HISTORY AND EPIDEMIOLOGY

Iron poisoning has become uncommon. This success may underscore the importance of prevention by interventions gleaned from poison center data and poison prevention advocacy. Blister packaging, smaller dosages, and education of parents and health care professionals have led to a great decline in iron poisoning in the past two decades. Unfortunately, however, significant iron poisonings still occur, and clinician must be aware of the nuances of presentation and diagnosis to optimize iron poisoning management. Clinicians must be vigilant for signs of serious iron poisoning and be ready to intervene if gastrointestinal (GI) toxic effects are followed by acid–base disturbances, altered mental status, or hemodynamic compromise.

Iron salts such as ferrous sulfate have been used therapeutically for thousands of years and continue to be available, both with and without prescription, for the prevention and treatment of iron deficiency anemia in patients of all ages. Despite this long history of use, the first reports of iron toxicity only occurred in the mid-twentieth century. Since then, numerous cases of iron poisoning and fatalities have been reported, mostly in children. In 1950, the manufacturer of “fersolate,” an iron supplement, included a package warning: “Excessive doses of iron can be dangerous. Do not leave these tablets within reach of young children, who may eat them as sweets with harmful results.”

The incidence of iron exposures continued to increase in the 1980s, ultimately becoming, in the 1990s, the leading cause of poisoning deaths reported to poison centers among children younger than 6 years (Chap. 136). This problem was publicized in a case series of tragic fatalities involving five toddlers in Los Angeles during a 6-month period in 1992, all of whom were exposed to prenatal vitamins containing iron. The association between death and prenatal vitamins highlights the availability of these potentially lethal medications in the homes of families with young children, ironically as a result of more attentive prescribing of prenatal iron. A case control study in Canada identified a fourfold increase in the risk of iron poisoning to the older sibling of a newborn during the first postpartum month. The authors concluded that almost one-half of all hospital admissions of young children for iron poisoning could be prevented by safer storage of iron supplements in the year before and the year after the birth of a sibling.

In 1997, the US Food and Drug Administration (FDA) mandated that all iron salt-containing preparations display warning labels regarding the dangers of pediatric iron poisoning. In addition to the warning labels, the FDA launched an educational campaign to alert caregivers and prescribers of the potential toxicity of iron supplements. Other preventive initiatives instituted by the FDA in 1997
included unit dosing (blister packs) of prescriptions for preparations containing more than 30 mg of elemental iron and limitations on the number of pills dispensed (ie, maximum 30 day supply). These efforts to prevent unintentional exposure dramatically decreased the incidence of poisoning and were pivotal in decreasing morbidity and mortality associated with iron poisoning (Chap. 135). However, in 2003, the FDA rescinded the blister packaging requirement in response to a lawsuit charging that the FDA did not have jurisdiction over the packaging of dietary supplements. Although isolated fatalities continue to occur, the trend in the National Poison Data System suggests they are becoming less common (Chap. 136). Iron poisoning may also occur after ingestion of other iron salts used in industry, such as ferric chloride. Ingestion of metallic iron does not result in toxicity.

**PHARMACOLOGY, PHARMACOKINETICS, AND TOXICOKINETICS**

Iron is an element critical to organ function. As a transition metal, iron can easily accept and donate electrons, thereby shifting the ferric (Fe$^{3+}$) and ferrous (Fe$^{2+}$) oxidation states (Chap. 12). This redox capacity elucidates the role of iron in multiple protein and enzyme complexes, including cytochromes and myoglobin, although it is principally incorporated into hemoglobin in erythrocytes. Whereas insufficient iron availability results in anemia, excess total body iron results in hemochromatosis.

The body cannot directly excrete iron, so iron stores are regulated by controlling iron absorption from the GI tract. The absorption of iron salts (iron ions as Fe$^{2+}$ or Fe$^{3+}$) occurs predominantly in the duodenum, and is determined by the iron requirements of the body. In iron deficiency, iron absorption and uptake into intestinal mucosal cells may increase from a normal 10% to 35% to as much as 80% to 95%. After uptake into the intestinal mucosal cells, iron is either stored as ferritin and lost when the cell is sloughed or released to transferrin, a serum iron binding protein. In therapeutic doses, some of these processes become saturated, and absorption into the intestinal cell may be limited. However, in overdose, the oxidative effects of iron on GI mucosal cells lead to dysfunction of this regulatory balance, and passive absorption of iron increases down its concentration gradient (see Pathophysiology).

Iron supplements are available as the iron salts ferrous gluconate, ferrous sulfate, and ferrous fumarate and as the nonionic preparations carbonyl iron and polysaccharide iron. Additional sources of significant quantities of iron are vitamin preparations, especially prenatal vitamins (Table 46–1). Toxic effects of iron poisoning occur at doses of 10 to 20 mg/kg elemental iron which is defined as the amount of iron ion present in an iron salt (Table 46–1). Significant GI toxic effects occurred in human adult volunteers who ingested 10 to 20 mg of elemental iron/kg. In one volunteer study, six participants who ingested 20 mg/kg elemental iron developed nausea and voluminous diarrhea within 2 hours, and five of the six subjects had serum iron concentrations above 300 µg/dL.

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<th>TABLE 46–1. Common Iron Formulations and Their Elemental Iron Contents</th>
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In another study of human volunteers who ingested 5 to 10 mg/kg elemental iron in the form of chewable iron containing vitamins, peak serum iron concentrations occurred between 4.2 and 4.5 hours in all participants. In overdose, peak concentrations of iron are thought to occur 2 to 6 hours after ingestion, depending on the iron preparation. Chewable vitamins continue to entice children with their sweet taste and recognizable character shapes, increasing the risk of significant exposure. Children’s chewable multivitamins contain less iron per tablet (10–18 mg of elemental iron) than typical prenatal vitamins (65 mg of elemental iron). Iron toxicity still results when large quantities of chewable children’s vitamins are ingested, but the therapeutic-to-toxic ratio is improved. One animal study paradoxically demonstrates higher iron concentrations after ingestion of equivalent elemental iron doses of chewable versus solid iron tablets. This finding was attributed, in part, to the limited gastric irritation associated with the chewable iron preparations, resulting in less vomiting.

Iron supplements are also available in two nonionic forms, carbonyl iron and iron polysaccharide, both of which appear to be less toxic after overdose than are iron salts, despite their high elemental iron content. Carbonyl iron is a form of elemental iron that is highly bioavailable in therapeutic doses compared to other forms of iron because of its high elemental iron content and its very fine, spherical particle size (5 µm). In a rat model of iron toxicity, carbonyl iron had a median lethal dose (LD₅₀) of 50 g/kg compared with an LD₅₀ of 1.1 g/kg for ferrous sulfate. No significant toxicity in humans exposed to carbonyl iron has been reported. Iron polysaccharide contains approximately 46% elemental iron by weight. It is synthesized by neutralization of a ferric chloride carbohydrate solution. This form of iron also appears to have much lower toxicity than iron salts. The estimated LD₅₀ in rats is more than 5 g/kg body weight. Retrospective poison center data have shown little toxicity from either of these products.

Parenteral iron, such as iron dextran, intravenously administered to patients with kidney failure and chronic anemia, may also result in toxicity, as well as anaphylactoid reactions. Newer parenteral formulations, including iron sucrose and sodium ferrous gluconate, appear to be safer.

**PATHOPHYSIOLOGY**

Iron is active in many oxidation reduction (redox) reactions. Iron catalyzes the generation of hydroxyl radicals intracellularly through the Fenton reaction and Haber-Weiss cycle and mediates its toxicologic effects as an inducer of oxidative stress and inhibitor of several key metabolic enzymes (Chap. 12). Reactive oxygen species oxidize membrane-bound lipids and cause loss of cellular integrity and tissue injury.

The initial oxidative damage to the GI epithelium produced by iron-induced reactive oxygen species permits iron ions to enter the systemic circulation. Iron ions are rapidly bound to circulating binding proteins, particularly transferrin. After transferrin is saturated with iron, “free” iron (ie, iron not bound to a transport protein) is widely distributed to the various organ systems, where it promotes
damaging oxidative processes. A postmortem series of 11 patients who died from iron ingestion substantiated these findings with measurements of elevated iron concentrations in most major organs examined, including the stomach, liver, brain, heart, lung, small bowel, and kidney. Congestion, edema, necrosis, and iron deposition in the gastric and intestinal mucosa, as well as hemorrhage and congestion in the lungs, are noted on postmortem examination.

Iron ions disrupt critical cellular processes such as mitochondrial oxidative phosphorylation. Subsequent buildup of unused hydrogen ions normally incorporated into the synthesis of adenosine triphosphate leads to liberation of H+ and development of metabolic acidosis (Chap. 13). In addition, absorption of iron from the GI tract leads to conversion of ferrous iron (Fe2+) to ferric iron (Fe3+). Ferric iron ions exceed the binding capacity of plasma, leading to formation of ferric hydroxide and release of three protons (Fe3+ + 3H2O → Fe(OH)3 + 3H+).

Decreased cardiac output contributes to shock in animals. Although this finding is often attributed to decreased preload and relative bradycardia, a direct negative inotropic effect of iron on the myocardium is also demonstrated in animal models. Reports of early coagulopathy unrelated to hepatotoxicity led to the identification of free iron as an inhibitor of thrombin formation and the reduction of the effect of thrombin on fibrinogen.

CLINICAL MANIFESTATIONS

Classic teaching posits five clinical stages of iron toxicity based on the pathophysiology of iron poisoning. Although these stages are conceptually important, they are of limited benefit to clinicians managing poisoned patients. Although the stages are typically described in approximate post-ingestion time frames, a clinical stage should never be assigned based solely on the number of hours post-ingestion because patients do not necessarily follow the same temporal course through these stages.

The first stage of iron toxicity is characterized by nausea, vomiting, abdominal pain, and diarrhea. These “local” toxic effects of iron predominate, and subsequent salt and water depletion contribute to the ill appearance of the iron poisoned patient. Intestinal ulceration, edema, transmural inflammation, and, in some extreme cases, small-bowel infarction and necrosis may occur. Hematemesis, melena, or hematochezia may cause hemodynamic instability. GI symptoms always occur after significant overdose. Conversely, the absence of signs and symptoms, specifically vomiting, in the first 6 hours following ingestion, essentially excludes serious iron toxicity.

The second, or “latent,” stage of iron poisoning commonly refers to the period 6 to 24 hours after ingestion when resolution of GI symptoms occurs, but systemic toxicity has not yet developed. Delineation of this stage may have evolved from early case reports of patients whose GI symptoms had resolved before subsequent deterioration. This second stage is not a true quiescent phase because ongoing cellular organ toxicity occurs during this phase. Although clinicians should be wary of patients who no longer have active GI complaints after iron overdose, most such patients have, in fact, recovered and are not in the latent phase. Patients in the latent phase generally have lethargy,
tachycardia, or metabolic acidosis. They should be readily identifiable as clinically ill despite resolution of their GI symptoms. In summary, patients who have remained well since ingestion and who have stable vital signs, a normal mental status, and a normal acid–base balance will have a benign clinical course.

Patients who progress to the third, or “shock,” stage of iron poisoning have profound toxicity. This stage may occur in the first few hours after a massive ingestion or 12 to 24 hours after a more moderate ingestion. The etiology of shock may be multifactorial, resulting from hypovolemia, vasodilation, and poor cardiac output, with decreased tissue perfusion and an ongoing metabolic acidosis. Iron-induced coagulopathy may worsen bleeding and hypovolemia. Systemic toxicity produces central nervous system effects with lethargy, hyperventilation, seizures, or coma.

The fourth stage of iron poisoning is characterized by hepatic failure, which may occur 2 to 3 days after ingestion. The hepatotoxicity is directly attributed to iron uptake by the reticuloendothelial system in the liver, where it causes oxidative damage.

The fifth stage of iron toxicity rarely manifests. Gastric outlet obstruction, secondary to strictures and scarring from the initial GI injury, may develop 2 to 8 weeks after ingestion. Patients treated for chronic iron overload are at increased risk for Yersinia enterocolitica infection. Iron is a required growth factor for Y. enterocolitica; however, the bacterium lacks the siderophore to solubilize and transport iron intracellularly. Because deferoxamine is a siderophore, it fosters the growth of Y. enterocolitica. Thus, patients with chronic iron overload or acute poisoning develop Yersinia infection or sepsis as a complication of iron poisoning or deferoxamine therapy. Yersinia infection should be suspected in patients who experience abdominal pain, fever, and bloody diarrhea after resolution of iron toxicity. In this setting, cultures should be obtained, fluid and electrolyte repletion accomplished, and fluoroquinolones or third-generation cephalosporin therapy initiated.

**DIAGNOSTIC TESTING**

**Radiography**

Iron is available in many forms, and the different preparations vary with respect to radiopacity on abdominal radiography. Factors such as the time since ingestion and elemental iron content of the tablets are also important. Liquid iron formulations and chewable iron tablets typically are not radiopaque. A retrospective review of iron ingestions in children revealed that abdominal radiographs were positive in only one of 30 patients who ingested chewable iron containing vitamin tablets. Because adult tablet preparations have a higher elemental iron content and do not readily disperse, they tend to be more consistently radiopaque. Finding radiopaque pills on an abdominal radiograph is helpful in guiding and evaluating the success of GI decontamination. However, the absence of radiographic evidence of tablets is not a reliable indicator to exclude potential toxicity. Most patients can be managed without abdominal radiographs, given their lack of sensitivity.
**Laboratory Studies**
Various laboratory studies are used as surrogate markers to assess the severity of iron poisoning. An anion gap metabolic acidosis and an elevated lactate concentration may develop in patients with serious iron ingestions. Serial electrolyte measurements may be used to assess progression and response to volume replacement. Anemia may result from GI blood loss, but may not be evident initially because of hemoconcentration secondary to plasma volume loss.

Although one small retrospective study of iron-poisoned children found that a white blood cell count (WBC) above 15,000/mm$^3$ or a blood glucose concentration above 150 mg/dL was 100% predictive of iron concentration above 300 µg/dL (a marker for clinical risk), three subsequent similar studies were unable to validate this association. In practice, an elevated WBC or glucose concentration in the setting of a known or suspected iron ingestion should raise concern about an elevated serum iron concentration; however, assessment of the signs and symptoms of the patient is more reliable. Most importantly, normal WBC and glucose concentrations do not reliably exclude toxicity.

Although iron poisoning remains a clinical diagnosis, serum iron concentrations can be used effectively to gauge toxicity and the success of treatment. In the previously mentioned human volunteer study of six adults who ingested 20 mg/kg of elemental iron, all six adults demonstrated significant GI toxicity, and the four who required intravenous (IV) fluid resuscitation had peak serum iron concentrations in the range of 300 µg/dL between 2 and 4 hours after ingestion. Serum iron concentrations between 300 and 500 µg/dL usually correlate with significant GI toxicity and modest systemic toxicity. Concentrations between 500 and 1000 µg/dL are associated with pronounced systemic toxicity and shock. Concentrations above 1000 µg/dL are associated with significant morbidity and mortality. Although elevated serum iron concentrations may be an additional indicator of potentially serious toxicity, lower concentrations cannot be used to exclude the possibility of serious toxicity. A single serum iron concentration may not represent a peak concentration or may be falsely lowered by the presence of deferoxamine unless an atomic absorption technique is used for measurement.

Total iron-binding capacity (TIBC) is a measurement of the total amount of iron that can be bound by transferrin in a given volume of serum. Previously, clinical iron toxicity was thought not to occur if the serum iron concentration was less than the TIBC, because insufficient circulating “free” iron was present to cause tissue damage. Although this is true, the error in interpretation results from the limitations of measuring TIBC values. Most importantly, the in vitro value of TIBC factiously increases as a result of iron poisoning and thus has a tendency to apparently increase above a concurrently measured serum iron concentration. Because of many confounding issues, the TIBC as currently determined has no value in the assessment of iron-poisoned patients.

**MANAGEMENT**

**Initial Approach**
As with any serious ingestion, initial stabilization must include supplemental oxygen, airway assessment, and establishment of IV access. Evidence of hematemesis or lethargy after an iron exposure may be a manifestation of significant toxicity. Intravenous volume repletion should begin while orogastric lavage and whole bowel irrigation (WBI) are considered. In any lethargic patient who likely will deteriorate further, early endotracheal intubation may facilitate safe GI decontamination measures. Abdominal radiography may be used to estimate the iron burden in the GI tract given the caveats discussed earlier. Laboratory values, including chemistries, hemoglobin, iron concentration, coagulation, and hepatic profiles, are necessary in the sickest patients. An arterial or venous blood gas or a lactate concentration rapidly identifies a metabolic acidosis. Patients who appear well and had only one or two brief episodes of vomiting can be observed pending discharge. A serum iron concentration and most other laboratory testing are not needed in patients who have minimal symptoms and normal vital signs.

**Limiting Absorption**

GI decontamination procedures should be initiated after stabilization. Adequate gastric emptying is critical after ingestion of xenobiotics, such as iron, that are not well adsorbed to activated charcoal. Because vomiting is a prominent early symptom in patients with significant toxicity, induced emesis is not recommended. Orosratic lavage is more effective but may be of only limited value because of the large size and poor solubility of most iron tablets, their ability to form adherent masses, and their movement into the bowel several hours after ingestion. The presence and location of radiopaque tablets on abdominal radiography can help guide orogastric lavage. Orosratic lavage will likely not be successful after iron tablets move past the pylorus, so WBI may be more effective (Fig. 46–1).

**FIGURE 46–1A.**
A 17 month-old boy presented to the hospital with lethargy and hematemesis after a large ingestion of iron supplement tablets. Despite orogastric lavage and whole-bowel irrigation, iron tablets and fragments can be visualized in the stomach 4 hours after ingestion.

**FIGURE 46–1B.**
The same 17 month-old child 10 hours after ingestion. Persistent iron pills were removed from the stomach by gastrotomy. No further radiopaque fragments can be visualized; however, ARDS is now visible.

Many strategies were used in the past in attempts to improve the efficacy of orogastric lavage. At the present time, no data support the use of oral deferoxamine, bicarbonate, phosphosoda, or magnesium. Although some of these
techniques demonstrate efficacy, avoidance of the associated risks mandates using only 0.9% sodium chloride solution or tap water for orogastric lavage.

The value of WBI in patients with iron poisoning is supported primarily by case reports and one uncontrolled case series. However, the rationale for WBI use is logical, especially considering the limitations of other gastric decontamination modalities. The usual dose of WBI with polyethylene glycol electrolyte lavage solution (PEG-ELS) is 500 mL/h in children and 2 L/h in adults. This rate is best achieved by starting slowly and increasing as tolerated, often using a nasogastric tube and an infusion pump to administer large volumes. Antiemetics may be used to treat nausea and vomiting. A large volume (44 L) of WBI was administered safely over a 5-day period to a child who had persistent iron tablets on serial abdominal radiographs (Antidotes in Depth: A2 and Chap. 8).

For patients with life-threatening toxicity who demonstrate persistent iron in the GI tract despite orogastric lavage and WBI, upper endoscopy or gastrotomy and surgical removal of iron tablets adherent to the gastric mucosa may be necessary and lifesaving.

Deferoxamine
Deferoxamine has been available since the 1960s as a specific chelator for patients with acute iron overdose or chronic iron overload (eg, multiple transfusions). Deferoxamine, which is derived from culture of Streptomyces pilosus, has high affinity and specificity for iron. In the presence of ferric iron (Fe$^{3+}$), deferoxamine forms the complex ferrioxamine, which is excreted by the kidneys, usually imparting a reddish-brown color to the urine (Fig. 46–2). Deferoxamine chelates free iron and the iron transported between transferrin and ferritin but not the iron present in transferrin, hemoglobin, hemosiderin, or ferritin. Deferoxamine may work by other mechanisms in addition to binding excess systemic iron. Because 100 mg of deferoxamine chelates approximately 8.5 mg of ferric iron, recommended or typical therapeutic dosing of deferoxamine does not produce significant excretion of chelated iron in the urine, yet it does often result in dramatic clinical benefits (Antidotes in Depth: A7). Sufficient evidence suggests that deferoxamine can reach intracytoplasmic and mitochondrial free iron, thereby limiting intracellular iron toxicity.

**FIGURE 46–2.**
These timed sequential urines were obtained from a small child with a serum iron concentration of 990 µg/dL who was treated with intravenous deferoxamine. The characteristic color change is illustrated.

*(Used with permission of The New York City Poison Center Toxicology Fellowship Program.)*

IV administration of deferoxamine should be considered in iron-poisoned patients with any of the following findings: metabolic acidosis, repetitive vomiting, toxic appearance, lethargy, hypotension, or signs of shock. Deferoxamine administration is indicated for any patient with an iron concentration above 500 µg/dL. In patients manifesting serious signs and symptoms of iron poisoning,
Deferoxamine should be initiated as an IV infusion, starting slowly and gradually increasing to a dose of 15 mg/kg/h. Hypotension is the rate-limiting factor as more rapid infusions are used.\textsuperscript{38, 39, 96} Patients who appear toxic or have serum iron concentrations above 500 µg/dL should be treated with IV deferoxamine. Patients who have concentrations below 500 µg/dL and who do not appear toxic should be treated supportively without administration of parenteral deferoxamine (Fig. 46–3).

**FIGURE 46–3.**
Algorithm for decision analysis following iron salt ingestion.

Clinicians have attempted to define the earliest clear end points for deferoxamine therapy because of possible deferoxamine toxicity. In one report, a urine iron-to-creatinine ratio (U/ Cr) was used to determine if free iron excretion into the urine continued during deferoxamine therapy.\textsuperscript{103} This ratio is a more objective measure of the presence of ferrioxamine in the urine than the less reliable and more subjective use of urinary color change.\textsuperscript{17, 47, 92} This method must be further studied clinically before its use can be advocated. Most authors agree that deferoxamine therapy should be discontinued when the patient appears clinically well, the anion-gap acidosis has resolved, and urine color undergoes no further change.\textsuperscript{55} In patients with persistent signs and symptoms of serious toxicity after 24 hours of IV deferoxamine, continuing therapy should be undertaken cautiously, if at all, and perhaps at a lower dose due to the risk of adverse events (Antidotes in Depth: A7).

**Adverse Effects of Deferoxamine.**
Most adverse effects of deferoxamine are reported in the setting of chronic administration for the treatment of hemochromatosis.\textsuperscript{39, 63, 74} The same effects, such as acute respiratory distress syndrome (ARDS), are also described after treatment for acute iron overdose.\textsuperscript{44} Four patients with serum iron concentrations ranging from 430 to 620 µg/dL developed ARDS after IV administration of deferoxamine for 32 to 72 hours.\textsuperscript{44} An animal study revealed significantly increased pulmonary toxicity when high-dose deferoxamine therapy was administered in the presence of high concentrations of oxygen (75%–80% FiO\textsubscript{2}).\textsuperscript{1} The authors suggested that this effect was mediated via an oxygen free radical mechanism (Antidotes in Depth: A7).

**Experimental Therapies**
**Deferasirox** is an oral iron chelator approved by the FDA for the treatment of chronic iron overload that was studied as a potential iron antidote in human volunteers following supratherapeutic iron ingestion. In a randomized, double blind, placebo-controlled study, volunteers were administered 5 mg/kg iron followed by deferasirox or placebo.\textsuperscript{34} Deferasirox resulted in lower iron concentrations in the treated group. However, concerns included the possibility that deferasirox may increase the absorption of iron complex and that the deferasirox dosing may need to be too high in patients with large exposures to effect these results. Further study is warranted before this therapy can be considered.
Patient Disposition

Many patients who ingest iron do not develop significant toxic effects. Recommendations for hospital referral of toddlers who ingest iron range from those with potential exposures of 20 mg/kg up to 60 mg/kg. These wide ranges probably result from the interpretation of retrospective studies in possibly “exposed” toddlers for whom the actual doses were estimated. Many authors suggest that doses were overestimated in patients who subsequently did not develop toxicity (Chap. 136). If a toddler remains asymptomatic or develops minimal or no GI manifestations after a 6 hour observation period in the emergency department, then discharge to an appropriate home situation can be considered. Patients who develop GI symptoms and signs of mild poisoning including vomiting and diarrhea can be observed as inpatients outside the intensive care unit. Patients who manifest signs and symptoms of significant iron poisoning, such as metabolic acidosis, hemodynamic instability, or lethargy, should be monitored and treated in an intensive care unit. Except in the case of carbonyl iron, hospital evaluation is recommended for any child with an estimated unintentional ingestion of more than 20 mg/kg of elemental iron. Children who appear well with unintentional ingestions between 10 and 20 mg/kg elemental iron and fewer than two episodes of vomiting should be closely followed at home in consultation with the poison control center.

Pregnant Patients

The frequent diagnosis of iron deficiency anemia during pregnancy has led to serious and even fatal iron ingestions in pregnant women. In all cases of toxic exposures during pregnancy, maternal resuscitation should always be the primary objective, even if an antidote poses a real or theoretical risk to the fetus. Unproven concerns regarding possible deferoxamine toxicity to the fetus have inappropriately, and at times, disastrously delayed therapy. These fears about fetal deferoxamine toxicity are not supported in either human or animal studies, which have demonstrated that neither iron nor deferoxamine is transferred to the fetus in appreciable quantities. An animal study demonstrated that fetal serum iron concentrations were not elevated and fetal deferoxamine concentrations could not be detected in pregnant near-term ewes poisoned with iron and treated with deferoxamine. Fetal demise under these circumstances presumably results from maternal iron toxicity and not from direct iron toxicity to the fetus. Thus, deferoxamine should be used to treat serious maternal iron poisoning and should never be withheld because of unfounded concern for fetal exposure to deferoxamine.

Adjunctive Therapies

Another modality used experimentally for treatment of iron intoxication is continuous arteriovenous hemofiltration (Chap. 10). In a study of five iron poisoned dogs, increased elimination of ferrioxamine in the ultrafiltrate was demonstrated when increasing doses of deferoxamine were infused into the arterial side of the system. A variant of this approach was utilized successfully in an iron poisoned toddler, who was treated with deferoxamine and venovenous hemofiltration. Although the authors demonstrated a decreasing serum iron concentration, only a minimal concentration of iron was measured in the ultrafiltrate. This was presumed secondary to the large volumes of infusate used. Theoretically, ferrioxamine in the blood could be dialyzable with new high molecular-weight (large-pore) dialysis filters, but this technique has not been studied.
In toddlers with severe poisoning, exchange transfusion may help to physically remove free iron from the blood while replacing it with normal blood. Exchange transfusion in children is effective for poisonings such as aspirin or theophylline when the volume of xenobiotic distribution is small and removal from the blood compartment can be expected. Treatment with exchange transfusion has been suggested in iron poisoning based on early reports and more recently reported in the successful treatment of an 18 month-old child with iron poisoning. However, removal of blood volume must be performed cautiously because it may not be well tolerated by iron poisoned patients with hemodynamic instability.

SUMMARY

- Iron is available in multiple formulations: prenatal vitamins, ferrous gluconate, ferrous fumarate, and ferrous sulfate are most toxic.
- Iron toxicity is determined by the amount of elemental iron present: signs and symptoms occur following ingestions of 20 mg/kg of elemental iron.
- GI decontamination, including orogastric lavage and WBI using PEG-ELS, should be initiated when indicated as activated charcoal is ineffective in binding iron.
- Abdominal radiography may be helpful in determining the iron burden in the GI tract. However, not all preparations are radiopaque.
- GI signs and symptoms of nausea, vomiting, diarrhea, hematemesis, and abdominal pain are prominent in iron poisoning.
- Systemic iron toxicity leads to metabolic acidosis, hypotension, coagulopathy, and multiorgan system failure.
- Diagnosis and treatment of shock and metabolic acidosis, as well as chelation with deferoxamine, are critical.

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