Protocol for Iron poisoning management

**Category/Use:** Iron supplements are used for the prevention and treatment of iron deficiency anemia, and as a nutritional supplement to provide additional iron during pregnancy. Iron dextran, iron sucrose, and sodium ferric gluconate are parenteral products which are used for the treatment of iron deficiency in patients for whom oral administration is ineffective or not feasible. Iron may also be contained in multivitamins.

**Specific substances:** Carbonyl Iron; Elemental Iron; Fe; Ferric Gluconate; Ferrous Fumarate; Ferrous Gluconate; Ferrous Iron; Ferrous Sulfate; Iron Dextran Complex; Iron Sucrose; Polysaccharide-Iron Complex

**Range of toxicity:**

All patients (children and adults) suspected of ingesting ≥40 mg/kg of elemental iron in the form of adult iron preparations or those with severe or persistent symptoms (persistent vomiting and diarrhea, alterations in consciousness, hematemesis, bloody diarrhea). Children who ingest multiple vitamins with iron preparations are unlikely to develop toxicity unless the amount of elemental iron exceeds 60 mg/kg; however, a poison center should always be consulted regarding any patient who has ingested >40 mg/kg of elemental iron.

The outcome of an oral exposure to iron-containing products may be anticipated if the amount of elemental iron ingested per unit of weight (mg/kg) can be quantitated. The ingestion of <20 mg/kg of elemental iron is unlikely to result in toxicity. The ingestion of carbonyl iron is unlikely to result in toxicity. In a pregnant patient, the prepregnancy weight should be used in the calculation. The percentage of elemental iron in commonly used iron salts is:

- Ferrous sulfate: 20% (every 100 mg = 20 mg of elemental iron)
- Ferrous fumarate: 33% (every 100 mg = 33 mg of elemental iron)
- Ferrous gluconate: 12% (every 100 mg = 12 mg of elemental iron)

Pediatric and adult patients who have ingested <40 mg/kg of elemental iron with mild symptoms (eg, vomiting and diarrhea) can be observed at home. If symptoms escalate (persistent vomiting, CNS depression), the patient must be evaluated in the emergency department.

**Mortality rate:** Not available

**Clinical presentation:**

- **Ingestion:** Severe symptoms of iron poisoning include coagulopathy, coma, erosion of the gastric mucosa, esophageal ulceration, hematemesis, hepatic and renal impairment, metabolic acidosis, and profound hypotension.
Classically, there are five stages of acute iron poisoning.

Stage I (30 minutes to 6 hours): Abdominal pain, hematemesis, hematochezia, diarrhea, nausea, and vomiting. The absence of GI symptoms suggests severe poisoning is unlikely.

Stage II (4-12 hours): A latent period of quiescence during which improvement of gastrointestinal symptoms occurs; however, subclinical hypoperfusion and metabolic acidosis may be present. This latent period may not be observed in severe poisonings.

Stage III (6-72 hours): Profound hypotension and metabolic acidosis occur and are the most common cause of death. Coagulopathy (early onset) and coma may also occur.

Stage IV (12-96 hours): Hepatotoxicity, coagulopathy (late onset), and renal insufficiency may occur.

Stage V (2-4 weeks): Primarily delayed GI complications, including gastric or duodenal fibrosis and scarring resulting in bowel obstruction

Comprehensive listing by system (listed alphabetically):

Cardiovascular: Flushing, heart failure, hypotension, myocardial depression, sinus tachycardia, vasodilation

Central nervous system: Chills, coma, dizziness, fever, headache

Endocrine & metabolic: Dehydration, metabolic acidosis (anion gap)

Gastrointestinal: Abdominal pain, dark stools, diarrhea, esophagitis, gastrointestinal irritation, heartburn, hematemesis, hematochezia, metallic taste, nausea, vomiting

Hematologic: Coagulopathy (early and late), leukocytosis

Hepatic: Hepatic failure, hepatic necrosis, jaundice, steatosis

Local: Pain, phlebitis, staining of skin at the site of I.M. injection

Neuromuscular & skeletal: Arthralgia

Renal: Hematuria, renal failure, renal insufficiency

Mechanism of Toxicity:

The human body has no means of excreting iron and iron homeostasis is normally maintained by regulating gastrointestinal absorption. Dietary ferrous (Fe$^{2+}$) iron is absorbed in the duodenum and proximal jejunum where it is bound to ferritin within intestinal mucosal cells and subsequently bound as ferric iron (Fe$^{3+}$) to the carrier protein transferrin and transported throughout the body as needed. In the overdose setting, toxicity may occur when the quantity of iron present exceeds the capacity of transferrin to bind the iron, but this mechanism is just postulated. The interaction of free ferrous iron with peroxides results in free radical production and damage to DNA, proteins, lipids, and other biologically important molecules.
Gastrointestinal injury is the result of local toxicity and may occur with even smaller ingested doses of iron, especially when a bezoar occurs. Serious gastrointestinal injury is unlikely following small overdoses of chewable children's vitamins that contain iron. Cardiovascular toxicity and hepatic necrosis are due to the systemic effects of absorbed iron and are associated with larger amounts of ingested iron.

Causes for the development of metabolic acidosis include lactic acidosis due to hypoperfusion and disruption of oxidative phosphorylation. The hydration of free iron by water to form iron hydroxide \([\text{Fe(OH)}_3]\) releases three protons, leading to the further development of metabolic acidosis.

**Pharmacokinetics:**

Route of exposure: Oral ingestion

Absorption: Iron is absorbed in the duodenum and upper jejunum. Because serum iron rapidly distributes into tissue, a serum iron concentration obtained 2-4 hours after the ingestion is most useful for assessing the degree of toxicity unless enteric-coated tablets have been ingested.

**Criteria for hospital admission:** Patients requiring deferoxamine therapy and any symptomatic patient with elevated iron levels

**Monitoring parameters:**
Blood Gases and pH, Arterial, Iron and Total Iron Binding Capacity/Transferrin, X-ray, Abdominal Series

**First aid measures:** Same as decontamination method explained in treatment part

**Treatment:**

**Oral exposure:**

**Stabilization**

Initially, evaluate and correct immediate life-threatening complications (eg, airway, breathing, and circulation). The serious complications of iron toxicity are hypotension, gastric erosion, and hepatic necrosis.

**Decontamination method**

**Ingestion:**

**Emesis:** Emesis is not recommended. Also Cathartics are not recommended.

**Activated charcoal:** Not recommended because iron bind weakly to activated charcoal. If potential high toxic ingestion of iron, activated charcoal can be given.

If the patient presents **within 1 hour** of ingestion, consider the following decontamination procedure(s):
**Gastric aspiration and lavage**: In rare situations when gastric lavage is deemed appropriate, it is most effective if initiated within 1 hour of ingestion; however, gastric aspiration and lavage have not been proven to be beneficial and are not routinely recommended due to the risk of complications and the lack of demonstrated efficacy. Use is contraindicated in patients with unprotected airways, in patients in whom its use increases the risk and severity of aspiration, and in patients who are at risk of hemorrhage or gastrointestinal perforation due to pathology.

If the patient presents following an ingestion of a potentially toxic amount of iron, even if >1 hour has elapsed since the ingestion, consider the following decontamination procedure(s):

**Whole bowel irrigation (WBI)**: WBI has not been well documented to improve the outcome of poisoned patients; however, WBI may be considered for ingestions of substances that carry a relatively high degree of morbidity and/or mortality (e.g., substances not bound to activated charcoal; sustained-release formulations of selected agents). Consultation with a poison control center is highly recommended. WBI is contraindicated in the presence of ileus, bowel obstruction, bowel perforation, clinically-significant GI hemorrhage, hemodynamic instability, intractable or uncontrollable vomiting, or an unprotected compromised airway.

**Polyethylene glycol-electrolyte solution**: Oral or NG: **Note**: Continue treatment at least until the rectal effluent is clear; treatment duration may be extended based on corroborative evidence of continued presence of poisons in the GI tract. Confirm the efficacy of WBI by x-ray visualization of the abdomen for the presence of iron.

- Children 9 months to 6 years: 500 mL/hour
- Children 6-12 years: 1000 mL/hour
- Children >12 years and Adults: 1500-2000 mL/hour

**Specific Antidote(s):**

**Deferoxamine**:

**Indications for use**: Deferoxamine therapy uses are not firmly established but may include:

- Significant toxicity (shock, altered mental status, metabolic acidosis)
- Serum iron concentrations ≥500 mcg/dL (drawn 4-6 hours after ingestion)

**Note**: Prior to initiating chelation therapy with deferoxamine, hypovolemia should be corrected with intravenous crystalloid solutions to prevent possible renal injury. Avoid chelation therapy in the absence of clinical and/or laboratory indications of toxicity despite radiopaque material in the gastrointestinal tract.
**Mechanism of action:** A chelating agent that binds with free iron to form ferrioxamine which is excreted renally. This compound may turn the urine orange or pink-red (vin rose).

**Goal of therapy:** Resolution of clinical symptoms and laboratory abnormalities; no additional changes in urine color

**Dosage:** Acute iron toxicity: Children and Adults: I.V. infusion: Initial dose: 15 mg/kg/hour; monitor blood pressure closely

**Dose:**

**Intravenous Dose** - Administer by continuous infusion at a rate of up to 15 mg/kg/hour.  
1b) Faster rates or IV boluses may cause hypotension in some individuals.  
c) Infusion rates of up to 35 mg/kg/hour have been used in children with severe overdoses without adverse effects.

**Intramuscular Dose** - Administer 90 mg/kg, up to a maximum of 1 gram/dose, every 8 hours as needed. Pain and induration at the injection site are often experienced. Intravenous infusion is much preferred because of more reliable absorption. Six to 12 grams/day have been successfully administered in daily intravenous doses every 12 hours to chronic iron-overloaded patients without significant adverse dosing effects.

Duration of infusion is guided by the patient's clinical condition. Patients with moderate toxicity are generally treated for 8 to 12 hours, those with severe toxicity may require deferoxamine for 24 hours. Patients should be re-evaluated for evidence of recurrent toxicity (hypotension, metabolic acidosis) several hours after the infusion is discontinued. Infusion duration of greater than 24 hours has been associated with the development of acute lung injury and should generally be avoided.

**Supportive Treatment**

**Hypotensive episode:**

Treat with isotonic crystalloids and vasopressors, if necessary. Initial intervention should include fluid resuscitation. Refractory hypotension may require treatment with a vasopressor (eg, dopamine, norepinephrine).

**Dopamine:** Starting 5 microgram/kg/minute progressing in 5 micrograms/kg/minute increments as needed. Norepinephrine should be added if more than 20 micrograms/kilogram/minute of dopamine is needed.

[PREPARATION: Add 400 milligrams to 250 milliliters of normal saline or dextrose 5% in water to produce 1600 micrograms per milliliter or add 400 milligrams to 500 milliliters of normal saline or dextrose 5% in water to produce 800 micrograms per milliliter.

**Norepinephrine:**
Adult dose: Start infusion at 0.5 to 1 microgram/minute and titrate to maintain adequate blood pressure.

Child dose: Start infusion at 0.1 microgram/kilogram/minute and titrate to maintain adequate blood pressure.

[PREPARATION: Add four milligram norepinephrine to 250 milliliters of dextrose 5% in water to produce a concentration of 16 micrograms/milliliter.]

Hypovolemia: Treat with isotonic crystalloids.

Elimination enhancement method:

Surgical decontamination: Concretion formation (bezoar) is an occasional complication of large iron ingestions. When gastric decontamination with whole bowel irrigation proved unsuccessful, laparotomy and gastrotomy were used to remove iron tablet concretions; however, this should be considered only when other measures have failed.

Hemodialysis: In the event of renal failure, hemodialysis may enhance the elimination of ferrioxamine or the iron-deferoxamine complex in patients with renal failure; however, hemodialysis is not effective at removing iron itself.

Eye exposure:

Decontamination: Corneal rust rings around the foreign body are usually absorbed by phagocytic pathways and softening of the surrounding cornea. They can also be removed mechanically or surgically by those trained in this procedure.

Treatment: Treating with deferoxamine several times a day as eye drops or 10% ophthalmic ointment can help in ridding these rings.

Treatment should include recommendations listed in the ORAL EXPOSURE section when appropriate.

Criteria for emergency department discharge:

Asymptomatic patients without radiological evidence of iron ingestion may be discharged from the emergency department after 6 hours of observation.

Asymptomatic patients are unlikely to develop symptoms if >6 hours have elapsed since the ingestion.

Complications of Exposure:

Liver failure: May require transplantation

Pregnant women with stage III toxicity: A review of 61 cases of iron overdose during pregnancy found that although women with peak serum iron levels >400 mcg/dL were more frequently symptomatic, iron levels >400 mcg/dL were not associated with increased risk of spontaneous
abortion, preterm delivery, congenital anomalies, or maternal death; however, patients with stage III toxicity were more likely to spontaneously abort, deliver preterm, or experience maternal death

**Contraindications:** Information not available

**References:**


3. www.lexi.com