free-based extract w/ alkali and mix w/ solvent ether  
Onset - seconds; Duration - 1 hr

**Caffeine:** Acts like a stimulant in high doses  
Ingredient in most OTC stimulants

OTC diet and decongestant agents - Pseudoephedrine, Phenylpropanolamine, Ephedrine

## Signs and Symptoms = Assess for excited delirium

HEENT	Pupils dilated Cocaine (IN): Bleeding, ulcerations, rhinitis, erythema, perforation of nasal septum, sinusitis Smoked: Acute asthma, hemoptysis, pulmonary infarcts, hypersensitivity, pneumonia
NEURO	Restlessness, irritability, hyperactivity, talkativeness, wild agitation, insomnia, HA, tremors, seizures, coma, stroke, paranoid, suspicious, hallucinations
RESP	Initial hyperpnea, may be followed by depression
CV	Vasospasm causes <b>HTN</b> , tachycardia, chest pain, palpitations, dysrhythmias, MI May be followed by hypotension and shock
GI	Decreased appetite, nausea, vomiting, diarrhea, cramps, weight loss (increased BMR), dehydration. May see ischemic bowel if swallowed cocaine packets rupture.
Skin	Temp may go as high as 112-115° F in cocaine abuse during the summer; diaphoresis

## Treatment

- Routine toxicology management; ECG
- Cocaine is a potent CNS and CV stimulant. Myocardial ischemia, infarction seen most commonly in young men who are "smokers". Pain within 3 hours of use; endocarditis (cocaine destroys endocardial surface); aortic rupture and stroke have been reported.
- Treat with midazolam IVP; may need rapid cooling

# HALLUCINOGENS

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Lysergic acid diethylamide (LSD), phencyclidine (PCP, Angel dust, TIC); cannabis, ketamine, methoxetamine (MXE) -analog of ketamine, (structural similarity to PCP). Synthetic cannabinoids come as white/off-white powders or may be combined with plant products and sold as *Spice, K2, Chill Zone, Sensation, Chaos, Aztec Thunder, Red Mercury, and Zen*. May be ingested or insufflated (if powdered chemicals) or smoked when mixed with other plant products. Liquid forms increasingly popular for use in electronic cigarette devices. Belong to varied classes of designer drugs and do not resemble THC in chemical structure.

**Signs and Symptoms** Variable (mild to significant paranoia and agitation resulting in self-harm);

HEENT	Nystagmus, blank stare
NEURO	AMS (out-of-body experiences), severe psychosis, paranoid, distortion of sensory perception, hallucinations, decreased sensitivity to pain, bizarre slow and dull or agitated, abusive, combative behavior, muscular rigidity, seizures, coma with eyes open
RESP	Respiratory depression
CV	Tachycardia, hypertension Hyperthermia may occur

## MARIJUANA (Cannabis)

**Signs and Symptoms**

HEENT	Reddening of the conjunctive
NEURO	Mild perceptual changes, mood alterations, feeling of being well, euphoria, heightened sensory awareness, depersonalization, alteration of time perception, memory impairment, decreased motor coordination, ataxia, slurred speech, drowsiness, lethargy
RESP	Irritation, coughing, chronic respiratory syndrome
CV	Tachycardia, postural hypotension
GI	Dry mouth, increased appetite, decreased bowel motility

**Complication:** 59 case reports of cannabis-related stroke (mean age, 33 years) have been described. Most cases were in men, with a male-to-female ratio of 4.9:1. Of the 59 cases, 49 were classed as ischemic strokes, 5 were transient ischemic attacks, and 1 was a hemorrhagic stroke; in 4 patients, a diagnosis of stroke was suspected but not confirmed because no neuroimaging was done. Cannabis appears to be associated with multifocal intracerebral stenosis, which can cause a stroke. These stenoses have been seen in people who are regular cannabis smokers and when they stop smoking the stenoses disappear. The stenoses are caused by shrinkage of the blood vessels and can occur in several different areas of the brain. It appears that cannabis may cause the arteries to constrict.

*Stroke*. 2013;44:1-6. Published online December 27, 2012. [Abstract](#)

**Treatment**

- Routine toxicology management
- Talk down
- Provide safe environment – Restraints prn
- Decrease sensory stimuli, including lights, noise and touch
- Midazolam for agitation and seizures

## Digging Deeper

# Bath Salts: What the EMS Provider Needs to Know

by Scott R. Snyder, BS, NREMT-P

Created: April 1, 2011

EMS providers must be prepared to protect the patient and themselves.

Bath salts have been described as a white or off-white powder that can be smoked, snorted, injected or ingested

There has been increasing law enforcement and media interest in a new product that is currently unregulated, but is causing significant medical issues for emergency providers. With this new group of drugs hitting the streets across the United States, there is a high level of alarm with law enforcement, poison control centers, lawmakers and physicians alike.



The drugs, referred to as "bath salts," were never intended for the tub, and you won't find them at Bath and Body Works. These salts, with names like "Ivory Wave," "White Lightning" and "Vanilla Sky," seem harmless, though they are anything but, having been blamed for up to four deaths in the U.S. Unbelievably, this product is legally available and can be easily purchased at convenience stores, head shops and online for about \$20-\$40 per gram. It is sold as a powder in sealed envelopes and can be purchased by consumers of any age. There are no limitations on quantity and no need to register the purchases.

In Louisiana, after the state poison center received more than 125 calls in the last three months of 2010 involving exposure to the chemicals, they alerted the appropriate authorities. In response, the state legislature issued a Declaration of Emergency and enacted a temporary order on January 6, 2011, banning the sale of bath salts and placing these toxic chemicals on the state's Controlled Dangerous Substances list. In addition to Louisiana, lawmakers in Texas, Mississippi, North Carolina and Kentucky are considering proposals to ban the sale of the powder. The DEA has weighed in recently, calling them a "drug of concern."

## BATH SALTS: THE SCIENCE

So what is this new drug? What are the active chemicals in it, and what effects do they have on the human body? How should you manage the patient who has ingested a bath salt?

Bath salts contain the active ingredients methylenedioxypyrovalerone (MDPV) and mephedrone. MDPV is a synthetic psychoactive drug with stimulant properties that have been likened to ecstasy. Mephedrone is a synthetic stimulant with amphetamine-like or cocaine-like effects. These molecules are very similar to amphetamines, cocaine and other stimulants. The substances have been described as a white or off-white powder that can be smoked, snorted, injected, or wrapped in pieces of paper and ingested (bombed). Both are considered analogs of illegal substances that are prohibited by the Federal Analog Act, a section of the United States Controlled Substances Act. However, since this act only applies to drugs sold for human consumption, they can be sold legally in products labeled as "bath salts." The appearance is similar to cocaine and other illicit substances, so law enforcement may or may not be able to do field testing to identify them.

## EFFECTS ON HUMANS

The drugs have profound effects on the central nervous and cardiovascular systems, similar to other stimulants. To date, complications have been reported at three levels. With small quantities, users report feelings of euphoria, increased alertness and awareness, diminished need for food and sleep, and overall feeling of well-being.

At higher doses, the substances can cause hallucinations, anxiety, agitation, paranoia and erratic behavior. In one case that was well-publicized in the national media, an abuser used his skinning knife to slice his face and stomach repeatedly. Effects on the cardiovascular system include tachycardia and hypertension, increasing the risk of stroke and acute myocardial infarction. Increased activity and metabolism common with use of the drugs can lead to renal failure secondary to rhabdomyolysis and hyperthermia. Rhabdomyolysis is the breakdown of muscle fibers that results in the release of myoglobin

**Toxicology emergencies**

into the bloodstream, which damages kidneys and can result in renal failure.

With frequent use, persons report insatiable cravings for the drug, and have been reported to engage in days-long binges. Almost nothing is known of the long-term, but users can be expected to experience the compulsive use and psychological and physical dependence that are characteristic of amphetamine-type drugs. There have been cases of severe depression after "coming down" from a bath salt high, as well as reports of suicide attempts and success during these episodes.

**PREHOSPITAL EMERGENCY CARE**

Management of the patient presenting with acute bath salt toxicity is driven by the symptoms exhibited, and the spectrum of possible presentations is quite varied. A patient may present with simple depression after a bath salt binge, or with an altered mental status, hyperthermia and renal failure. As with any patient, the airway, breathing and circulation should be evaluated and any immediate life threats promptly corrected.

EMS providers must be prepared to protect the patient and themselves related to the use or overuse of these substances. Patients who present with depression after a binge episode will require reassurance, support and basic monitoring. The EMS crew should attempt to create an environment that reduces stimulation. For example, turning down the lights, avoiding unnecessary use of the siren and driving smoothly can help prevent a patient from becoming more agitated and complicating the situation. A patient who is agitated, combative or in some other way dangerous to himself or you may require soft restraints. The use of soft restraints is not without risk, however, as hyperthermia or rhabdomyolysis can result secondary to the patient struggling against them. For the paramedic, chemical sedation with a benzodiazepine (lorazepam, midazolam, Valium) or a barbiturate (phenobarbital) can be considered, but medical control should be consulted prior to administration.

Any patient presenting with an altered mental status, altered level of consciousness, tachycardia or hypertension should be administered oxygen via the appropriate delivery device to assure a SpO<sub>2</sub> above 95%. The hyperthermic patient should be cooled in accordance with your local protocol. Possible methods include misting with tepid (59°F) water and application of cold packs to the axillae, groin and anterior neck.

EMS providers should stay informed regarding this class of substances, with cooperative efforts involving local law enforcement, poison control centers, emergency departments and medical control. Information regarding bath salts is still evolving and may change with intervention by federal authorities.

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Add to this:

The active ingredient in most formulations of bath salts is 3,4-methylenedioxypyrovalerone, better known as MDPV. MDPV is a potent inhibitor of dopamine and norepinephrine re-uptake transporters and is thought to inhibit each transporter with a potency much greater than that of cocaine.<sup>[1]</sup> Thus, many of the signs and symptoms associated with intoxication mimic sympathetic overstimulation, including tachycardia, hypertension, hyperthermia, diaphoresis and arrhythmias.<sup>[2]</sup>

Bruxism, a clenching of the jaw and/or grinding of the teeth, has been noted as a relatively common presentation of bath salts intoxication.<sup>[3]</sup> Bruxism can be caused by a wide array of conditions and substances ranging from sleep disorders to SSRI's to Obsessive-Compulsive Disorder to MDMA (Ecstasy). However, the combination of the above sympathetic overdrive signs and symptoms with bruxism should raise suspicion for a bath salts intoxication.

Just remember, bruxism and bath salts!

American Academy of Emergency Medicine > [Modern Resident](#)  
Haas, N. (Feb. 12, 2013). Clinical Pearl: Bruxism and Bath Salts

## Synthetic Marijuana Sending Teens to the ED

Megan Brooks

Synthetic cannabinoid compounds are increasingly popular among adolescents and young adults in the United States, and many are ending up in the hospital after smoking these products, a [report](#) published March 19 in *Pediatrics* warns.

The herbs and spices found in these products — commonly known as K2, Spice, Aroma, Mr. Smiley, Zohai, Eclipse, Black Mama, Red X Dawn, Blaze, and Dream — have been sprayed with toxic chemicals that produce euphoric and psychoactive effects akin to those associated with delta-9-tetrahydrocannabinol (THC), the active ingredient in marijuana.

However, it is becoming apparent that these synthetic marijuana products can cause agitation, aggressive behavior, catatonia, intense sweating, and trouble speaking, Joanna Cohen, MD, of the Division of Emergency Medicine, Children's National Medical Center, Washington, DC, and colleagues note in their report.

Until recently, these products were sold in [gas stations](#), convenience stores, and over the Internet. From 2010 to 2011, the American Association of Poison Control Centers reported 4500 calls involving synthetic cannabinoid toxicity.

On March 1, 2011, the US Drug Enforcement Administration (DEA) listed 5 chemicals used to make synthetic marijuana as schedule 1 controlled substances (ie, JWH-018, JWH-073, JWH-200, CP-47,497, and cannabicyclohexanol). These chemicals "have not been approved by the FDA for human consumption, and there is no oversight of the manufacturing process," the DEA wrote in a statement.

Synthetic cannabinoids are relatively novel substances of abuse, and there is "little information" in the medical literature on it, said Dr. Cohen in a statement.

"Recognition of the signs and symptoms of intoxication of synthetic cannabinoids and a high index of suspicion are necessary to diagnose toxicity," the investigators write. These chemicals are hard to detect with available drug tests, increasing their popularity among youth.

### Typical Symptoms

The report highlights 3 case studies of teenagers seen in the emergency department (ED) with suspected synthetic cannabinoid intoxication and discusses typical signs and symptoms of intoxication with these substances.

Case 1 involved a 16-year-old girl transferred from an outside hospital with altered mental status; she was awake with her eyes [open](#) but was not responding to verbal or painful stimuli. Her boyfriend reported that they had been smoking marijuana containing K2.

She was catatonic on arrival at the ED at Children's National; her lower extremities were rigid and flexed. Her heart rate was 105 beats/min, her respiratory rate was 18 breaths/min, and her [blood pressure](#) was 118/73 mm Hg. She had sinus tachycardia and remained unresponsive to verbal and painful stimuli.

The patient was treated with single dose of 50 mg intravenous (IV) diphenhydramine, after which she began to move her lips in an attempt to speak. She was subsequently treated with lorazepam 2 mg IV twice, after which she began to speak slowly. She was observed overnight, during which time she slowly recovered her motor and verbal functions and was discharged.

Case 2 involved an 18-year-old boy who was brought to the ED after he became agitated and was sweating profusely at a party. In the ED, he was uncooperative, restless, and aggressive. On examination, his vital signs included a temperature of 37.6° C (99.68° F), a heart rate of 131 beats/min, and a blood pressure of 131/89 mm Hg. He remained diaphoretic and anxious. His pupils were dilated and "sluggishly reactive." He too had sinus tachycardia.

When the patient continued to be aggressive and agitated, he was given a dose of lorazepam 2 mg IV. He finally admitted to smoking Spice at the party. He was given 50 mg diphenhydramine IV and was admitted to the hospital. Over the next several hours, he showed clear signs of recovery and was discharged.

### Toxicology emergencies

Case 3 involved a 16-year-old previously healthy boy who was a resident of a group home. He was brought to the ED by his case worker when she noticed that his face seemed "frozen" and that his speech was slowed. She also reported that he was agitated and seemed to be hallucinating. The boy said he had smoked Spice roughly 5 hours before.

Upon arrival at the ED, the patient was agitated and dysarthric with pressured speech. He appeared dystonic. He was alert and able to answer simple questions but seemed confused. He received a normal saline bolus of 1000 mL and 4 mg of lorazepam IV. A urine toxicology screen was negative, as was an expanded serum toxicology screen. After 3 to 4 hours, he began to recover and was discharged at his baseline neurologic status.

#### Potential for Long-Term Effects

Dr. Cohen and colleagues note that the dystonic reactions seen in 2 of the cases are "unusual side effects." It is also possible that the dystonia observed was actually a combination of catatonia and catalepsy combined with agitation. "Dystonia from synthetic cannabinoids would be a curious phenomenon," because the effects of THC on the basal ganglia have been studied in the treatment of dystonia.

No antidote is currently available for synthetic cannabinoid intoxication. And although symptoms are usually short-lived and self-limited, "the potential for multiple long-term effects, including immunomodulation and carcinogenicity, memory loss, psychiatric complications, and dependence, have been described," the authors write.

As [reported by Medscape Medical News](#), there is evidence that synthetic cannabis may pose an even greater risk for psychosis than natural cannabis, even among users with no history of a psychiatric disorder.

"Given the sensitivity of the developing brain and association between early cannabis use and psychosis, adolescent use of these new synthetic cannabinoids is particularly concerning," the authors write.

"Recognition of the signs and symptoms of patients with synthetic cannabinoid ingestion can help physicians who treat adolescents be better prepared to diagnose and manage patients presenting with this toxicity," they conclude. *Pediatrics*. 2012;129:e1064-e1067

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## K-2

NEW YORK (Reuters Health) Nov 07, 2011 - Three 16-year-olds had heart attacks after smoking K2, a blend of herbs and spices laced with synthetic cannabis-like chemicals, Texas doctors reported Monday.

While there is no proof that the drug is to blame, the doctors worry it might have been the cause.

"Lots of teenagers get chest pain, but very few teenagers get that from a heart attack," said Dr. Colin Kane, a pediatric cardiologist at UT Southwestern & Children's Medical Center in Dallas. "I am certainly suspicious that there was something in the K2 that would have caused these heart attacks."

A few earlier reports have linked marijuana use to heart disease, but this appears to be the first time K2 has surfaced in that context, Dr. Kane told Reuters Health.

K2 is one of several "fake pot" products that have become increasingly popular among young Americans. Other brands include Blaze, Spice and Red X Dawn.

The herbs and spices in these products have been sprayed with synthetic cannabinoids that mimic the effects of natural cannabis.

Once legal, five of these substances were banned nationwide by the Drug Enforcement Administration in March of this year. The DEA explained in a statement that it had received reports from poison control centers, hospitals and law enforcement about K2 and similar products.

"Emergency room physicians report that individuals that use these types of products experience serious side effects which include: convulsions, anxiety attacks, dangerously elevated heart rates, increased blood pressure, vomiting, and disorientation," the agency said.

## Toxicology emergencies

With the new report, published online today in Pediatrics, myocardial infarction has been added to the list.

Dr. Kane and his colleagues said the three teenage boys who came separately to their hospital complaining of chest pain had none of the typical risk factors for heart disease.

After questioning the boys, who came to the hospital within three months of each other, the doctors found out that all three of them had smoked K2 a few days before their symptoms began.

While it's impossible to know for certain what caused the heart attacks, Dr. Kane and his colleagues suggest the K2 might have caused temporary coronary artery spasms that were severe enough to cause infarction.

Dr. Kane said his hospital hasn't seen more cases since these three, which happened about a year ago.

"I'm not sure if use is going down or if there was something particular about this batch" of K2, he said.

He added that the boys have normal cardiac function now, so it appears they got off with a warning.

"The real take-home message is that these products -- K2 and Spice and other products like that -- might initially be attractive because they are easy to get and they don't show up on a drug screen, but they might have some harmful effects," Dr. Kane said.

## Spice

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### Potent 'Spice' Drug Fuels Rise in Visits to Emergency Room

By [ALAN SCHWARZ](#) APRIL 24, 2015

A sharp rise in visits to emergency rooms and calls to poison control centers nationwide has some health officials fearing that more potent and dangerous variations of a popular drug known as spice have reached the nation's streets, resulting in several deaths.

In the first three weeks of April, state poison control centers received about 1,000 reports of adverse reactions to spice — the street name for a family of synthetic substances that mimic the effects of marijuana — more than doubling the total from January through March, according to the American Association of Poison Control [Centers](#).

The cases, which can involve spice alone or in combination with other substances, have appeared four times as often this year as in 2014, the organization said. On Thursday alone there were 172 reports, by far the most in one day this year.

Health departments in Alabama, Mississippi and New York have issued alerts this month about more spice users being rushed to hospitals experiencing extreme anxiety, violent behavior and delusions, with some of the cases resulting in death. Similar increases have occurred in Arizona, Florida, New Jersey and Texas.

The total number of fatalities nationwide this year is not available, health officials said. One person in Louisiana died Wednesday and two others were in intensive care, said Mark Ryan, the director of the Louisiana Poison Center.

"We had one hospital in the Baton Rouge area that saw over 110 cases in February. That's a huge spike," Dr. Ryan said. "There's a large amount of use going on. When one of these new ingredients — something that's more potent and gives a bigger high — is released and gets into distribution, it can cause these more extreme effects."

Experts were unsure whether the increase this month in spice-related emergencies reflected greater use of the drug or a particularly dangerous formulation. Dr. Ryan said a large portion of cases appeared to involve a form called mab-chminaca.

Law enforcement agencies, from the Drug Enforcement [Administration](#) to local police departments, have struggled to control the flow of synthetic cannabinoids, substances that look like marijuana that are sprayed with a hallucinogenic chemical and then smoked.

Those chemicals, typically imported from China by American distributors, come in hundreds of varieties; new formulations appear monthly, with molecules subtly tweaked to try to skirt the [D.E.A.](#)'s list of illegal drugs as well as drug-detecting urine tests.

## Toxicology emergencies

Although the entire class of drugs is illegal because of the psychological effects, each new variety can present distinct health risks caused by its underlying chemistry or contaminants in renegade manufacturing facilities.

Synthetic cannabinoids seized by agents in Alabama. Credit Alabama Alcoholic Beverage Control Board, via Associated Press

Experts warn that the popular term “synthetic marijuana” is a misnomer, as the substances merely resemble marijuana but can be 100 times as potent.

The use of synthetic cannabinoids as well as calls to poison control centers had decreased from 2011 through 2014, as awareness of their danger and illegality has spread, national data [indicates](#).

Still, about one in 20 high school students used the drugs in 2014; about one in 30 adults age 19 to 28 used them in 2013, the most recent [data](#) available for that age group.

More than 400 emergency-room visits in Mississippi were attributed to synthetic cannabinoids in April, according to the state health [department](#).

Two of those cases involved Jeffrey and Joey Stallings of McComb, who spent several days in intensive care in medically induced comas, their mother, Karen, said in a telephone interview.

Ms. Stallings said that Jeffrey, 24, and Joey, 29, smoked a type of spice known as “mojo” that they received from a dealer.

She said that Jeffrey became delusional, thinking that a woman was bleeding in their hallway, and extremely violent; Joey became extremely agitated before she took them to the hospital.

Ms. Stallings said that her sons were released from the hospital after about a week and that doctors told her that Jeffrey might have permanent [kidney damage](#). Efforts to reach the brothers for comment were unsuccessful.

“I told them, ‘This is killing you and you don’t see it,’ ” Ms. Stallings said. “There’s no telling what that stuff was. There’s no telling at all.”

A unique case occurred earlier this year in Texas. The death of Kendrick Sneed, a soldier at Fort Hood, on Jan. 13 had been considered to be possibly caused by Ebola, because he had recently returned from deployment to a hot zone for the disease in West Africa.

The local police department, however, [announced](#) on April 16 that an autopsy determined the cause to be “synthetic cannabinoid intoxication.”

The increases in cases in Mississippi and Alabama demonstrate the challenge facing law enforcement officials.

Last year, [D.E.A.](#) agents made about 40 arrests and seized more than 400 pounds of synthetic drugs in those states as part of a wider national operation. Yet supply chains clearly remain.

“Is it frustrating? Yes, but when you’re in this business what you come to understand is that total eradication of a drug threat just isn’t going to happen,” said Keith Brown, the special agent in charge of the D.E.A.’s New Orleans field division, which covers Alabama, Arkansas, Louisiana and Mississippi. “Until we can control the demand there’s going to be someone with supply.”

Mr. Brown added: “We had success last year, and now it’s coming back. It’s like a guy who tends a garden or tends a yard. It’s impossible to eradicate weeds. They come back. They grow again.”

Mr. Ryan said his Louisiana call center had fielded fewer calls in the past several years partly because emergency-room doctors had begun to recognize the effects of certain variations of spice and knew how to handle those cases themselves, leaving most of the calls from worried individuals. The tenor of recent calls has been different, he said.

“It’s been more than 90 percent hospitals this year,” Mr. Ryan said. “It’s not, ‘Hey, I smoked this thing and I don’t feel well.’ It’s, ‘This guy’s trying to tear up the E.R. and we have him locked down in restraints. We don’t know what he’s taken. What do we do?’ ”



# N-Bomb

<http://exclusive.multibriefs.com/content/meet-the-designer-drug-n-bomb-and-its-effects/medical-allied-healthcare>

Lynn Hetzler Thursday, April 23, 2015



Recreational use of designer psychoactive drugs is rising dramatically. Designer drugs have gained popularity since law enforcement and legislation have made it more difficult for recreational users to secure cocaine, ecstasy, heroin, opioids and cannabis. These restrictions have encouraged suppliers and users to seek alternatives.

Illicit drug makers usually create designer drugs by modifying the molecular structures of existing illegal drugs in hopes of producing similar effects. These designer drugs are often less expensive, readily available, difficult to detect with routine drug screens, and have a more potent and desirable pharmacological effect. One such drug that emergency care providers and law enforcement officials need to watch for is 25I-NBOMe, also known as the "N-bomb."

25I-NBOMe has been associated with at least 17 deaths in the United States since it first became available on the Internet in 2010. Often marketed as "natural" or "legal" LSD, N-bomb is a derivative of the psychedelic phenethylamine 2C-C that produces potent psychedelic effects.

Discovered in 2007 by Free University of Berlin chemist Ralf Heim, 25I-NBOMe was developed to map serotonin receptors in the brain. Today, it is one of the most frequently abused psychoactive substances. 25I-NBOMe is the chemical abbreviation for e 1-(4-Iodo-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine.

Users purchase N-bomb as blotted paper, loose or encapsulated powder, and liquids. Consumers can administer N-bomb by ingesting under the tongue, sniffing or inserting into the body vaginally or rectally. The drug is active at low submilligram doses. The effects of N-Bomb last from four to 10 hours, depending on route of administration, dosage and other factors.

Because it is so new, there is little research into the side effects of N-bomb. Consumers have presented peripheral vasoconstriction requiring medical attention. Symptoms typically begin with coldness, bluing of the skin, tingling and numbness in the nose, lips, fingers, toes and other extremities. Some patients presented swelling in the hands, feet and face.

Since N-bomb is manufactured and sold in unregulated labs, quality control is nonexistent. Misjudging a dose can potentially lead to significant toxicity, presenting symptoms such as hypertension, tachycardia, arrhythmia, hyperthermia, mydriasis, agitated or aggressive behavior, delirium and hallucinations, seizures and renal failure. Coma and death may occur.

One case study, reported in *Clinical Toxicology*, details an encounter with an 18-year-old male presenting to the emergency department with severe agitation and hallucinations. His pulse was 150 to 160 bpm, and his blood pressure was 150 to 170/110. Serum assays returned a value of 0.76 ng/ml of 25-I. The patient required physical restraints and IV Lorazepam. Symptoms and vital signs gradually returned to normal within 48 hours, punctuated by periods of aggression.

N-bomb is a dangerous and potentially deadly drug. Emergency room doctors and nurses, first responders, law enforcement and parents need to be aware of the existence of 25I-NBOMe and its potentially toxic effects.

Treatment goals include management of agitation and prevention of organ damage. Sedation may be necessary to calm particularly aggressive or violent patients. Patients with hyperthermia may require external cooling measures.

Designer drugs change quickly in response to legislative controls. Emergency department personnel and other healthcare providers must remain current on the toxicological effects of these ever-emerging designer drugs, like 25I-NBOMe.

Legislators have already moved many designer drugs to the DEA's Schedules of Controlled Substances list, including the phenethylamine 2C-C from which 25I-NBOMe is derived. N-bomb has been on this DEA list since November 2013.

# CYANIDE

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**Examples:** Industrial - Electroplating, metal cleaning, nylon manufacture, recovery of silver from x-rays and photographs  
Cherry, apricot, peach, apple, pear seeds, Laetrile  
Product of combustion in some fires

**Action:** **Blocks cellular use of O<sub>2</sub>** by inactivating the cytochrome oxidase system inside the cells.  
**Rapid onset can produce death in minutes.**  
Can enter the body through ingestion, absorption or inhalation

## Signs and Symptoms

HEENT Bitter almond odor on breath or body (however, only 20-40% population can smell this)  
Burning sensation of mouth and throat  
Retinal arteries and veins equally red  
Mucus membranes may be cherry red

NEURO H/A, vertigo, agitation, combative, rapid onset of coma, seizures

RESP RR and depth increased initially, followed by respiratory depression and pulmonary edema

CV BP and P increased initially, followed by decreased BP and P; dysrhythmias

GI Nausea, vomiting

## Treatment

1. PPE including SCBA; evacuate danger area
2. **IMC** per Drug OD/Poisoning SOP; decontaminate pt as necessary. Do NOT direct water jet on liquid. Absorb liquid in sand or inert absorbent and remove to a safe place. Remove vapor cloud w/ fine water spray. Remove contaminated clothing and wash skin with soap and water for 2-3 min.
3. Establish OLMC ASAP so receiving hospital is prepared for your arrival
4. If hypotensive or pulseless: **IV/IO NS wide open**. CPR as indicated.  
**AMYL NITRITE** inhalants 1 per minute X 12 minutes (followed ASAP by IV sodium thiosulfate at hospital) *OR*  
**HYDROXOCOBALAMIN** 5 gm IV. May repeat X 1 if needed w/ or w/o sodium thiosulfate. Converts cyanide to vitamin B<sub>12</sub> (cyanocobalamin).  
<http://emergency.cdc.gov/agent/cyanide/erc506-77-4pr.asp> *and*  
<http://emergency.cdc.gov/agent/cyanide/erc74-90-8pr.asp>  
Hyperbaric oxygen and hemodialysis may be useful  
Emesis is contraindicated

## Digging deeper

### Antidotes for Cyanide Poisoning

In the United States, there are now two types of cyanide antidotes available. The Lilly Cyanide Antidote Kit was the first and, for many years, the only such kit available; it contained amyl nitrite, sodium nitrite, and sodium thiosulfate. This combination of agents is now available as the branded Cyanide Antidote Package or as the generic Cyanide Antidote Kit, and the components are sold separately by various manufacturers.<sup>[41]</sup> Nithiodote, recently approved by FDA, contains sodium nitrite and sodium thiosulfate.<sup>[42]</sup> In 2006, [FDA approved](#) hydroxocobalamin, a novel cyanide antidote, available as the branded Cyanokit.<sup>[43]</sup>

Cyanide binds to the ferric ion on cytochrome oxidase and abruptly halts the electron transport chain and aerobic respiration, producing profound toxic effects. Cyanide also preferentially binds to the ferric ion of methemoglobin, but endogenous concentrations of methemoglobin are quite low.

Exposure to cyanide can occur during house fires, [industrial accidents](#), and attempted suicides, and cyanide is a potential agent of chemical warfare. Smoke inhalation is one of the more common sources of exposure to cyanide in the United States.<sup>[44,45]</sup> Suicide attempts involving the ingestion of commercially

## Toxicology emergencies

available cyanide salts have been reported.<sup>[46]</sup> Cyanide overdose has been reported among workers in the gold, jewelry, and textile industries, in which the salts are frequently used. Cyanide exposure causes rapid, severe systemic toxicity and rapid cardiovascular collapse. Although there is no rapid test for the diagnosis of cyanide poisoning, an elevated lactate concentration (>8 mmol/L, or 72 mg/dL)<sup>[47]</sup> and a venous blood gas with a high partial pressure of oxygen and a high [oxygen saturation](#) are, in the appropriate clinical context, highly suggestive of cyanide toxicity and warrant empiric antidotal therapy.

### Amyl Nitrite and Sodium Nitrite

The mechanism of action of amyl nitrite and sodium nitrite as antidotes for cyanide poisoning is to produce methemoglobinemia and vasodilation.<sup>[48]</sup> Vasodilation may contribute to their therapeutic and adverse effects.

Intravenous sodium nitrite produces significant methemoglobinemia.<sup>[49]</sup> The cyanide bound to cytochrome oxidase is then preferentially bound to methemoglobin, forming cyanomethemoglobin. Rhodanese, an endogenous enzyme, then facilitates the formation of thiocyanate, a much less toxic metabolite, which is renally excreted.

The creation of methemoglobinemia through the use of nitrites for cyanide poisoning entails some risk and, in particular, may be detrimental or even lethal to a patient with smoke inhalation and concurrent carboxyhemoglobinemia or lung injury.<sup>[50]</sup> Neither carboxyhemoglobin nor methemoglobin is capable of carrying oxygen, so such patients can develop functional hypoxia. Therefore, the administration of the nitrite component of therapy for cyanide poisoning should be avoided in patients with smoke inhalation unless it can be demonstrated that the carboxyhemoglobin level is negligible. The dosage of nitrites should not be adjusted to achieve a predetermined methemoglobin concentration, since the formation of cyanomethemoglobin can potentially be misread as methemoglobin formation by an oximeter during [patient monitoring](#). (A methemoglobin concentration above 20% should halt further nitrite administration.)

In the context of cyanide poisoning, the differences between nitrites lie in the route of administration and the degree of methemoglobinemia they produce.<sup>[49,51]</sup> Amyl nitrite is inhaled, produces a minimal amount of methemoglobin, and is designed to be administered pending the establishment of i.v. access, as is often the case in the prehospital setting. Sodium nitrite is administered intravenously and results in a methemoglobin concentration of about 15% in healthy adults.<sup>[49]</sup> In other scenarios of cyanide toxicity, particularly the intentional ingestion of cyanide salts, amyl nitrite can be given to adults as one ampul (0.3 mL) inhaled until i.v. access is obtained, followed by 300 mg (10 mL of 3%) i.v. sodium nitrite over two to four minutes.<sup>[41]</sup> Children should receive 6 mg/kg (0.2 mL/kg of 3%) sodium nitrite up to the adult dose, at the same rate. This dosing strategy has been established as safe in children with a hemoglobin concentration of  $\geq 7$  g/dL). Half of the recommended dosage can be administered if cyanide toxicity reappears or, for prophylaxis, two hours after the initial dosage.

### Sodium Thiosulfate

As noted above, cyanide is metabolized by the enzyme rhodanese to a less toxic metabolite, thiocyanate, which is renally eliminated. However, this metabolic pathway is capacity limited. Thiosulfate enhances the activity of rhodanese by donating a sulfur group, thereby increasing the amount of thiocyanate that rhodanese can produce.<sup>[52]</sup> Sodium thiosulfate is relatively well tolerated, but there is a potential for nausea and vomiting, as well as rate-related hypotension.

Because of its relatively favorable adverse-effect profile, sodium thiosulfate should be given to all patients with suspected cyanide toxicity, including those with smoke inhalation. The recommended dosage of sodium thiosulfate for adults is 12.5 g i.v. (50 mL of 25% solution); for pediatric patients, it is 0.5 g/kg i.v. (2 mL/kg of 25% solution) up to the adult dose. One half of the initial dose can be administered two hours later if toxicity reappears or as a preventive measure. Intravenous sodium thiosulfate should be administered either as a bolus injection or infused over 10–30 minutes immediately after sodium nitrite via the same i.v. line.<sup>[41]</sup>

### Hydroxocobalamin

Vitamin B<sub>12a</sub>, or hydroxocobalamin, detoxifies cyanide and forms cyanocobalamin, which is renally excreted. Hydroxocobalamin is an appealing cyanide antidote because it is relatively safe, does not compromise the blood's oxygen-carrying capacity, and, unlike the nitrites or sodium thiosulfate, does not produce hypotension. These features make hydroxocobalamin an ideal agent for empiric use in patients with smoke inhalation who are suspected to have cyanide toxicity.<sup>[53,54]</sup> Hydroxocobalamin has been found

**Toxicology emergencies**

effective for the treatment of acute cyanide poisoning in animal models; in one study of laboratory dogs rendered cyanide toxic, mortality was greatly reduced among dogs given hydroxocobalamin in comparison with those given placebo (21% versus 82%, respectively).<sup>[55]</sup>

In healthy volunteers, the use of hydroxocobalamin has been linked to chromaturia, dose-dependent erythema, headache, GI distress, pruritus, dysphagia, and infusion-site reactions. Allergic reactions are less frequent but occasionally are severe enough to require intervention. In one study, 25% of volunteers who received hydroxocobalamin experienced a substantial rise in diastolic blood pressure, and three also had a rise in systolic blood pressure; these blood pressure changes were attributed to the effects of hydroxocobalamin on nitric oxide scavenging.<sup>[56]</sup> A delayed pustular rash appeared on the face and neck of a few participants in that study and took several weeks to resolve.

Hydroxocobalamin is known to cause a reddish discoloration of the urine that typically resolves within 48 hours.<sup>[57]</sup> Once hydroxocobalamin is administered, the use of laboratory tests that depend on colorimetric techniques is no longer valid, as both hydroxocobalamin and cyanocobalamin are bright red and will cause interference; assays for bilirubin, creatinine, aspartate transaminase (AST), iron, glucose, magnesium, and hemoglobin and most urine assays are among the tests affected. There was a recent case report of a hydroxocobalamin-related colorimetric change resulting in problems with hemodialysis; the machine interpreted the discoloration as a blood leak and shut down automatically.<sup>[58]</sup> Discoloration of urine by hydroxocobalamin also has been reported to interfere with a spectroscopic assay for urinary thiocyanate that is often used to confirm cyanide exposure.

The use of hydroxocobalamin can also skew the results of serum carboxyhemoglobin determinations, falsely increasing or falsely decreasing the measured concentration. Therefore, if possible, blood samples should be drawn before the administration of hydroxocobalamin.<sup>[59-62]</sup>

The empiric adult dose of hydroxocobalamin is 5 g, which can be infused over a period of 15 minutes, with the infusion repeated if necessary; the pediatric dose is 70 mg/kg, up to a maximum of the adult dose, administered at the same infusion rate.<sup>[43]</sup>

There are no published data on the compatibility of hydroxocobalamin with other substances, and the drug should therefore not be administered through the same line as other agents.<sup>[43]</sup> If another line is not available, sodium thiosulfate can be administered through the same line after hydroxocobalamin administration is completed, with care taken to avoid mixing and inactivating the hydroxocobalamin with sodium thiosulfate.

**Implications for the practitioner** Cyanide toxicity should be considered in patients with sudden cardiovascular collapse, especially in the appropriate context of occupational exposure (e.g., laboratory or industrial work) or in a fire victim with hemodynamic instability, elevated lactic acid, or coma. Ideally, cyanide antidotes should be immediately available in the field and must be available in the ED.

Marraffa, J. M., Cohen, V., and Howland, M.A., (2012). Antidotes for toxicological emergencies: A practical review. *American Journal of Health-System Pharmacy*; 69(3), 199-212. [On-line] Posted: 02/14/2012.

# CARBON MONOXIDE

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Produced during incomplete burning of organic fuels

**Examples:** Auto, home, heating (furnaces, water heaters), fires, fireplaces, cigarette smoking (smoke from tip contains 2.5 times more CO than inhaled smoke)

**Characteristics:** Colorless, odorless gas

**Actions:** CO binds with Hb (200 x stronger than O<sub>2</sub>) to form carboxyhemoglobin that decreases the blood's ability to carry O<sub>2</sub> to cells causing tissue hypoxia. Once CO binds with hemoglobin, it is very resistant to removal.

**Incidence:** About ½ of all adult suicides

**S&S:** Often vague, frequently misdiagnosed

HEENT	Roaring sensation in ears, dilated pupils, visual complaints
NEURO	Anxious, restless, <b>confusion, headache</b> , dizzy, twitching, seizures, coma
RESP	Hypoxia, dyspnea on exertion, SOB, <b>tachypnea</b>
CV	Pulse bounding, dysrhythmias, hypotension late
GI	<b>Nausea, vomiting</b>
SKIN	Cyanosis, cherry-red color rarely seen

## Carboxyhemoglobin level and symptoms

5%	None or mild headache
10%	Slight headache, dyspnea on vigorous exertion
20%	Throbbing headache, dyspnea on moderate exertion
30%	Severe headache, irritability, fatigue, dimness of vision
40-50%	Headache, tachycardia, confusion, lethargy, collapse
50-70%	Coma, convulsions
80%	Rapidly fatal

## Factors influencing severity include:

Concentration of CO, ventilation, PMH of anemia or CVD, duration of exposure, physical activity

## Treatment

- Move to fresh air; begin immediate ventilation of the area if possible
  - Draw CO level
  - Oxygen 100% via tight fitting NRM
  - Hyperbaric (HBO) will increase delivery
    - CO half-Life Room Air = 6 hrs
    - CO half-Life 100% O<sub>2</sub> = 30 - 90 min
    - CO half-Life Hyperbaric = 15 - 20 min
- Continue until CO less than 5-10% and patient asymptomatic
- Keep patient at rest to minimize O<sub>2</sub> requirements

## Special considerations

- SpO<sub>2</sub> readings are meaningless in the presence of CO poisoning
- Take awake, alert and oriented patients to the nearest hospital
- Take awake but very confused patients directly to LGH
- Take unstable patients or those in cardiac arrest to the nearest hospital

# PHENOTHIAZINES

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**Examples** Antipsychotics, Stelazine, Mellaril, Haldol, Compazine, Thorazine

Incidence: Life threatening OD relatively rare, more common are side effects

## **Signs and Symptoms** (dystonic reaction)

HEENT Stiff neck, torticollis, protruding tongue, oculogyric eye movements, trismus, lip smacking, facial grimacing, difficulty swallowing

NEURO CNS depression, psychomotor slowing, agitation, seizures, coma

CV Hypotension, tachycardia and bradycardia may be seen

MS Parkinsonian syndrome with rigidity and rest tremor

Akathisia with incessant movement and restlessness

Dysarthria, bizarre movements

## **Treatment**

- Routine toxicology management
- Diphenhydramine for dystonic reactions

# HEAVY METALS

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## IRON (Fe)

**Examples:** Vitamins, pesticides, paint

**Signs and symptoms** - occur when > 20 mg/kg of elemental iron are ingested

NEURO	Decreased LOC, coma, peripheral neuropathies, encephalopathy, seizures, coma
RESP	Tachypnea, congestion, pulmonary edema, cyanosis, respiratory failure
CV	Hemorrhage, shock
GU/GI	Vomiting, hematemesis, abdominal pain, (from <i>concretions</i> or lumps of iron formed when tablets fuse together after being swallowed), bloody diarrhea, hepatotoxicity, GI tract necrosis with possible obstruction, renal failure
Acid/base:	Acidosis may occur
Metabolic:	Fever

## Treatment

- Routine toxicology management
- Charcoal will not bind to any metal, so is ineffective
- Chelating agents at hospital - Deferoxamine therapy - up to 15 mg/kg/hr IV  
Turns urine pink-orange

## LEAD and MERCURY

### Signs and symptoms

NEURO	Headache , irritability, confusion, coma Memory disturbances Tremor, weakness, agitation
GI	Abdominal pain

## Treatment

- Routine toxicology management
- Chelating agents: DMSA, BAL, CDE at the hospital

# POISONOUS PLANTS AND MUSHROOMS

**Examples:** Multiple plants and mushrooms can be poisonous.  
*Amanita* and *Galerina* belong to the deadly *cyclopeptide* group. Toxin is poisonous to the liver with a mortality of 50%.  
Try to obtain a sample of the plant including leaf, stem and any flowers.

## Signs and symptoms

HEENT	Examine mouth and throat for redness, blisters or edema Excessive salivation, lacrimation
NEURO	Decreasing LOC progressing to coma
RESP	
CV	
GU/GI	Abdominal cramps, N/V, diarrhea
SKIN	Diaphoresis

## Treatment

- Routine toxicology management

# **DEXTROMETHORPHAN (DXM)**

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**Examples:** Cough syrups

**Action:** Opium-like derivative, but not classified as a hard drug. Structurally similar to PCP (phencyclidine) so may produce false positive urine drug test results.

Often abused by teens as they can obtain the source legally and they think it is a safe over-the-counter agent

## **Signs and Symptoms**

HEENT  
NEURO

Intoxicating effects range from mildly euphoric to hallucinogenic depending on the person's weight, health status, amount of drug ingested and other drug interactions, such as alcohol. Some web sites advertise 4 different plateaus of intoxicated states. At the first plateau, users experience effects comparable to light social drinking as it frees inhibitions. The second plateau is similar to heavy social drinking leaving the user oriented to surroundings. Visual and auditory stimuli are more enhanced and a sense of euphoria may be present. The third plateau is considered most desirable for the DXM user. They may experience profound philosophical insight, distortions in mental perceptions, and a free, uninhibited feeling. The fourth plateau, reached after ingesting 375 mL, is like taking LSD. Users report out of body experiences with additional physical effects similar to heavy alcohol intoxication.

RESP  
CV

Respiratory depression

GI

Vomiting

SKIN

Risk of liver failure if mixed with significant amounts of acetaminophen like in NyQuil

Diaphoresis

Risk:

Possibly life threatening

Loss of consciousness

## **Treatment**

- IMC; supportive care
- Gastric gavage or activated charcoal at hospital

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**Study questions**

1. Any chemical that causes adverse effects on an organism that is exposed to it is called a/n \_\_\_\_\_.
2. The term, \_\_\_\_\_ is used to describe exposure to nonpharmacological substances
3. Ingestion is the most common route of entry for toxic exposure. Other routes of entry include all **except**
  - A. tertiary.
  - B. injection.
  - C. inhalation.
  - D. surface absorption.
4. Which **IS NOT** a typical route of entry for cyanide?
  - A. Injection
  - B. Ingestion
  - C. Inhalation
  - D. Absorption
5. The process of minimizing toxicity by reducing the amount of toxin absorbed into the body is called \_\_\_\_\_.
6. N-Acetylcysteine is the antidote for \_\_\_\_\_
7. Ethyl alcohol is considered the antidote for \_\_\_\_\_
8. A group of typical signs and symptoms consistently associated with exposure to a particular type of toxin is called a/n \_\_\_\_\_
9. \_\_\_\_\_ is an odorless, tasteless gas that is often the byproduct of incomplete combustion.
10. What drug is used IVPB to reverse cyanide? \_\_\_\_\_
11. Aspirin overdoses may require urine alkalinization with \_\_\_\_\_
12. A compulsive and overwhelming dependence on a drug is called a/n \_\_\_\_\_
13. The need to progressively increase the dose of a drug to reproduce the effect originally achieved by a smaller dose is called \_\_\_\_\_
14. **True or false**  
\_\_\_\_ Syrup of Ipecac is used widely by EMS and in the hospital to decontaminate poisoning cases  
\_\_\_\_ Naloxone has been found to be beneficial to reverse benzodiazepine overdoses.  
\_\_\_\_ Severe cases of CO poisoning may require treatment in a hyperbaric chamber to remove CO from hemoglobin more quickly.  
\_\_\_\_ Activated charcoal binds well with heavy metals such as lead and mercury.

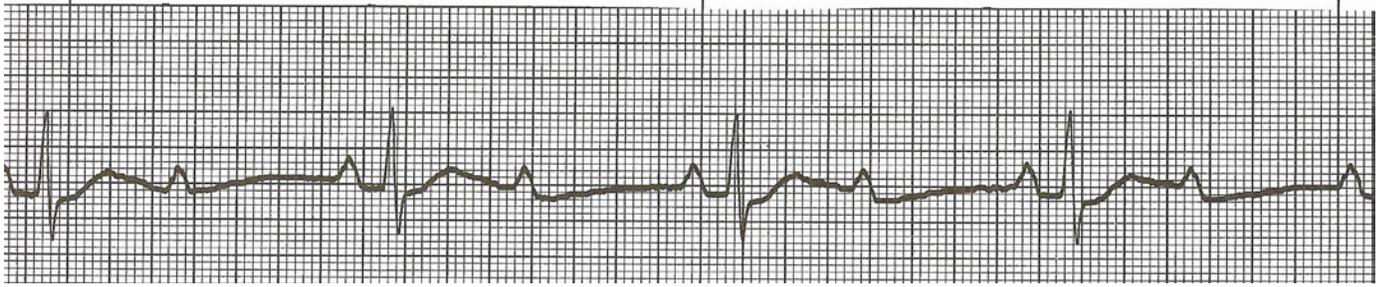
**Toxicology emergencies**

15. A substance that neutralizes a poison or the effects of a poison is called a/n
- 
16. Which is true when caring for a patient with carbon monoxide poisoning?
- A. CO has a distinctive "rotten egg" odor
  - B. Once CO molecules bind with hemoglobin, it is very resistant to removal
  - C. Oxygen has more than 200 times the affinity of CO to bind with hemoglobin
  - D. Because CO binds with RBCs, internal hemorrhage is a serious complication of exposure
17. Which of these is a major objective when treating all poisoning patients?
- A. Induce vomiting
  - B. Prevent aspiration
  - C. Administer activated charcoal
  - D. Administer an empiric coma cocktail
18. An adult has been working in the fields of his farm for several hours. On arrival, the pt presents with sweating, constricted pupils, tearing, drooling, wheezing, abdominal cramps, vomiting, diarrhea, and urinary incontinence. What should a paramedic suspect?
- A. Spider bite
  - B. Heat stroke
  - C. Cyanide poisoning
  - D. Organophosphate poisoning
19. Which of these reflects the range between curative and toxic doses of a medication?
- A. Toxic window
  - B. Curative level
  - C. Therapeutic index
  - D. Cumulative dosage
20. Which of these is true regarding salicylate overdoses?
- A. About 150 mg/kg is the dose required to cause toxicity.
  - B. ASA OD can result in severe metabolic alkalosis and organ failure.
  - C. S&S are likely to include hyperthermia, confusion and rapid respirations.
  - D. The antidote, N-acetylcysteine, is most effective when given rapidly in the field.
21. Which of these is a S&S of poisonous mushroom ingestion?
- A. Dry mouth
  - B. Diaphoresis
  - C. Constipation
  - D. Hallucinations
22. An adult overdosed on medication taken for obsessive-compulsive disorder. The patient is c/o a headache, nausea and palpitations; is very agitated, restless and you note tremors of the hands. Which agent has the patient likely ingested?
- A. Prozac
  - B. Lithium
  - C. An MAO inhibitor
  - D. A tricyclic antidepressant
23. Which of these is evident if a patient reacts severely when deprived of an abused substance?
- A. Addiction
  - B. Tolerance
  - C. Withdrawal
  - D. Dependence

24. What is the treatment for a patient who is agitated and hypertensive from a cocaine overdose?
- A. naloxone
  - B. flumazenil
  - C. midazolam
  - D. nitroglycerin
25. Which benzodiazepine is commonly referred to as a "date rape" drug?
- A. PCP
  - B. Restoril
  - C. Halcyon
  - D. Rohypnol
26. For which class of drugs is flumazenil used to counteract adverse effects?
- A. Barbiturates
  - B. Hallucinogens
  - C. Benzodiazepines
  - D. Marijuana derivatives
27. Which of these should be given to a patient with an organophosphate poisoning?
- A. atropine
  - B. epinephrine
  - C. diphenhydramine
  - D. sodium bicarbonate
28. Which designer drug should be suspected if a patient is found at a rave party with altered mental status, respiratory depression, clenched teeth and a pacifier around their neck?
- A. GHB
  - B. Ecstasy
  - C. Rohypnol
  - D. Speed ball
29. What is the agent in cough syrups that produces intoxicating effects and causes teens to abuse these over-the-counter medications?
30. If you are presented with a patient who says he has "entered the third dimension" and believes that he can fly, what type of ingestion should a paramedic suspect?
- A. Narcotic opiate
  - B. Hallucinogen
  - C. Amphetamine
  - D. Barbiturate
31. An adult presents with CNS depression, small pupils, respiratory depression, hypotension, and bradycardia. What type of overdose should a paramedic suspect?
- A. Narcotic
  - B. Amphetamine
  - C. Hallucinogenic
  - D. Benzodiazepine
32. What drug should be given to reverse the clinical S&S in the above patient?
- A. atropine
  - B. glucagon
  - C. naloxone (Narcan)
  - D. sodium bicarbonate

**Toxicology emergencies**

33. An elderly male has overdosed on Inderal (propranolol). BP 80/palp, P 30; R 12. Identify his rhythm.



- A. Second degree block Mobitz II
  - B. Third degree AV block
  - C. Idioventricular rhythm
  - D. Sinus bradycardia w/ PVCs
34. After IMC, if pacing and dopamine are unsuccessful for the above patient, which of these is indicated first based on the current SOPs?
- A. Atropine 1 mg IVP
  - B. Glucagon 1 mg IVP.
  - C. Albuterol 10 mg / HHN
  - D. Epinephrine 1:10,000 1 mg IVP
35. Which of these is indicated to treat a symptomatic patient with a tricyclic antidepressant overdose?
- A. atropine
  - B. glucagon
  - C. naloxone
  - D. sodium bicarbonate
36. What is the classification of cocaine?
- A. Narcotic
  - B. Hallucinogen
  - C. Amphetamine
  - D. CNS stimulant
37. Tricyclic antidepressant overdoses bind and block the alpha receptors on the blood vessels and block the Na channels in the heart resulting in
- A. hypotension and wide QRS complexes.
  - B. tachycardia and vasoconstriction.
  - C. hypertension and atrial fibrillation.
  - D. bradycardia and seizure activity.
38. If an unconscious female patient presents with respiratory depression & nystagmus after euphoria and what appeared to be seizure-like activity, what type of ingestion should a paramedic suspect?
- A. GHB
  - B. Ecstasy
  - C. Angel dust
  - D. Amphetamines
39. Which alcohol ingestion can rapidly cause blindness?
40. Why do acetaminophen overdoses carry such a high morbidity and mortality? What organ do they damage?