CYANIDE

Description

Includes:
Hydrogen cyanide (hydrocyanic acid, prussic acid, HCN) used in manufacture of fibers, plastics, and as a fumigant. Hydrogen cyanide is a gas which may be liquefied to hydrocyanic acid.

Cyanide salts (e.g. potassium, sodium, calcium, silver cyanide), used in electroplating, metal cleaning and polishing, jewelry making, ore refining, metal extraction and metallurgy. Also used as a fumigant powder in agriculture and restricted use as a rodenticide in Canada and other countries.

Cyanide-releasing compounds (also called cyanogens or nitriles) Compounds which liberate cyanide upon decomposition or chemical reaction:
cyanogen (gas) and its halides (e.g. *cyanogen chloride, cyanogen iodide*).
Burning *polyurethanes* and *plastics* can release cyanide; cyanide poisoning should be suspected in smoke inhalation victims.

Compounds which liberate cyanide within the body following exposure include:
acetonitrile (methyl cyanide, used as general solvent in manufacture of pesticides, acrylic fibres, present in some artificial nail removers, **see also** NAIL CARE PRODUCTS)
acrylonitrile (used in manufacture of nylon, polymers, and as a fumigant). Metabolism involves conjugation with glutathione; N-acetylcysteine treatment may be useful.
sodium nitroprusside (releases cyanide when metabolized)
cyanogenic glycosides (amygdalin, laetrile; found in plants including pits or seeds of cherry, apricot, apple, **see** PLANTS - CYANOGENIC GLYCOSIDES).

Ferrocyanides and *ferricyanides* can release cyanide, but rarely cause toxicity because of tight binding between metal and cyanyl group.

SI Unit Conversion

cyanide (µg/mL OR mg/L) = 0.026 x cyanide (µmol/L)

Toxicity

Severe acute cyanide poisoning is commonly associated with rapid onset of CNS symptoms (coma, seizures), cardiovascular effects (hypotension, tachycardia), and metabolic acidosis. Symptoms may be mistaken for other illnesses, and diagnosis requires a high index of suspicion. Hydrogen cyanide and inorganic cyanide salts tend to produce symptoms rapidly following acute exposure. Death may occur within minutes. Exposure to cyanide-releasing compounds may result in delayed onset of symptoms.

Mechanism of Toxicity

Cyanide inhibits numerous enzymes including cytochrome oxidase a3 in the mitochondrial electron transport chain resulting in inhibition of ATP production, inhibition of cellular aerobic metabolism, cellular anoxia, accumulation of hydrogen ions and acidemia. Subsequent shift to anaerobic metabolism results in excess production of lactate. There is a significant association between lactate level and cyanide level including in victims of smoke inhalation without significant burns.
In one study of cyanide poisoned patients a lactate ≥ 8 mmol/L had a sensitivity of 94%, a specificity of 70%, a positive predictive value of 64%, and a negative predictive value of 98% for a blood cyanide concentration of ≥ 38 µmol/L. Effects are most pronounced in brain and cardiovascular system.
Chronic cyanide exposure may cause neurotoxicity (mechanism unclear).
Alkaline salts (potassium, sodium) may cause caustic injury as well as systemic effects.
Thiocyanate metabolite is toxic if high concentrations accumulate. **See also** SODIUM THIOSULFATE antidote monograph.

Toxic Dose

Hydrogen cyanide and cyanide salts Air concentrations of 200-300 ppm *hydrogen cyanide* may be rapidly fatal. "Bitter almond" odour of hydrogen cyanide is *not* a reliable indicator of danger; many individuals are unable to detect or recognize this odour. Estimated adult lethal oral dose is 50 mg of *hydrocyanic acid* and 200-300 mg of cyanide salts. Patients have survived > 1 g *potassium cyanide* ingestions with antidote therapy.
Acetonitrile Ingestion of as little as 5 mL of 85-100% solution may produce life-threatening toxicity in children or adults. Reported lethal air concentrations vary.

Nitroprusside Toxic cyanide concentrations *may* accumulate under following conditions:
Short-term infusion (1-2 hours): total dose > 0.5-1.5 mg/kg
Long-term infusion (> 2 hours): rates > 4 µg/kg/minute
Post-operative or malnourished patients and individuals with renal dysfunction may be more susceptible.

Cyanide levels can be used retrospectively to confirm poisonings; not readily available. Whole blood cyanide levels > 38 µmol/L are generally associated with toxicity; however, whole blood or plasma levels may be a poor predictor of toxic effects. Red blood cell cyanide concentrations may be preferred: normal < 1 µmol/L.
Cyanide levels drawn after antidote administration are difficult to interpret; antidotal treatment will increase measured cyanide levels.

Case Reports
acetonitrile A 2-year-old ingested 5-10 mL of an artificial nail remover containing 84% *acetonitrile*. Within 14 hours post ingestion, patient developed restlessness, vomiting and seizures. Patient arrived at hospital comatose with RR of 36/minute, HR 176 beats/minute, BP 104/80 mmHg, pH 7.08, pO_2 38 mmHg, pCO_2 22 mmHg and bicarbonate 6.6 mmol/L. Patient received oxygen, amyl nitrite, sodium nitrite, sodium thiosulfate and awakened within 10 minutes. Patient was maintained on oxygen for 24 hours and discharged after 2 days with no apparent sequelae.
laetrile/amygdalin **See** PLANTS-CYANOGENIC GLYCOSIDES.
potassium cyanide A 34-year-old ingested 1 g and became comatose within 45 minutes; apnea, seizures and metabolic acidosis developed rapidly. Supportive care was initiated within 45 minutes, and antidotes (sodium nitrite, sodium thiosulfate) administered within 75 minutes. Patient made a full recovery in less than one day.
A 17-year-old was intentionally administered up to 1.5 g potassium cyanide and within minutes felt unwell and developed "seizure-like" activity. Paramedics responded but history of cyanide ingestion was not provided. Patient was intubated and given naloxone with no response. On admission to hospital BP was 98/49 mmHg, HR 79 beats/minute, RR 4/minute. Patient had GCS of 3, with absent corneal, gag and cough reflexes, 5 mm non-reactive pupils, and weak peripheral pulses. ABGs showed pH 7.25, bicarbonate 9 mEq/L. He was treated with fluids, bicarbonate, dopamine. He developed atrial fibrillation and was cardioverted. Condition worsened over next hour and he developed bradycardia, with systolic pressure in mid-50s. By 4 hours post ingestion, anion gap was 38, lactate 20 mmol/L, bicarbonate 7 mEq/L, pH 7.11, and an elevated venous oxygen was noted. Based on clinical effects, profound acidosis, elevated lactate and venous oxygen, cyanide poisoning was suspected and patient was given IV sodium nitrite and sodium thiosulfate. Within minutes bradycardia resolved and hypotension improved. Patient required multiple repeated doses of antidote. Over next 48 hours, patient remained hemodynamically unstable and MRI revealed multiple brain infarctions and edema. Brain death criteria were met about 60 hours post ingestion.

Pharmacokinetics
Hydrogen cyanide and cyanide salts Rapidly absorbed by ingestion, inhalation and through mucosal surfaces. Symptoms may be seen within seconds to minutes of inhalation or ingestion; death within minutes to hours depending on route of exposure. May be absorbed through intact skin, although most reported cases involve extensive burns from molten cyanide salts or immersion in vats of cyanide solution.
Primarily detoxified via several mitochondrial enzymes to form less toxic *thiocyanate*, which is excreted in urine. Detoxification pathways are inadequate in significant cyanide exposure.
Elimination half-life from blood varies (1-66 hours) depending on type of cyanide, dose, route of exposure and effects of antidotal therapy.
For half-life of *thiocyanate*, **see** SODIUM THIOSULFATE antidote monograph.
Acetonitrile Absorbed following ingestion, inhalation or dermal application. Metabolized in liver; partially converted to cyanide. Onset of cyanide toxicity may be delayed 3-12 hours or more; cyanide release may continue for several days after exposure.
Acrylonitrile Metabolism involves conjugation with glutathione; N-acetylcysteine treatment may be useful.
Nitroprusside Each molecule contains five cyanide moieties. Does not appear to be absorbed orally; however, liberated cyanide may be absorbed. Following IV infusion, converted to free cyanide in plasma or extracellular space, which combines with thiosulfate to produce *thiocyanate*. Onset of cyanide toxicity may appear within hours to days after starting infusion. Elimination half-life of nitroprusside is approximately 2 minutes. May also result in thiocyanate toxicity if high levels accumulate, **see also** SODIUM THIOSULFATE antidote monograph, for thiocyanate toxicity and elimination.

Clinical Effects

- **General:** Symptom onset may be very rapid or delayed several hours depending on chemical form of cyanide and route of exposure. Inhalation of *hydrogen cyanide* usually produces effects within minutes depending on concentration. Ingestion of *inorganic cyanide salts* can be expected to cause symptoms within 30 minutes. Ingestion of *cyanide-releasing compounds* may result in a delay of symptoms up to 24 hours. Hypothermia is common.

- **Topical:** Exposure to concentrated solutions of cyanide salts can cause skin burns as well as systemic toxicity. Marked flushing may be observed from systemic effects (**see** Ingestion). Chronic skin exposure can result in corrosive dermatitis.

- **Ocular:** Possible irritation. *Hydrogen cyanide* vapours can cause conjunctivitis, corneal edema. Systemic toxicity has not been reported following ocular exposure but should be considered.

- **Inhalation:** Respiratory tract irritation. Massive exposure may produce sudden loss of consciousness and death from respiratory arrest within minutes. Cyanogen chloride can cause delayed pulmonary edema. Systemic effects as for Ingestion.
  Low-level chronic inhalation exposure can result in irritation of mucous membranes and respiratory tract (with caustic salts). Headache, fatigue, dizziness, optic neuropathy, myelopathy, thyroid dysfunction have been reported (uncommon).

- **Ingestion**:
  HEENT: Burning of tongue and mucous membranes, mydriasis.
  CVS: Tachycardia (common in early stage), transient mild hypertension; usually progresses to hypotension, bradycardia, cardiovascular collapse.
  Respiratory: Increased rate and depth of respiration (common initially); may progress to dyspnea, respiratory depression, apnea, respiratory arrest. Pulmonary edema may develop.
  Neurologic: Headache, anxiety, dizziness, agitation, confusion may progress rapidly to seizures and coma.
  GI: Nausea, vomiting, abdominal pain. Corrosive injury with bleeding and perforation may occur following ingestion of alkaline cyanide salts.
  Fluid/Lytes/Acid-Base: Anion gap metabolic acidosis with hyperlactatemia is characteristic of severe cyanide poisoning. Elevated mixed venous oxygen (requires central venous access; elevated results are not specific to cyanide).
  Blood: Hyperglycemia may be noted.
  Skin: Red colour due to increased oxygen in venous blood; however, patients may also appear cyanotic (blue).
  Late Sequelae of Acute Exposure: Delayed neurologic sequelae (rare) after significant cyanide poisoning include Parkinsonism, extrapyramidal syndromes, memory impairment and personality changes. May not respond to antiparkinsonian medications.
  Note: Death from cyanide poisoning does not prohibit organ transplant.

Treatment

General: Prompt rescue and treatment is required. Rescue of an unconscious victim exposed to cyanide gas should only be performed by personnel equipped with respiratory protection, protective clothing, and devices that can quickly measure cyanide air concentration.

1. **Topical**: Caregivers should wear gown, gloves, and protective eyewear. Decontaminate patient BEFORE entering hospital: remove and dispose of contaminated clothing and shoes, brush off any powder from skin and flush skin and wounds thoroughly with water (soap optional). Treat systemic effects as for ingestion.

2. **Ocular**: Flush eyes with a gentle stream of tepid water for 15 minutes. Obtain ophthalmologic opinion if irritation persists.

3. **Inhalation**: Remove from exposure. Rescuers should wear self-contained breathing apparatus. Protect airway and assist ventilation as needed. Remove and dispose of contaminated clothing. If patient is *asymptomatic*, observe closely for at least 4-6 hours. Treat systemic effects as for ingestion.

4. **Ingestion**: Caregivers should wear gown, gloves, and protective eyewear; avoid direct mouth-to-mouth resuscitation and direct contact with skin or gastric contents. There have been no reports of serious illness or death in health care workers caring for these patients.

5. **All patients should receive *100% oxygen* by nonrebreather facemask; intubate and ventilate patient as required**. Oxygen alone can partially reverse cyanide toxicity and is synergistic with other antidotes.

6. ***Asymptomatic*** patients with history of ingestion of hydrogen cyanide or cyanide salts, *should receive oxygen*; *antidotes are NOT indicated*.
   Observe and monitor for at least 6 hours (24 hours for nitriles or cyanide-releasing compounds).

7. *Oxygen, supportive care, and IV hydroxocobalamin* should be administered to ***symptomatic*** patients with
   - a history of cyanide exposure, ***OR***
   - when cyanide exposure is a consideration, especially if lactate is ≥ 8 mmol/L, ***OR***
   - pregnant women, ***OR***
   - life-threatening smoke inhalation with concurrent carbon monoxide and cyanide poisoning (lactate ≥ 8 mmol/L)

   Hydroxocobalamin should be considered as first-line therapy over sodium thiosulfate and nitrites. **See** HYDROXOCOBALAMIN antidote monograph.
   IV sodium thiosulfate can be considered for patients who have received maximum dose of hydroxocobalamin but have persistent effects of cyanide **OR** when hydroxocobalamin is unavailable. **See** SODIUM THIOSULFATE antidote monograph.

Observe and monitor until symptoms resolve and for 12 hours after last dose of antidote (24 hours after last antidote if exposed to nitriles or cyanide-releasing compounds).

8. Gastric lavage is seldom practical because of rapid absorption and onset of symptoms. Activated charcoal is of limited value but may be administered for recent ingestions of cyanide-releasing compounds.

9. **Monitor** vital signs, ECG, electrolytes, serum lactate, anion gap, arterial and venous blood gases (elevated venous oxygen may indicate cellular anoxia), renal and liver function. If nitrite therapy is used, monitor methemoglobin levels especially if repeat doses of sodium nitrite are required. Cyanide level (whole blood), may be useful for confirming exposure; do *not* delay treatment awaiting results. If obtaining a cyanide level, it is best to draw before hydroxocobalamin administration but only if drawing a level will not delay treatment. Perform chest X-ray if aspiration or inhalation occurred.

10. Hypotension unresponsive to IV fluids may require vasopressors.

11. Maintain fluid and electrolyte balance. Treat severe metabolic acidosis with IV sodium bicarbonate.

12. Seizures should be treated with IV benzodiazepines. Seizures refractory to high dose benzodiazepines should be treated with propofol or barbiturates.

13. **Antidotes**: Cyanokit® contains hydroxocobalamin (preferred antidote). Sodium thiosulfate may be used alone (with oxygen and supportive care), or with sodium nitrite if hydroxocobalamin in unavailable.
    Hydroxocobalamin: Administer IV over 15-30 minutes.
    Adult: 5 g IV infusion. Depending on the severity of the poisoning and the clinical response, a second dose may be given after 15 minutes. The maximum recommended total dose is 140 mg/kg body weight not exceeding 10 g. If patient is not responding, look for other causes/contributors for metabolic acidosis.
    Child: 70 mg/kg IV infusion. Depending on the severity of the poisoning and the clinical response, a second dose may be given after 15 minutes. The maximum recommended total dose is 140 mg/kg body weight not exceeding 10 g.
    For indications, administration, cautions and contraindications, **see** HYDROXOCOBALAMIN antidote monograph.
    Sodium Thiosulfate: Administer IV over a minimum of 10 minutes.
    Adult, first dose: 12.5 g (50 mL of a 25% solution).
    Child, first dose: 250 mg/kg (1 mL/kg of a 25% solution); maximum 12.5 g (50 mL of a 25% solution).
    See SODIUM THIOSULFATE antidote monograph.
    Sodium Nitrite: Administer over 5-20 minutes.
    Adult, first dose: 300 mg IV (10 mL of a 3% solution).
    Child, first dose: 4 mg/kg IV (0.13 mL/kg of a 3% solution); do not exceed 300 mg (10 mL of a 3% solution).
    Caution hypotension; do *not* exceed methemoglobin concentration of 25%, much lower levels may be adequate.
    For indications, administration, cautions and contraindications, **see** SODIUM NITRITE antidote monograph.

14. ***Hyperbaric oxygen*** may be useful as an adjunct to antidotal therapy in symptomatic patients not responding to conventional antidotal and supportive therapy, or in fire victims exhibiting manifestations of both cyanide and carbon monoxide toxicity.

15. Perform endoscopy in patients with GI symptoms who have ingested a caustic cyanide salt. **See also** ALKALI.

16. *Hemodialysis* and *charcoal hemoperfusion* do not have a role in treatment of cyanide poisoning.

17. Follow-up as an outpatient for possible development of delayed neurologic sequelae (rare).

18. In patients who do not survive, cyanide poisoning does not prohibit use of organs for transplantation.

Key Points

- Severe acute cyanide poisoning is commonly associated with rapid onset of CNS symptoms (coma, seizures), cardiovascular effects (hypotension, tachycardia), and metabolic acidosis. Symptoms may be mistaken for other illnesses, and diagnosis requires a high index of suspicion.

- Hydrogen cyanide and inorganic cyanide salts produce symptoms rapidly following acute exposure.

  Death may occur within minutes. Exposure to nitriles and cyanide-releasing compounds may result in delayed onset of symptoms.

- All patients with suspected cyanide exposure should be treated with supplemental oxygen and supportive measures.

- *Asymptomatic* patients should be monitored for 6 hours following acute exposure to hydrogen cyanide or inorganic cyanide salts. Monitoring period should be extended to 24 hours following exposure to nitriles and cyanide-releasing compounds.

- Antidotes include hydroxocobalamin (preferred), sodium thiosulfate, and sodium nitrite. **See specific antidote monographs.**

- Hydroxocobalamin is considered first-line antidotal therapy, if available.