Acute Iron Overdose (Pediatric: Adolescent)
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Target Audience: Emergency Medicine Residents, Medical Students

Primary Learning Objectives:

1. Recognize signs and symptoms of acute iron toxicity
2. Identify the need for fluid resuscitation
3. Recognize acid base disturbance
4. Discuss the utility of calculating the dose of elemental Fe and ordering a peak Fe level in determining potential toxicity
5. Name the stages of acute iron toxicity

Secondary Learning Objectives: detailed technical/behavioral goals, didactic points

1. Describe the utility and limitations of KUB in iron ingestion
2. Discuss the use of whole bowel irrigation (WBI) to decontaminate pill fragments visualized on KUB
3. Demonstrate basic knowledge of the antidote for acute iron toxicity
4. Obtain psychiatric evaluation for suicidal patients

Critical actions checklist:

1. Perform focused history and physical exam based on reported ingestion
2. Order basic screening labs (must include iron level)
3. Order KUB to evaluate for pill fragments
4. Volume resuscitate with normal saline
5. Consult Poison Center/Toxicology consultant
6. Consult the intensive care unit for admission
7. Discuss administration of deferoxamine

Environment:

1. Room Set Up – ED acute care area
    a. Manikin Set Up – Mid or high fidelity simulator, simulated vomiting
    b. Props – Standard ED equipment
2. Distractors – ED noise, Mom asking questions about iron overdose

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CASE SUMMARY

SYNOPSIS OF HISTORY/ Scenario Background

The setting is an urban emergency department.

Patient is a 15-year-old male with no significant past medical history who is brought to the emergency department by his mother after reportedly ingesting approximately 90 tablets of iron about 3 hours ago. He has no known history of depression or suicidal ideation. He took the pills after his girlfriend broke up with him. He developed nausea and vomiting within 30 minutes of ingestion. He decided to tell his mother about the ingestion after he vomited approximately five times at home. In the ED, he is actively vomiting and complains of 5 out of 10 upper abdominal pain.

PMHx: Denies
PSHx: None
Medications: Ibuprofen as needed for headache
Allergies: NKDA
SocHx: Denies tobacco, alcohol or drug use. He is a sophomore in high school. He lives at home with his mother and younger sister.

Patient is triaged to the acute care area in the pediatric emergency department. Mother brings in the medication bottle, which can be provided (ferrous sulfate 325 mg tablet, 20% elemental Fe, bottle of 100 tablets with 10 tablets remaining). Bottle was purchased a few days ago and was unopened per the patient's mother.

SYNOPSIS OF PHYSICAL

Patient is tachycardic and in mild distress due to active vomiting.
Airway is intact.
Abdominal exam with mild tenderness to palpation in the epigastric region.
Neurologic exam is normal.

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CRITICAL ACTIONS

1. **Perform focused history and physical exam based on reported ingestion**

   Asks key questions pertinent to the case and evaluates hydration status, abdominal exam, and mental status at a minimum.
   Cueing Guideline: Mom asks why he is vomiting so much.

2. **Order basic screening labs (must include iron level)**

   Asks for a BMP, CBC and iron level, at a minimum. May also order LFTs, coagulation studies, lactic acid, and toxicology labs (4hr acetaminophen level, and salicylate level), and ECG.
   Cueing Guideline: Nurse asks if the doctor would like to send off any blood work.

3. **Order KUB to evaluate for pill fragments**

   Orders imaging to look for radiopaque pill fragments in the GI tract.
   Cueing Guideline: Nurse asks if the doctor would like to order any imaging. Mom asks if there is a way to find out how many pills are still in his stomach.

4. **Volume resuscitate with normal saline**

   Administer 1 to 2 liters of normal saline for volume resuscitation.
   Cueing Guideline: Patient becomes more tachycardic and hypotensive without adequate volume resuscitation.

5. **Consult Poison Center or Toxicology Consultant**

   Call Poison Center or the Toxicology Consultant.
   Cueing Guideline: The nurse asks if anyone has called the Poison Center or the Toxicology Consultant yet.

6. **Consult the intensive care unit**

   Call intensivist for admission.
   Cueing Guideline: Mom asks who will admit the patient and to what location.

7. **Discuss administration of deferoxamine**

   Able to identify the proper antidote and indications for administration.
   Cueing Guideline: Mom asks if there is any medication that can be given to “counteract” the iron.

Critical Actions Checklist[1]

Resident Name	
Case Description	

Skills measured **Core competencies: PC** Patient care, **MK** Medical knowledge, **IC** Interpersonal and communication skills **P** Professionalism, **PB** Practice-based learning and improvement **SB** Systems-based practice	Very Unacceptable		Unacceptable		Acceptable		Very Acceptable	
Data Acquisition (D) PC MK I	1	2	3	4	5	6	7	8
Problem Solving (S) PC MK PB	1	2	3	4	5	6	7	8
Patient Management (M) PC MK IC P PB SB	1	2	3	4	5	6	7	8
Resource Utilization (R) PC PB SB	1	2	3	4	5	6	7	8
Health Care Provided (H) PC SB	1	2	3	4	5	6	7	8
Interpersonal Relations (I) IC P	1	2	3	4	5	6	7	8
Comprehension of Pathophysiology (P) MK PB	1	2	3	4	5	6	7	8
Clinical Competence (C) PC MK IC P PB SB	1	2	3	4	5	6	7	8

Critical Actions

Yes	No		Comments:
		Perform focused history and physical exam	
		Order basic screening labs (must include iron level)	
		Order KUB to evaluate for pill fragments	
		Volume resuscitate with normal saline	
		Consult Poison Center or Toxicology consultant	
		Consult intensive care unit	
		Discuss administration of deferoxamine	

	Yes	No	
			Dangerous actions

[1] Modified ABEM Oral Certification Examination checklist and scoresheet

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HISTORY

A 15-year-old male presents to the acute care area after ingesting iron tablets in a suicide attempt. You see an ill-appearing male who is actively vomiting.

Onset of Symptoms: Today

Background Info: 15-year-old male came home from school upset and spent most of the afternoon in his room. He came to his mom a few hours later stating that he took some of the iron tablets that were in the medicine cabinet. After vomiting several times, his mother decided to bring him to the emergency department.

Additional History

From Mother: She states that the patient has recently been a bit on edge. She believes he has been having "girl trouble."

Chief Complaint: Iron overdose

Past Medical Hx: None

Past Surgical Hx: None

Habits: Smoking: Never
ETOH: Never
Drugs: Never

Family Med Hx: Mother with depression and anemia, Father with high blood pressure

Social Hx: Lives at home with mother and 12-year-old sister. Parents are divorced. Father lives in the area. He is a sophomore in high school. He is a good student and has never been in trouble at school. His hobbies include playing baseball and video games.

ROS: All systems reviewed and otherwise negative.

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PHYSICAL EXAM

General Appearance: Well-nourished male in mild distress secondary to active vomiting

Vital Signs: BP: 95/60 mmHg P: 128/minute R: 16/minute T: 36.6C (97.9F)
POx: 100% (room air) Weight: 60 kg

Head: Normal

Eyes: Pupils are 4mm, equal, round and reactive to light. Conjunctivae are normal. Extra-ocular movements are intact.

Ears: TM's normal.

Mouth: Mucous membranes are dry, without lesions.

Neck: No tenderness or deformity on exam, full range of motion.

Skin: Warm, dry, no rashes.

Chest: Normal respiratory rate without any signs of respiratory distress.

Lungs: Breath sounds are clear and equal bilaterally.

Heart: Tachycardic, regular, no murmurs or rubs.

Back: Normal

Abdomen: Normal bowel sounds. Soft, mild tenderness to palpation in the epigastric region. No guarding or rebound.

Extremities: Range of motion is normal in all four extremities. No edema is noted. No cyanosis.

Genital: Deferred

Rectal: Normal tone, guaiac positive brown stool.

Neurological: Patient is alert and oriented. No gross motor or sensory deficit noted.

Required Actions at the Beginning of the Case

- Perform focused history and exam based on reported ingestion
- Start fluid resuscitation with IV NS 1 L
- Order a KUB to look for pill fragments
- Order iron level and basic screening labs

Branch Point:

- **IF A 20 ML/KG BOLUS OF ISOTONIC FLUID IS GIVEN,** then the patient's tachycardia and hypotension will initially improve. However, the patient will become recurrently tachycardic, requiring further fluid resuscitation.
- **IF A 20 ML/KG BOLUS OF ISOTONIC FLUID IS NOT GIVEN,** then the patient's tachycardia and hypotension will worsen: the patient's heart rate increases to 150/minute and the blood pressure drops to 80/30 mmHg.
- **REGARDLESS OF THE INTERVENTIONS MADE, THE PATIENT WILL DEVELOP BLOOD-TINGED EMESIS AS THE CASE PROGRESSES.**
- **IF A KUB (OR EQUIVALENT RADIOGRAPH) IS ORDERED,** it shows pill fragments in stomach and small intestine.
- **IF A SERUM IRON LEVEL IS ORDERED,** the initial result is 512 micrograms/dL.

Required Actions Over the Next Several Minutes of the Case

- Consider ordering an H_2 blocker or PPI after the patient develops blood-tinged emesis
- Discuss whole bowel irrigation (WBI) once vomiting controlled after visualizing multiple pill fragments on KUB
- Administer deferoxamine once iron level and labs results have returned
- Call Poison Center/Consult Medical Toxicology
- Call PICU for definitive disposition and admission

Branch Point

- **IF NO INTERVENTION OCCURS WITHIN THE FIRST TWO MINUTES,** tachycardia increases to the 130s.

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STIMULUS INVENTORY

#1	Complete blood count
#2	Basic metabolic panel
#3	Liver function tests
#4	Lactate
#5	Toxicology
#6	Coagulation studies
#7	Iron level
#8	KUB
#9	ECG

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LAB DATA & IMAGING RESULTS

Stimulus #1	
Complete Blood Count (CBC)	
WBC	5,700/mm^3
Hemoglobin	13 g/dL
Hematocrit	40%
Platelets	256,000/mm^3
Differential	
PMNLs	92%
Lymphocytes	5%
Monocytes	2%
Eosinophils	1%

Stimulus #2	
Basic Metabolic Profile (BMP)	
Sodium	142mEq/L
Potassium	3.8 mEq/L
Chloride	107 mEq/L
Bicarbonate	15 mEq/L
Glucose	96 mg/dL
BUN	14 mg/dL
Creatinine	0.6 mg/dL

Stimulus #3	
Liver Function Tests	
AST	45 U/L
ALT	35 U/L
Alk Phos	110 U/L
T. Bilirubin	1.0 mg/dL
D. Bilirubin	0.2 mg/dL
Albumin	4.3 mg/dL

Stimulus #4	
Lactate	
Value	3 mmol/L

Stimulus #5	
Toxicology	
Salicylate	Undetectable
Acetaminophen	Undetectable
Ethanol	Undetectable

Stimulus #6	
Coagulation Studies	
PT	11 seconds
INR	1.09
PTT	23.5 seconds

Stimulus #7	
Iron Level	
Value	512 micrograms/dL

Stimulus #8	
KUB	Multiple radiopaque fragments in the stomach and small intestine

Stimulus #9	
ECG	Sinus tachycardia No conduction delays

Stimulus #1

Complete Blood Count (CBC)

WBC	5,700/mm^3
Hemoglobin	13 g/dL
Hematocrit	40%
Platelets	256,000/mm^3
Differential	
PMNLs	92%
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Stimulus #2

Basic Metabolic Profile (BMP)

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Stimulus #3

Liver Function Tests

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Stimulus #4

Lactate

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Stimulus #5

Toxicology

Salicylate	Undetectable
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Stimulus #6

Coagulation Studies

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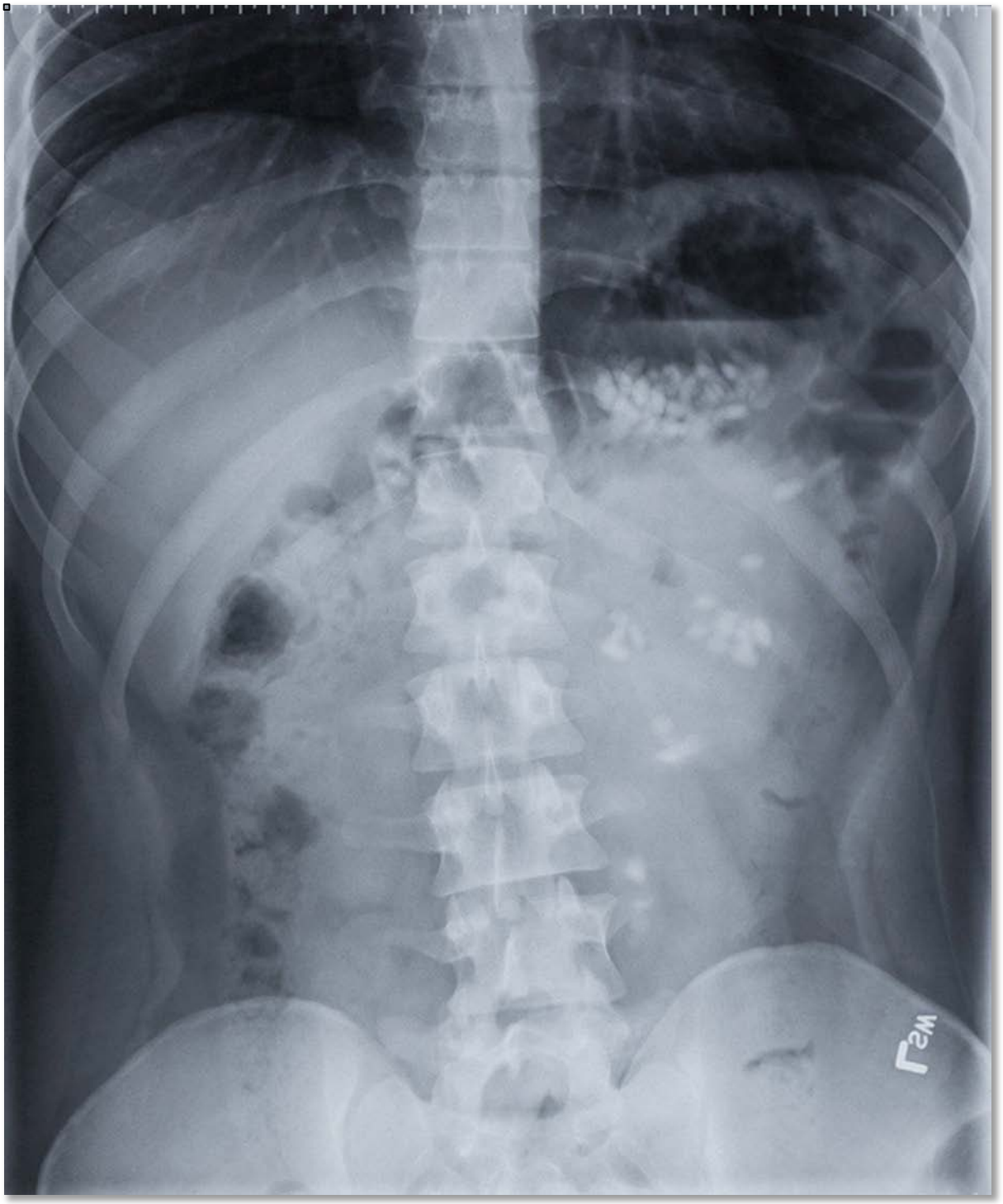
Stimulus #7

Iron Level

512 micrograms/dL

Stimulus #8



Stimulus #9	
ECG	Sinus tachycardia No conduction delays

Debriefing Materials – Acute Iron Toxicity

Sources of Exposure:

- There are many iron preparations that contain various amounts of iron salts
- Toxicity is determined by the amount of elemental iron (Fe) ingested

Contents	Product Name	Elemental Fe (%)
Ferrous fumarate	Chromagen	33
Ferrous chloride	Ferro-66	28
Ferrous sulfate	Feosol	20
Ferrous lactate	Ferro-drops	19
Ferrous gluconate	Iromin-G	12

- Iron equivalents can be determined as below
    - (Strength x % elemental Fe/tablet) X # of tablets/weight (kg)
    - (325 mg x 20% elemental Fe/tablet) X 90 tablets/60 kg = 97.5 mg/kg

Pathophysiology:

- Direct corrosive effects and cellular toxicity
- Iron engages in redox reactions, resulting in the formation of free radicals and oxidative damage
- Cellular energy and metabolism are altered
- Uncouples oxidative phosphorylation
- Ultimately causes cellular death

Severity of Ingestion:

- Acute lethal dose in animal studies is 150 – 200 mg/kg of elemental iron
- Gastrointestinal symptoms start at 20 mg/kg of elemental iron
- ≥40 mg/kg is considered potentially serious and is the current level recommended for referral to the ED after accidental ingestion
- Severity of toxicity can be predicted by peak iron level:
    - Less than 300 mcg/dL – lacks significant clinical effect
    - 300-500 mcg/dL – mild-moderate effects, serious toxicity less likely
    - 500-1000 mcg/dL – moderate – severe systemic toxicity
    - Greater than 1000 mcg/dL – significant morbidity and mortality

Toxicokinetics:

- Humans do not synthesize or secrete Fe; total body Fe is regulated via absorption from the gastrointestinal tract
- Absorption occurs in the duodenum
    - Stored as ferritin in intestinal cells
        - Disposed via epithelial cell shedding OR
        - Released to transferrin, a serum Fe-binding protein
    - In iron overdose, corrosive effects of Fe on the gastrointestinal tract mucosa permit passive absorption of Fe
        - Once transferrin is saturated, “free” Fe is available to cause toxicity

Stages of Toxicity:

- Stage I: Local Toxicity
  - 0.5 – 6 hours post-ingestion
  - Nausea, vomiting, diarrhea
  - Abdominal pain
  - Gastrointestinal bleeding
- Stage II: Latent Toxicity
  - 6 – 24 hours post-ingestion
  - Resolution of local toxicity with ongoing cellular toxicity
  - Hypovolemia, markers of poor tissue perfusion (metabolic acidosis, elevated lactate levels)
- Stage III: Shock
  - 12 – 24 hours post-ingestion
  - Shock, acidosis, coagulopathy, coma
  - Multi-system organ failure
- Stage IV: Hepatic failure
  - 2 – 3 days post-ingestion
  - Periportal hepatic failure
- Stage V: Sequelae
  - 3 – 6 weeks post-ingestion
  - Gastric outlet obstruction (small bowel obstruction)

Diagnostic Testing:

- Fe level
  - Peak concentration occurs between 2 – 6 hours after ingestion
  - Consider repeat level after 8 – 12 hours to rule out delayed absorption
- Serum chemistry
- Lactate level
- Complete blood count
  - WBC > 15,000/mm^3 and glucose > 150 mg/dL had a 100% positive predictive value for serum Fe > 300 mcg/dL in one study (otherwise not supported in the literature)
- Coagulation studies
- Liver function tests
- TIBC (not recommended)
  - Initially believed the Fe toxicity would not occur if the serum Fe level was less than TIBC
    - TIBC is an indirect measure of transferrin level
    - Need 'free' Fe to cause tissue damage
    - Not supported in the literature
- Abdominal X-ray (KUB)
  - Useful if pill fragments are seen
  - Radiopacity varies with preparation, time since ingestion, and amount of ingestion
  - There are numerous reasons for negative abdominal X-ray including time since ingestion and Fe preparation.

Treatment:

- Decontamination

    - Gastric lavage may be considered in severe, large volume overdose. However, a lack of evidence supporting clinical benefit, the patient's concurrent hematemesis, and potential for iatrogenic injury limit its usefulness.
    - No utility for activated charcoal as iron does not bind well.
    - Consider whole bowel irrigation (WBI) if pill fragments noted on X-ray and if a risk/benefit discussion supports it. There are no controlled studies supporting efficacy. Can administer polyethylene glycol solution at recommended rates of 500 mL/hr in children and 1.5 – 2 L/hr in adolescents and adults.
- Administer volume resuscitation with crystalloid at 20 cc/kg and adjust to signs of volume and perfusion status.
- Treat hemorrhagic gastroenteritis and replace blood if needed.
- Consider chelation therapy with deferoxamine (DFO).
    - DFO has high affinity and specificity for Fe. It complexes with Fe^{3+} forming ferrioxamine which is excreted in the urine. Ferrioxamine has a brick-orange color (*vin rose).*
    - No study has determined the optimal dosing regimen, maximum dose, or length of administration.
    - General dose is 15 mg/kg/hr IV.
    - Indications for chelation are not well defined. Consider with serious toxicity, such as the presence of a metabolic acidosis, lethargy/coma, shock, toxic appearance and Fe > 500 mcg/dL.
    - Adverse effects of DFO can be divided into early and late manifestations
        - Early effects include urticaria and hypotension. Both are rate related. Adequate fluid resuscitation is important.
        - Late effects include Yersinia sepsis and acute respiratory distress syndrome. DFO is a siderophore that fosters Yersinia growth. ARDS is more common with prolonged DFO infusions (> 24 hours).

Consultations:

- Consult the regional poison center or a local medical toxicologist for additional information and patient care recommendations.
- Consult psychiatric service personnel for stabilized patients with intentional overdose.

Disposition:

- Admit patients with major signs and symptoms to an ICU.
- Patients with self-limited mild GI symptoms or who remain asymptomatic for 6 hours are unlikely to develop serious intoxication.

Take-Home Points:

- Iron preparations come in a variety of forms with varying toxicities.
- Gastrointestinal symptoms occur early and can result in significant volume loss.
- Aggressive fluid resuscitation is very important with iron poisoning.
- There are several stages of iron poisoning that can ultimately lead to multisystem organ dysfunction.
- It is important to determine peak iron level which typically occurs within 2 to 6 hours of ingestion.
- Abdominal X-rays may show pill fragments which may assist in treatment decisions (consideration of WBI).

- There are no well-defined indications for chelation with deferoxamine; however, consider in patients with serious toxicity.

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