

# Lecture 4: Heavy Metals

Iron is the most important for the exam,  
the other metals are just for reading.

# Iron

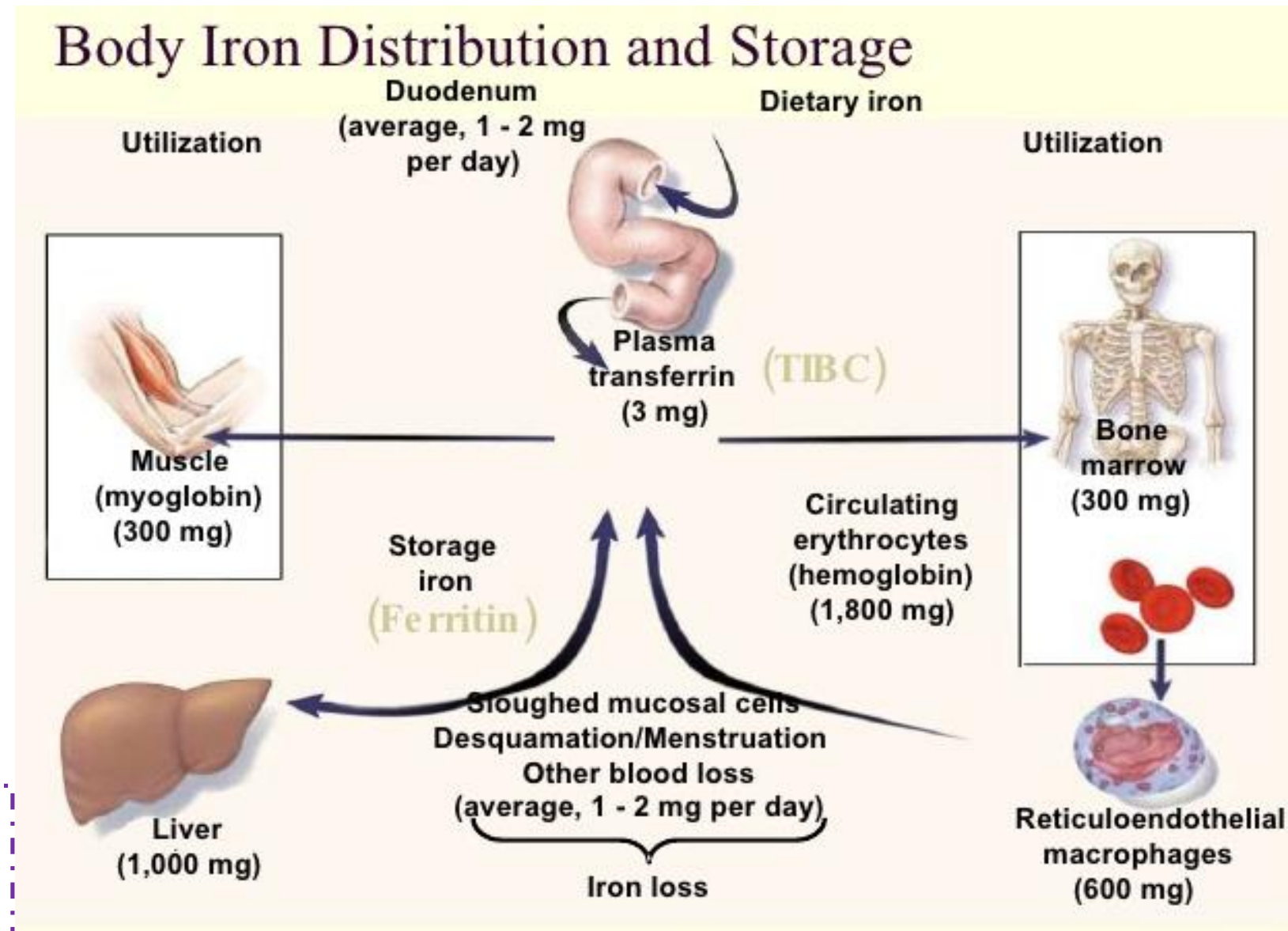
children younger than age 6 years : minimally toxic  
Adult : suicide attempts.

## Principles of disease Pharmacology:

- Normal serum iron levels : 50 to 150 micg/dL.
- The total iron-binding capacity (TIBC), a crude measure of the ability of serum proteins—including transferrin—to bind iron, ranges from 300 to 400 micg/dL.
- It is higher than the serum iron level due to a low degree of saturation.
- When iron levels rise following a significant iron overdose, transferrin becomes saturated so that excess iron circulates as free iron in the serum.
- **This unbound iron is directly toxic to target organs.**

# Remember We're talking here about acute iron overdose, while chronic overdose (hemosiderosis) is a different story.

# In pregnancy or patient with anemia, the iron level in the blood is very low, and the serum iron is very low and the capacity is high, that's why the level of transferrin in pregnancy is high, because it wants to carry more iron.



# Iron..

## Principles of disease Pharmacology:

- Ingestions of less than 20 mg/kg of elemental iron usually cause no symptoms
- Ingestion of 20 to 60 mg/kg results in mild to moderate symptoms
- **Ingestion of more than 60 mg/kg may lead to severe morbidity.**
- 50% mortality (LD50) is reported to be 200 to 250 mg/kg.

COMPOUND	PERCENTAGE OF ELEMENTAL IRON
Ferrous sulfate	20
Ferrous fumarate	33
Ferrous gluconate	12
Ferric pyrophosphate	30
Ferrocholate	14
Ferroglycine sulfate	16
Ferrous sulfate, dried	33
Ferrous carbonate, anhydrous	38
Carbonyl iron	100
Iron polysaccharide	46

# Toxic dose of iron for a child weighing 20kg is more than 1 gram.  
# Toxic dose of iron for a 70kg adult is more than 5 gram.  
# Toxic dose of iron for children is 60mg/kg  
# The weight is important in calculating the toxic dose.  
# Tablet Iron is not 100% elemental, the **only one that's 100% elemental is carbonyl iron.**  
#e.g. if a child ingested 10 tablets of Ferrous sulfate, the percentage of elemental iron would be  $20 \times 10 = 200\text{mg}$



# Iron..

## Pathophysiology:

- Two distinct toxic effects:
  1. It causes **direct caustic injury to the gastrointestinal mucosa**.
  2. It **impairs cellular metabolism**, primarily of the heart, liver, and the CNS.
- Unbound (free) iron moves into cells and localizes near the mitochondrial cristae, resulting in uncoupling of oxidative phosphorylation and impairment of adenosine triphosphate synthesis.
- Cell membranes are injured by free radical-mediated lipid peroxidation.
- Iron increases capillary permeability and induces both arteriolar and venodilation.
- Myocardial toxicity decreases cardiac output.
- Hydration of the iron molecule creates an excess of unbuffered protons, worsening metabolic acidosis.
- This multitude of effects, combined with severe gastrointestinal fluid losses, can lead to the development of shock, cardiovascular collapse, and death.

# Iron causes direct toxic injury to the GIT, which means if the child doesn't have nausea and vomiting (GI symptoms) it is very unlikely that he is going to die. (this is important to help us in decision-making of admission to the hospital).

# Paracetamol overdose is silent, whereas iron overdose shows these symptoms.

# Iron..

## Clinical features:

**Five stages.** Very Very important because they help us to decide the management.

### Phase I (sever GIT irritation.. You have to admit the patient to the hospital, don't discharge him)

Reflects the corrosive effects of iron on the gut. **Vomiting** occurs within 80 minutes of ingestion in more than 90% of symptomatic cases. **Diarrhea**, which can be bloody, follows.



### Phase II (silent phase last for 48 hours, very dangerous)

Represents an apparent (but not complete) recovery that lasts less than 24 hours but can extend up to 2 days. Most patients recover after this point.



### Phase III (clinical and critical phase, also called " Shock Face " , the body shutdown –hypotension, metabolic acidosis, renal failure and coma)

Characterized by the recurrence of GI symptoms, severe **lethargy** or **coma**, anion gap **metabolic acidosis**, leukocytosis, coagulopathy, renal failure, and cardiovascular collapse. Serum iron levels may have fallen to normal during this phase due to distribution into the tissues.



### Phase IV (fatal, all you have is supporting)

Characterized by **fulminant hepatic failure**, occurs 2 to 5 days after ingestion. This is relatively rare, appears to be dose related, and is usually fatal.



### Phase V (recovery phase)

Represents the consequences of healing the injured gastrointestinal mucosa, and is characterized by pyloric or proximal bowel scarring, which is sometimes associated with obstruction.

# Iron..

## Diagnostic categories:

- The presence of gastrointestinal symptoms suggests a potentially serious ingestion, whereas their absence is reassuring.
- A **serum iron level**: 3 to 5 hours after ingestion, **is the most useful laboratory test** to evaluate the potential severity of an iron overdose.
  - ✓ Peak serum iron levels of less than 350 micg/dL are with minimal toxicity.
  - ✓ 350 to 500 micg/dL with moderate toxicity.
  - ✓ **and greater than 500 micg/dL with potentially severe toxicity. “ diagnostic “**

### Toxicity of Iron by Amount Ingested and Peak Serum Levels

ELEMENTAL IRON (MG/KG)	PEAK SERUM IRON ( $\mu$ G/DL)	TOXICITY
<20	50–150	None
20–40	150–300	Mild
40–60	300–500	Moderate
>60	>500	Severe

# Iron..

## Management:

### Gastric Emptying:

- Iron is not bound to activated charcoal
- Gastric lavage nor ipecac: **NOT EFFECTIVE**
- Iron tablets clump together as their outer coatings dissolve.

### Gastrotomy

- Has been performed to remove iron from the stomach.

### Whole-Bowel Irrigation

- Polyethylene glycol electrolyte lavage solution (PEG-ELS) (CoLyte, NuLytely, or GoLYTELY) is routinely recommended.
- The solution is either taken orally or administered through a nasogastric tube.
- Rate of administration of PEG-ELS is 20 to 40 mL/kg/hr in young children and 1.5 to 2 L/hr for teenagers or adults, continued until the rectal effluent is clear and there is no radiographic evidence of pill fragments
- **Whole-bowel irrigation is contraindicated in the presence of bowel obstruction, perforation, or ileus**

### Hemodialysis

- .. and hemoperfusion are not effective in removing iron due to its large volume of distribution.

### Exchange transfusions

- Have been recommended for severely symptomatic patients with serum iron levels exceeding 1000 micg/dL.

### Deferoxamine (the antidote)

- Deferoxamine chelates iron to form the water-soluble compound ferrioxamine, which can be renally excreted or dialyzed.
- 100 mg: chelate 9.35 mg of elemental iron.
- Because of its short half-life, it is administered as a continuous infusion at a dose of 15 mg/kg/hr for up to 24 hours.
- The maximum rate of administration is 35 mg/kg/hr.
- Rapid administration of deferoxamine can lead to hypotension, which is treated by reducing the initial rate of the infusion and slowly increasing it to the desired rate.
- **Pregnancy is not a contraindication to deferoxamine**
- The presence of ferrioxamine turns the urine a "vin ros?" color, which reflects the excretion of chelated iron.

# Title

## Questions:

**Q1: What is the toxic dose of Iron for child 15 Kg?**

A1: 60/kg

**Q2: calculate the amount of ingested iron for a 10-kg child who consumed ten 320-mg tablets of ferrous gluconate (12% elemental iron per tablet)?**

A2: 10 tablets X 38.4 mg elemental iron per tablet = 384 mg/10 kg = 38.4 mg/kg.

**Q3: child who ingested 5 tablets of ferrous sulfate and they brought him to you in the hospital and he is asymptomatic, what is the management?**

A3: Observation for 6 hours then discharge.

**Q4: -True or False - Regarding iron overdose:**

a) Patient remained asymptomatic after 4 hours of observation can be discharged F

b) Patients usually die of hepatic failure F

c) Metabolic acidosis is a poor prognosticator T

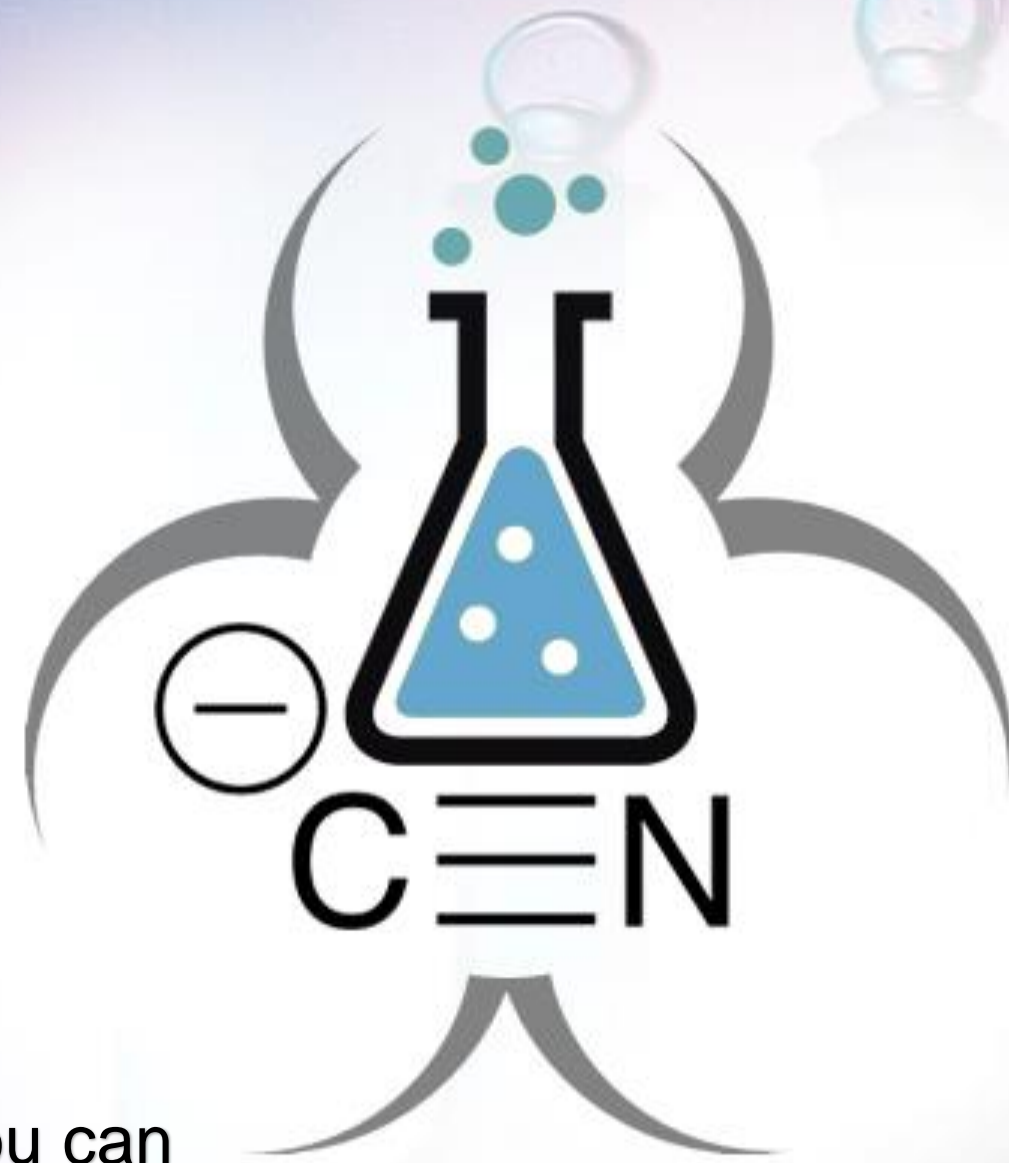
d) Total iron binding capacity (TIBC) is useful to guide treatment F

e) Whole bowel irrigation is usually the gut decontamination method of choice T

**Q5: comatose patient with hypotension, metabolic acidosis and renal failure, this patient is in which phase of iron toxicity?**

A5: phase III- critical phase.





If you have any questions You can  
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