



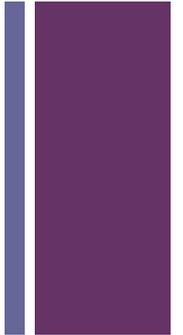
Iron Overload from Chronic blood Transfusion

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15th Oct 2016

Moncton patient education day

+ Preview



- What is the role of Iron.
- Iron metabolism.
- Why iron overload is a bad thing.
- How can we remove extra iron.
- Current recommendation for treatment of iron overload.

+ What does Iron do?

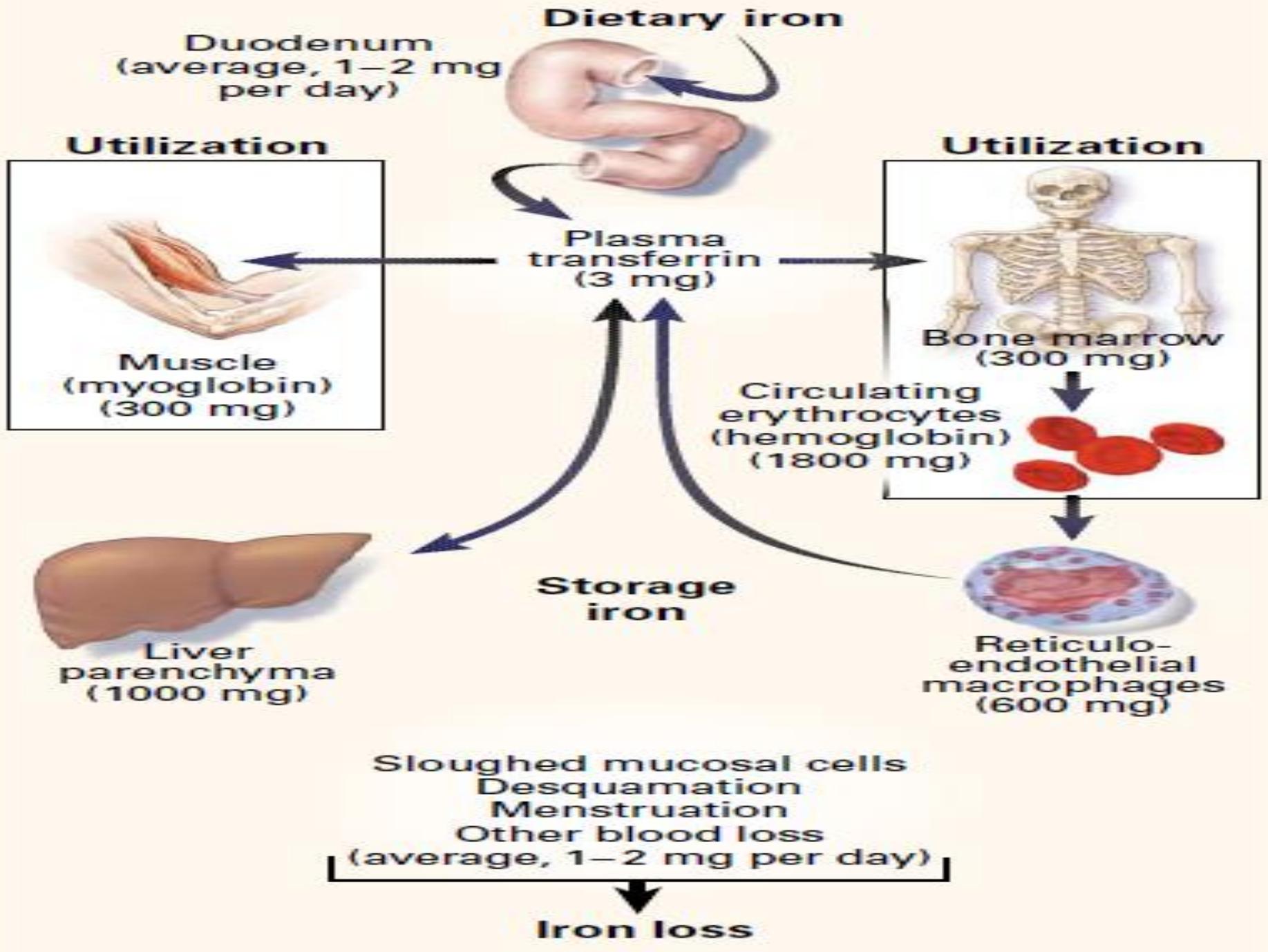
■ Oxygen transport

1- Hemoglobin RBC.

2- Myoglobin (muscle cells)

About 70 % of the body's
iron is in these proteins.





+ Iron Shortage

■ Iron Deficiency:

- Blood loss,
- Low intake.
- Malabsorption.



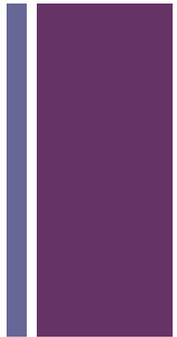
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About 1000 mg of iron is stored as ferritin. Intestinal absorption of iron increases in response to deficiency.



Iron Overload

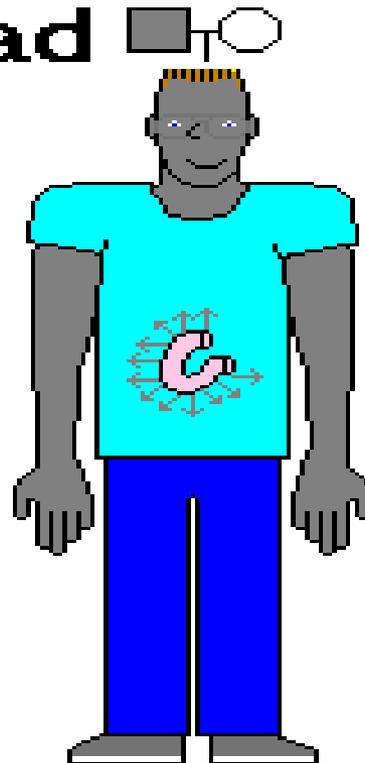
- Iron is excreted by shedding off intestinal cells.
- There is no renal excretion of iron.



Iron Overload

Easy to diagnose and treat -- if you think of it.

- diabetes
- gray skin
- joint pain
- dilated cardiomyopathy
- heart rhythm disturbances



Primary iron overload:
The duodenum absorbs iron too well. Genetic.

High Fe/TIBC ratio

elevated liver enzymes
cirrhosis
addisonism

Treat it BEFORE
cirrhosis develops!



+ Blood transfusion

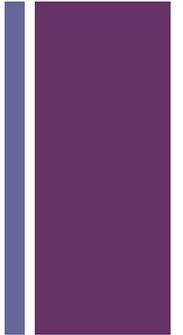
- Normal daily iron flux is 1-2 mg.
- Patients who receive transfusion, each unite of blood contains 200-250 mg.

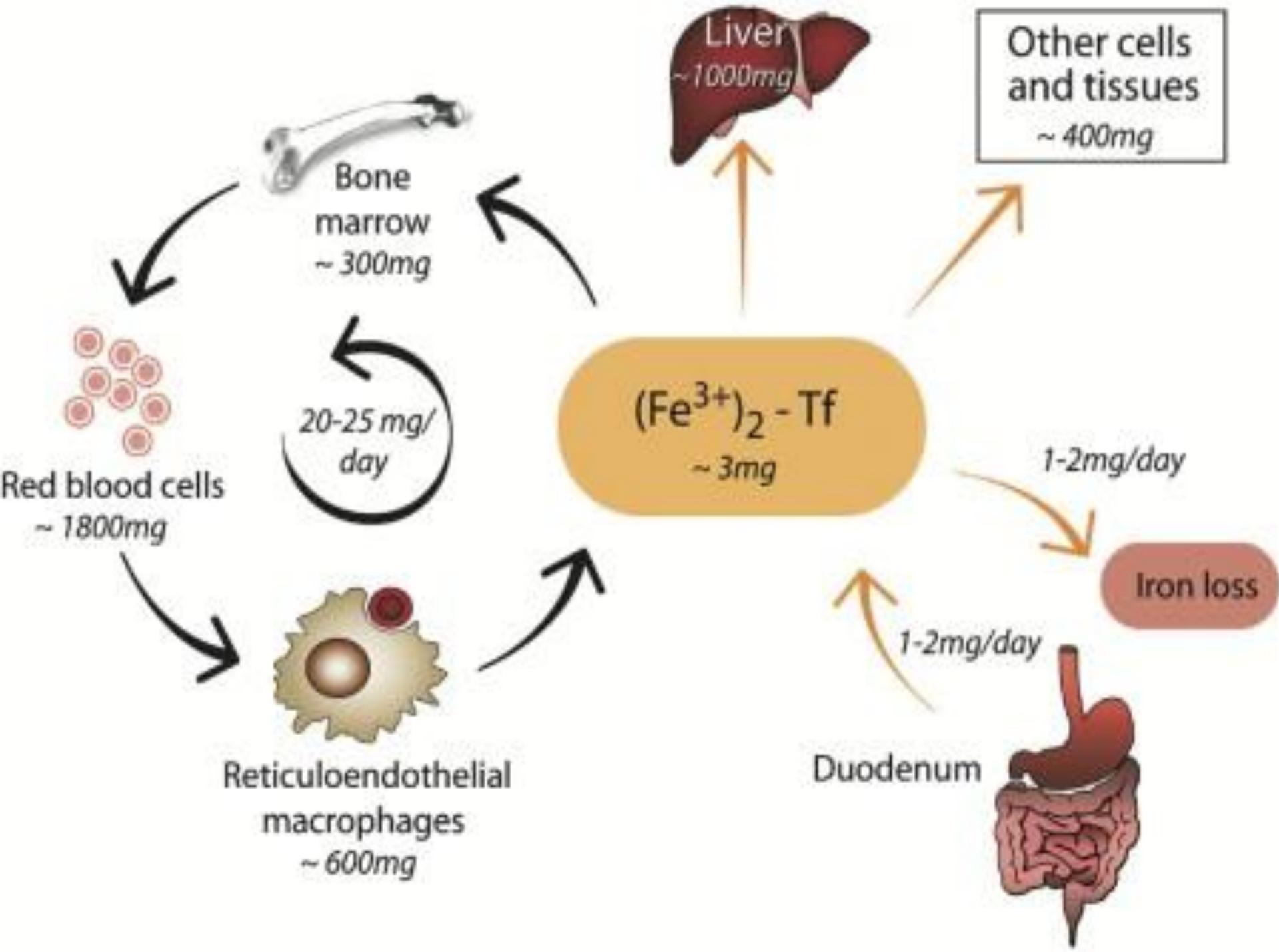




Iron balance

- Normally not much iron enters or leaves body.
- The body can't increase its excretion of iron.
- Blood transfusions contain much iron so patients who need frequent transfusions will build up excess iron.







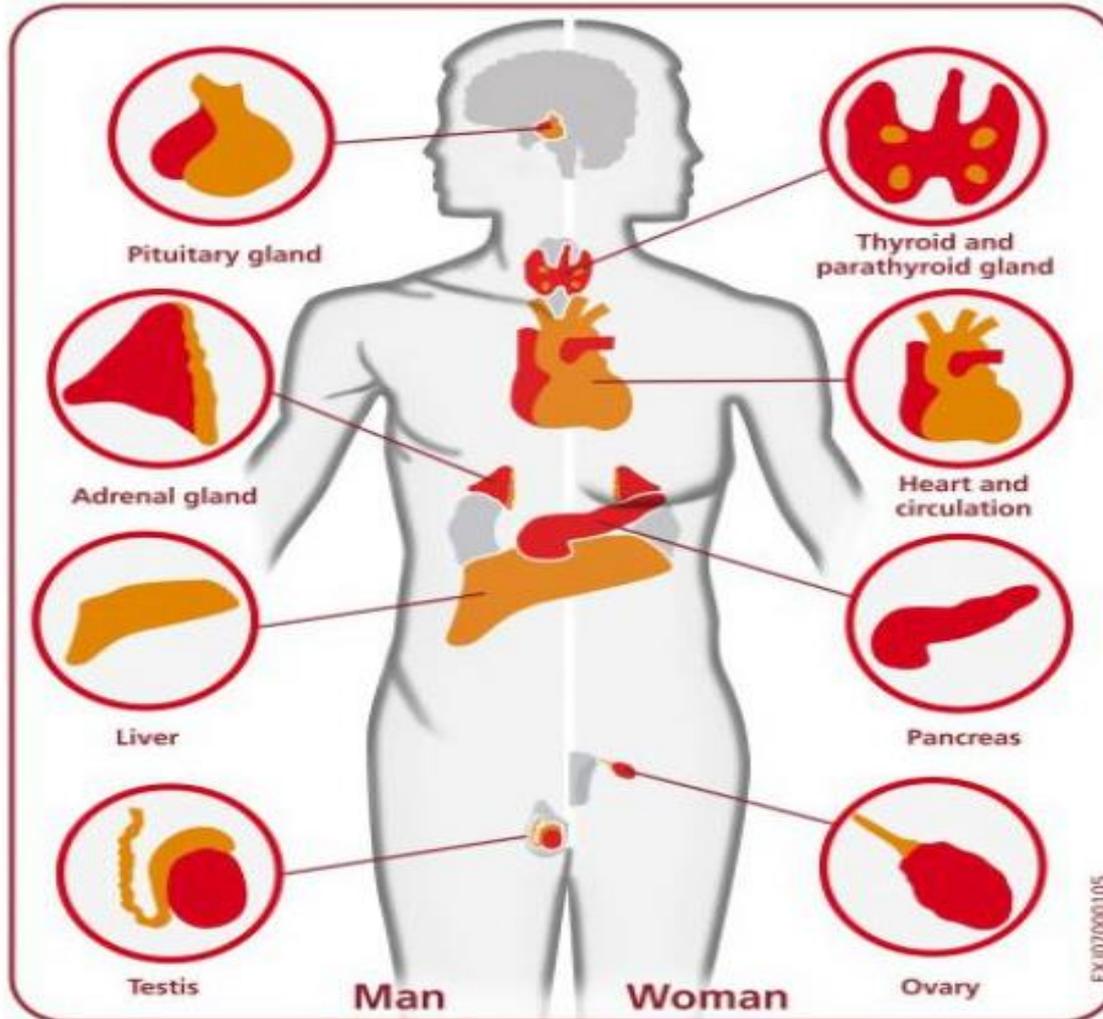
When does iron become a problem?



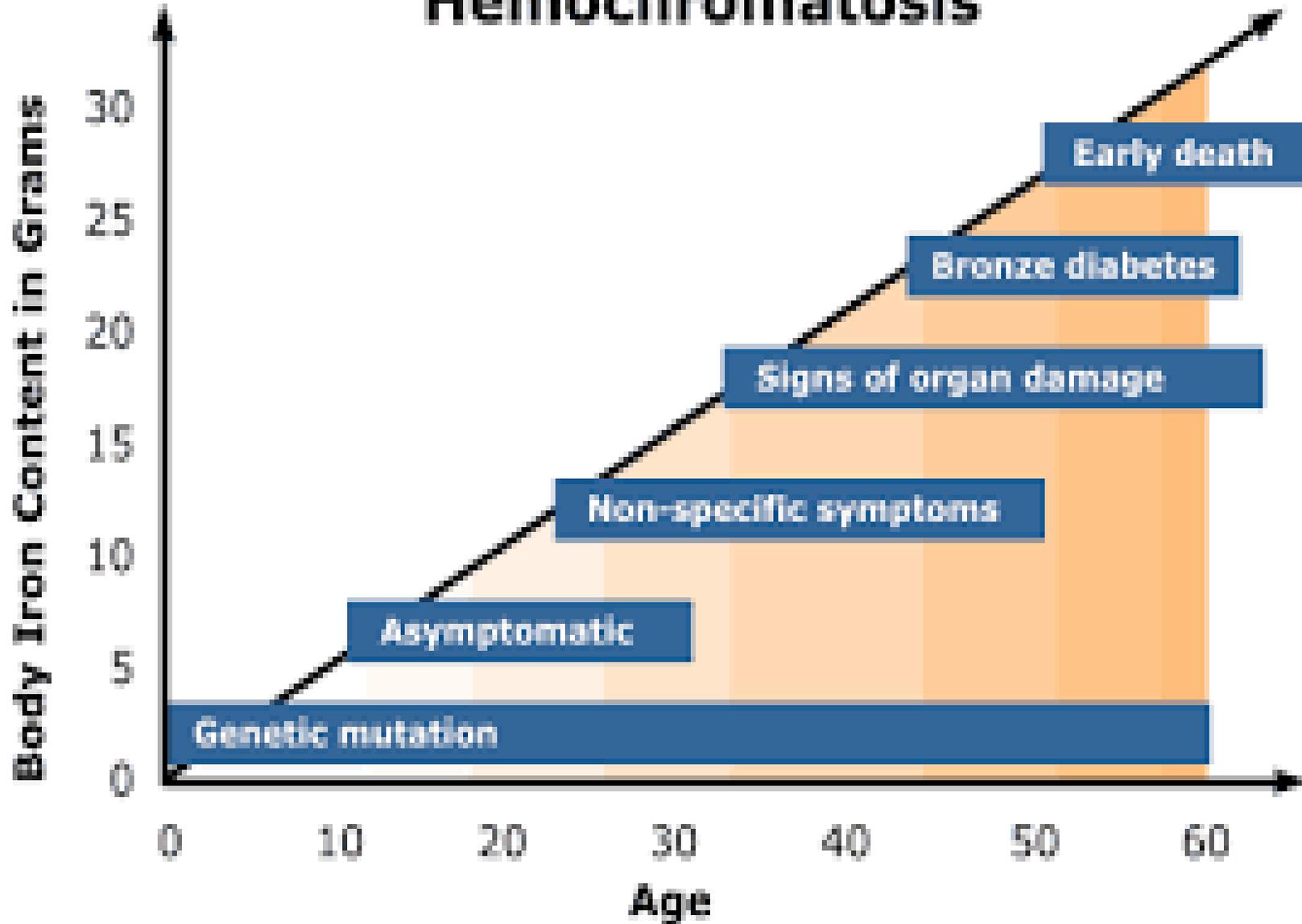
- Normally 2.5-3 grams of iron in the body.
- Tissue damage when total body iron is 7-15 grams. After 30-50 Unites of red blood cells.

+ Iron Overload

Organs that may be affected by iron overload



Course of Hereditary Hemochromatosis



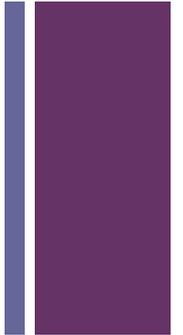


How do we diagnose iron Overload?



- History.
- Serum ferritin level.
- Liver Biopsy.
- Magnetic resonance imaging MRI.

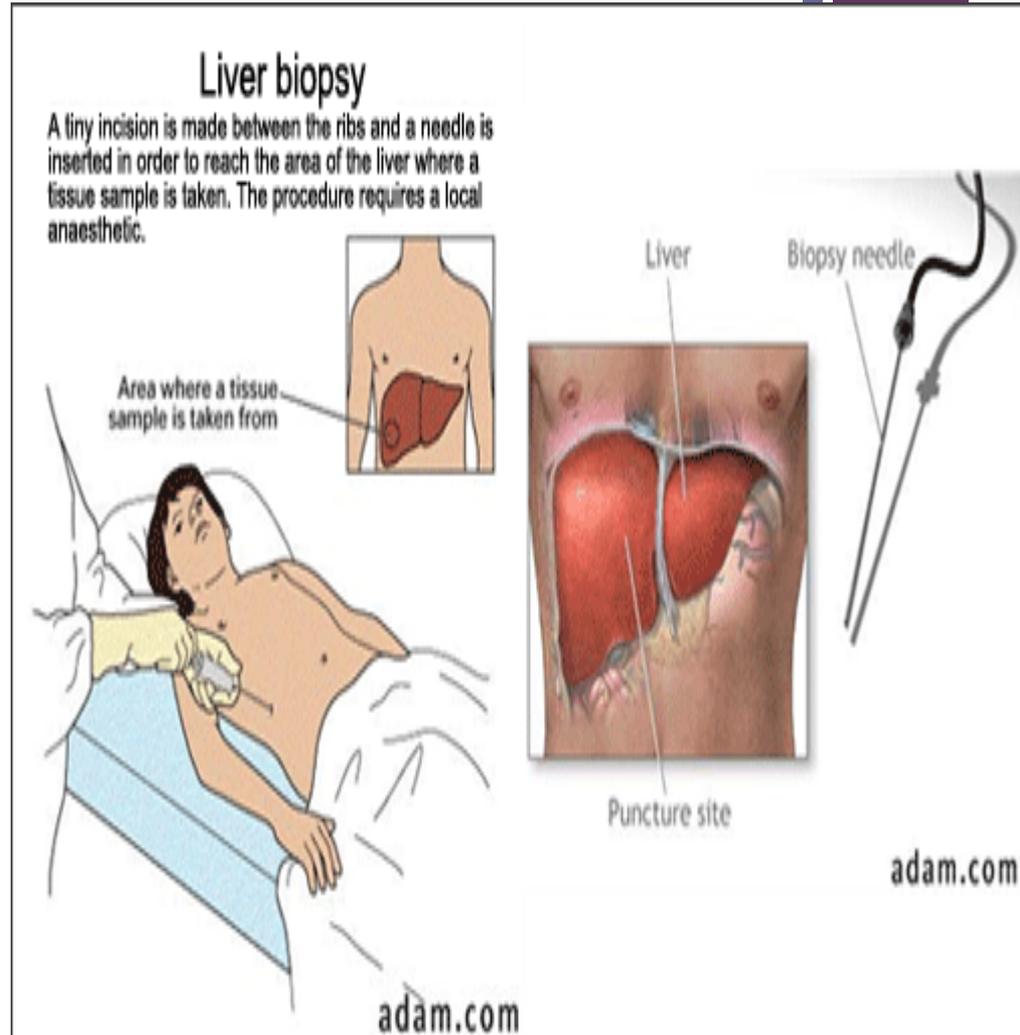
+ Serum Ferritin Level



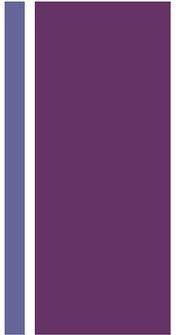
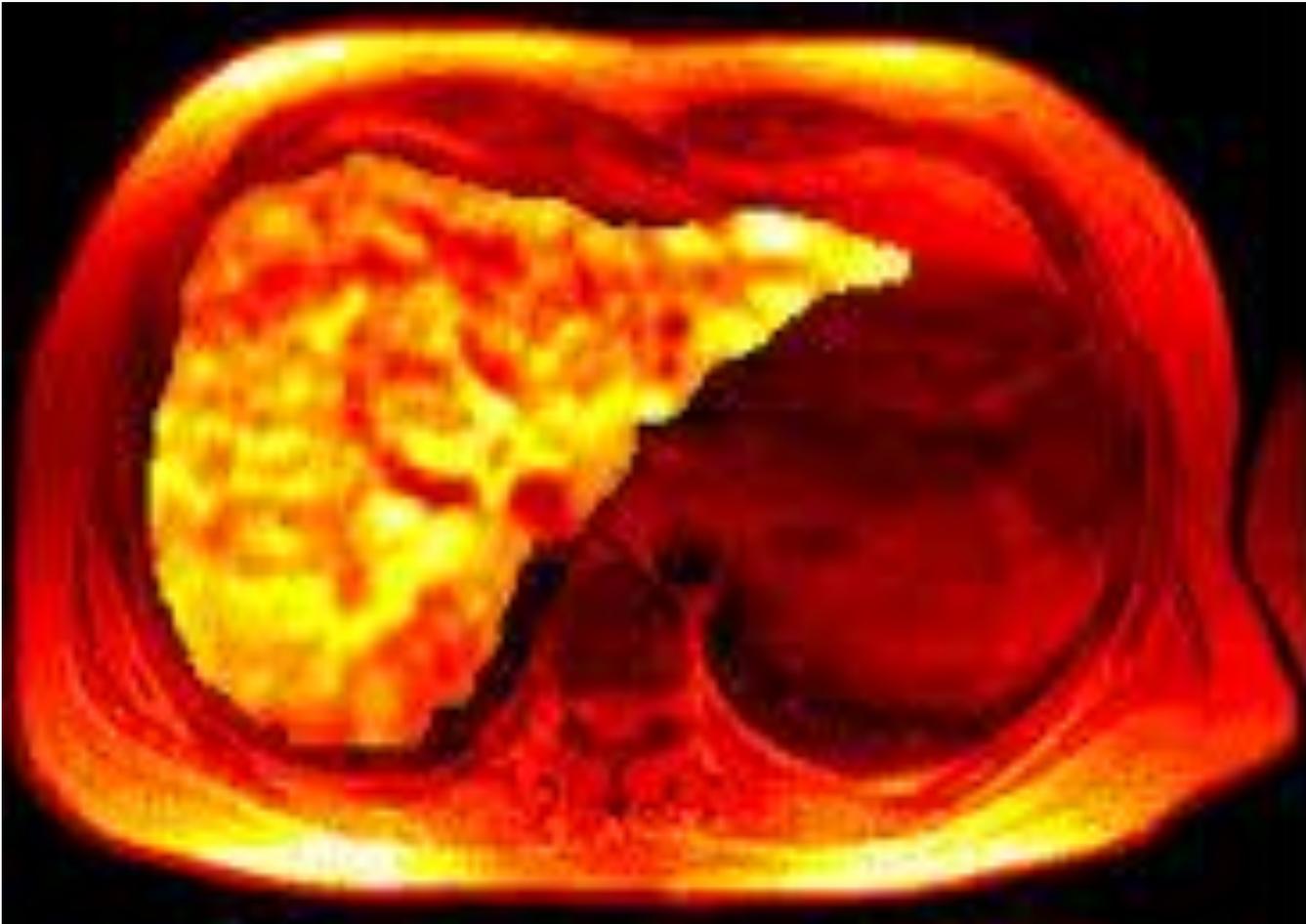
- Easy.
- Inexpensive.
- Can be misleading in cases of liver function abnormalities, or inflammation.

+ Liver Biopsy

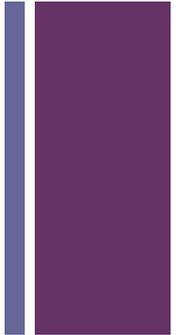
- Specific.
- Invasive, and potentially risky.
- Not often needed for patients with chronic transfusions.



+ Magnetic Resonance Imaging



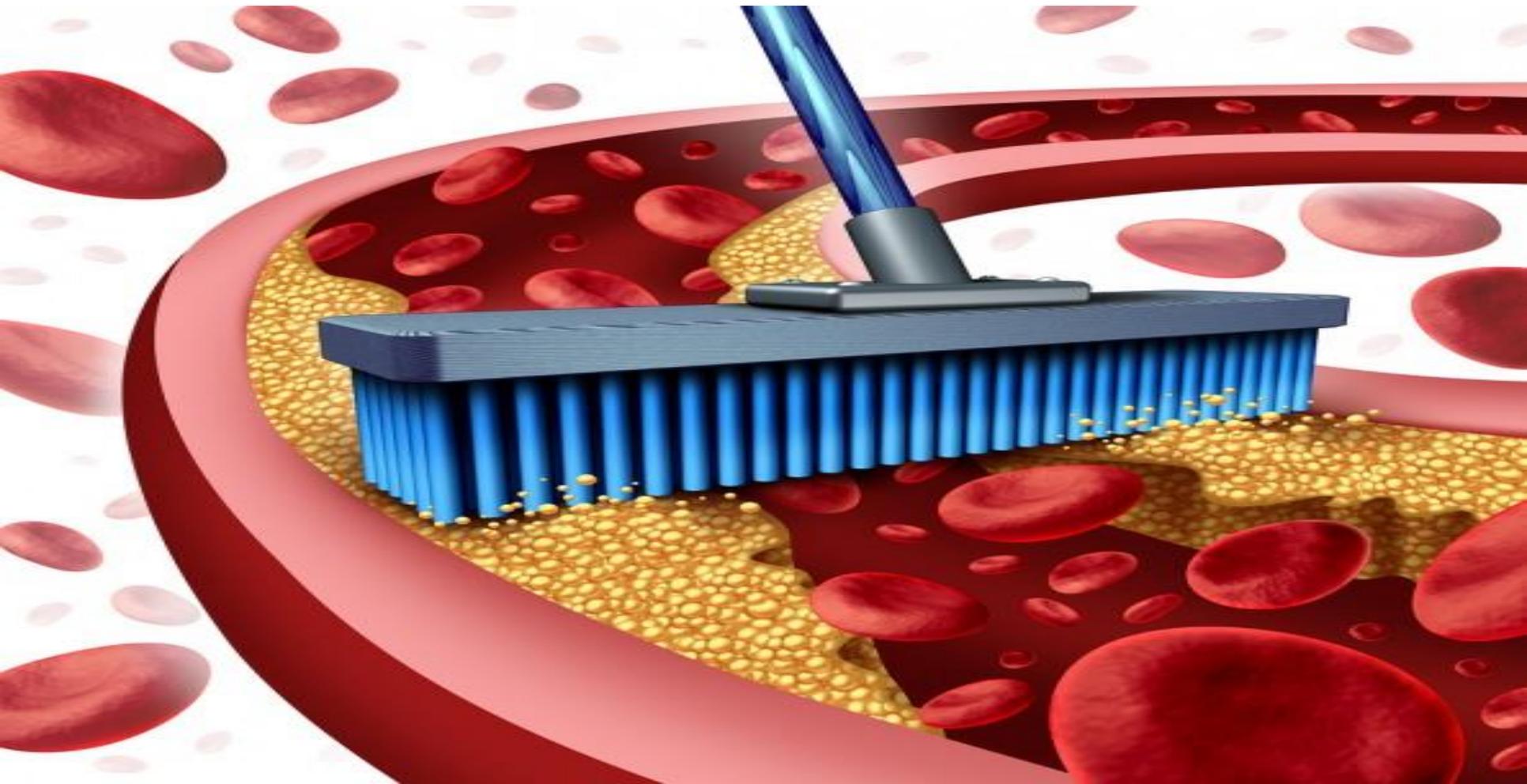
+ Iron Overload



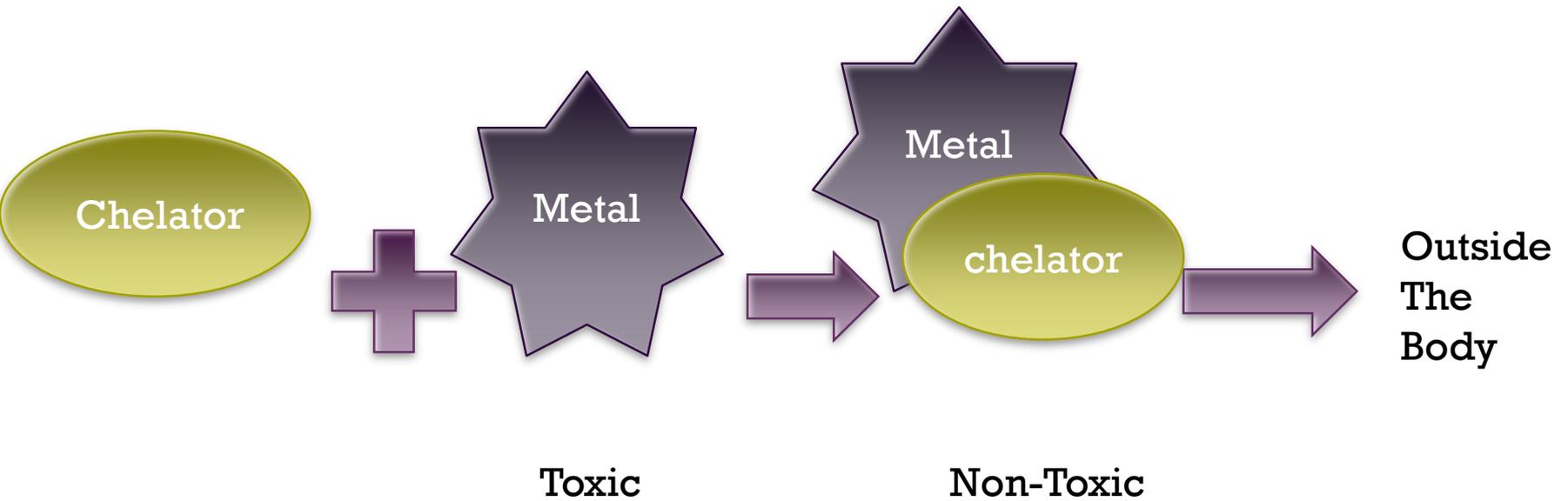
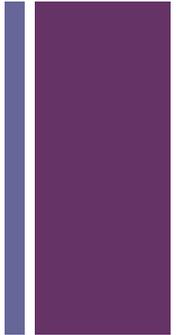
- Iron overload caused by transfusions causes malfunction of the liver, heart, and endocrine organs.
- Problems may begin after 30 unites of red blood cells.
- Serum Ferritin helps to estimate iron levels.
 - MRI.

+ How can we treat?

- Iron Chelation= pumping out iron.

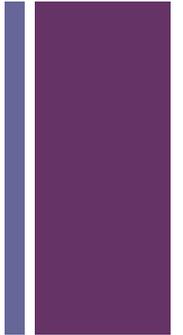


+ What is Chelation Therapy?

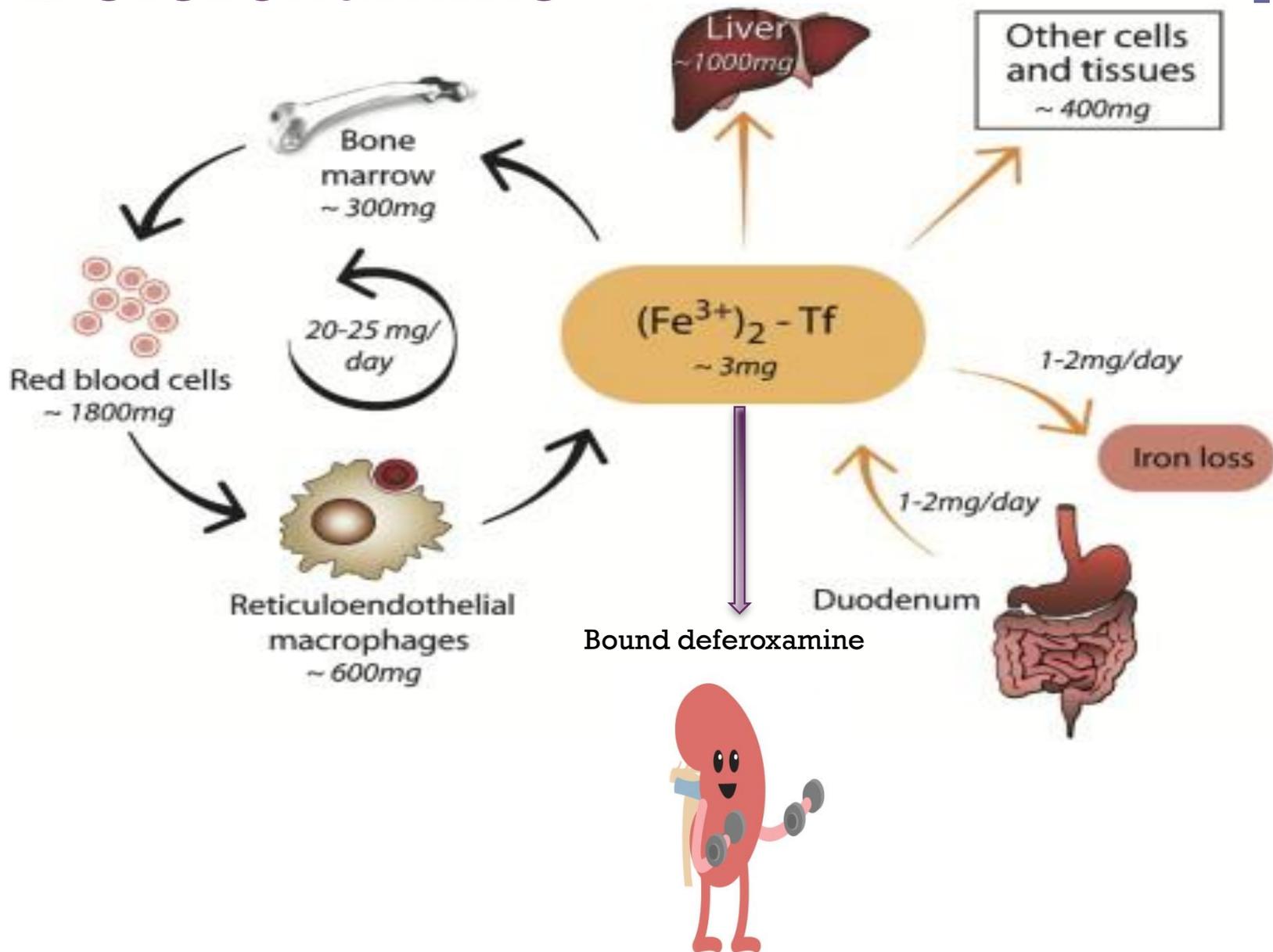


+ What are the available agents?

- Dferoxamine (Desferal)
- Deferasirox (ICL670, EXJADE)
- Alternative: Deferiprone (L1)

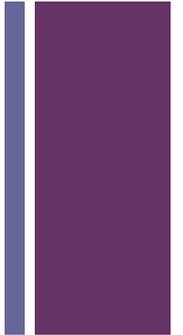


+ Deferoxamine





Challenges of Deferoxamine



- Subcutaneous/Intravenous route of administration
 - Expensive.
 - Cumbersome.
 - Uncomfortable.

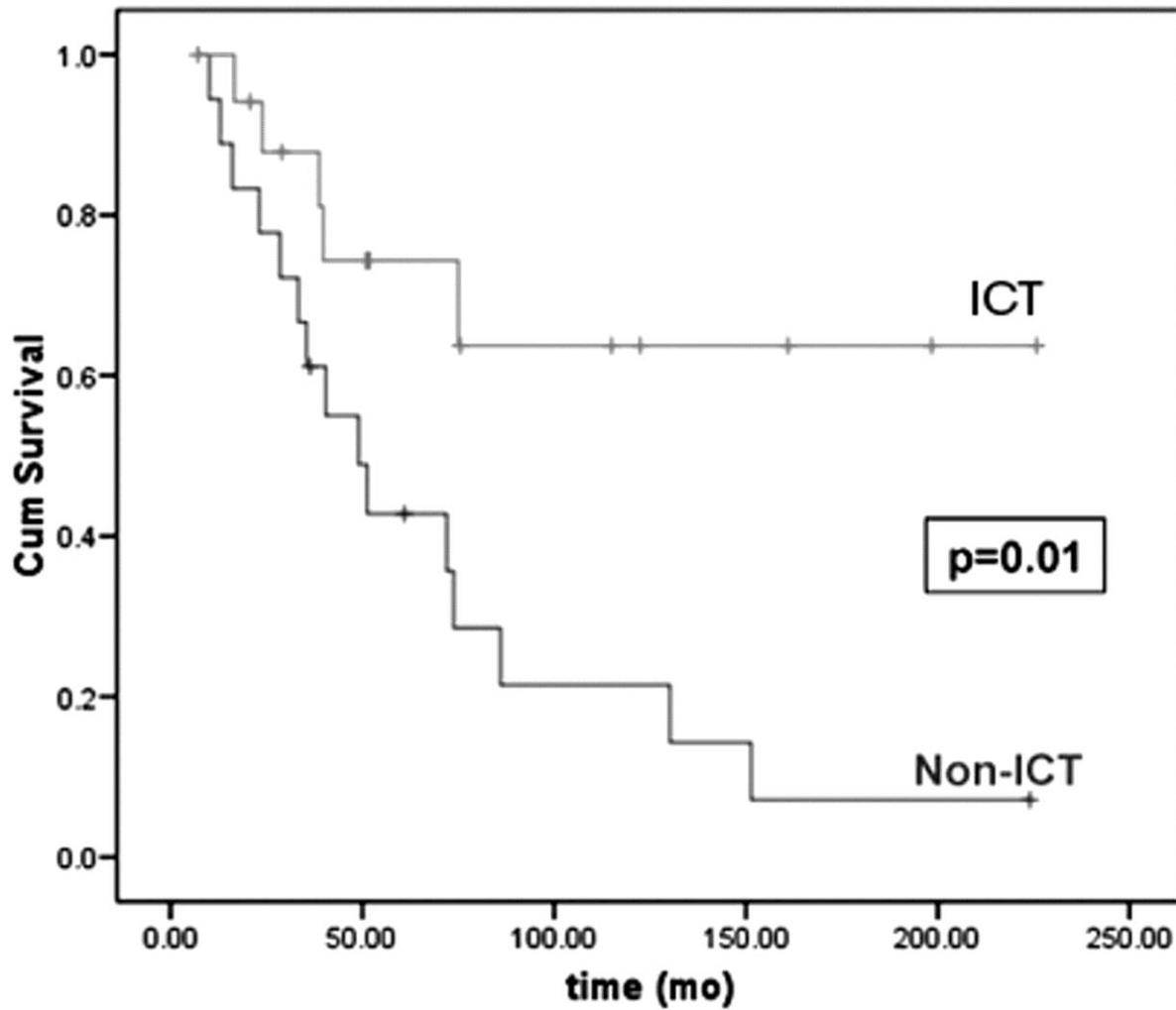
Rapid metabolism (30 min half life) necessitates prolonged infusion (12-15 hours)

Complications due to iron overload still occur due to poor compliance with therapy.

+ Deferoxamine infusion



Overall survival in patients with myelodysplastic syndromes (MDS) according to receipt of ICT in a subgroup analysis.



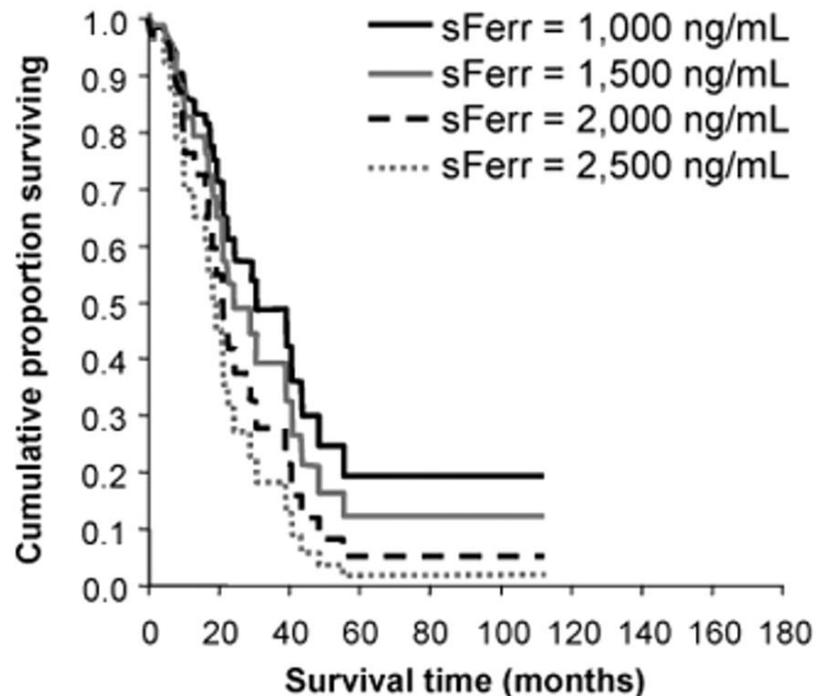
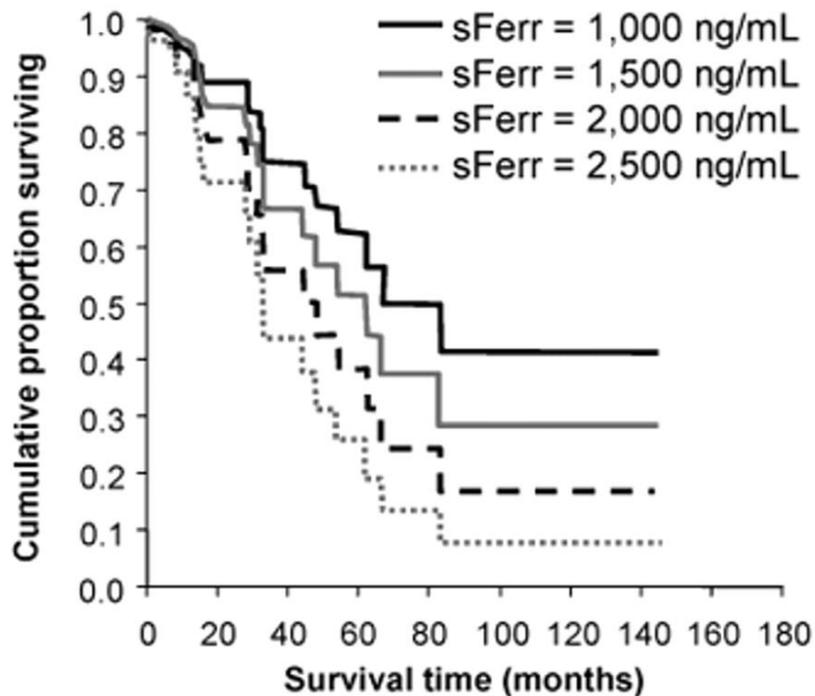
Heather A. Leitch, and Linda M. Vickars Hematology
2009;2009:664-672



Overall survival of transfusion-dependent patients with myelodysplastic syndrome (MDS) according to ferritin level.

RA/RARS/5q-
(HR = 1.42, p < 0.001)

RCMD/RCMD-RS
(HR = 1.33, p = 0.07)



Heather A. Leitch, and Linda M. Vickars Hematology
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+ Common Side Effects of Deferoxamine

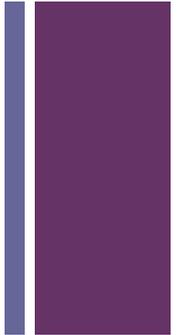
■ Local reactions

- Erythema (localized redness)
- Induration (localized swelling)
- Pruritus (itchiness)

Ophthalmologic

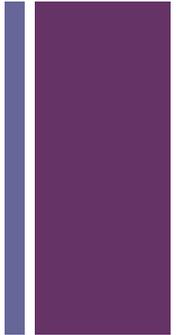
- Reduced visual acuity
- Impaired color vision
- Night blindness.
- Increased by presence of diabetes.

Hearing loss, Zinc Deficiency.



+ Iron Chelation and deferoxamine

- Chelation works by attaching a drug to iron, which allows the body to excrete it.
- Deferoxamine is inconvenient and uncomfortable but works.



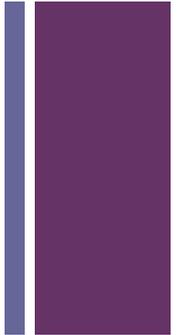
+ Deferasirox; Exjade

- Oral, dispersible tablet.
- Taken once daily.
- Highly specific for iron.
- Chelated iron excreted mainly in feces.
- Less than 10% excreted in urine.





Exjade is Generally Tolerable



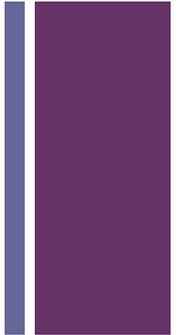
- The most common adverse events were mild and transient:
 - Nausea (10%)
 - Vomiting (9%)
 - Abdominal pain (14%)
 - Diarrhea (12%)
 - Skin rash (8%)

Rarely required discontinuation of drug.

There are reports of Kidney failure, worsening blood counts.

+ Exjade is Available.

- Approved in 2006 for chronic iron overload in patients with transfusion dependent anemias aged 6 years old and older.
- Chronic iron overload is patients with transfusion-dependent anemias aged 2-5 years old who can't be adequately treated with deferoxamine.



+ Exjade works

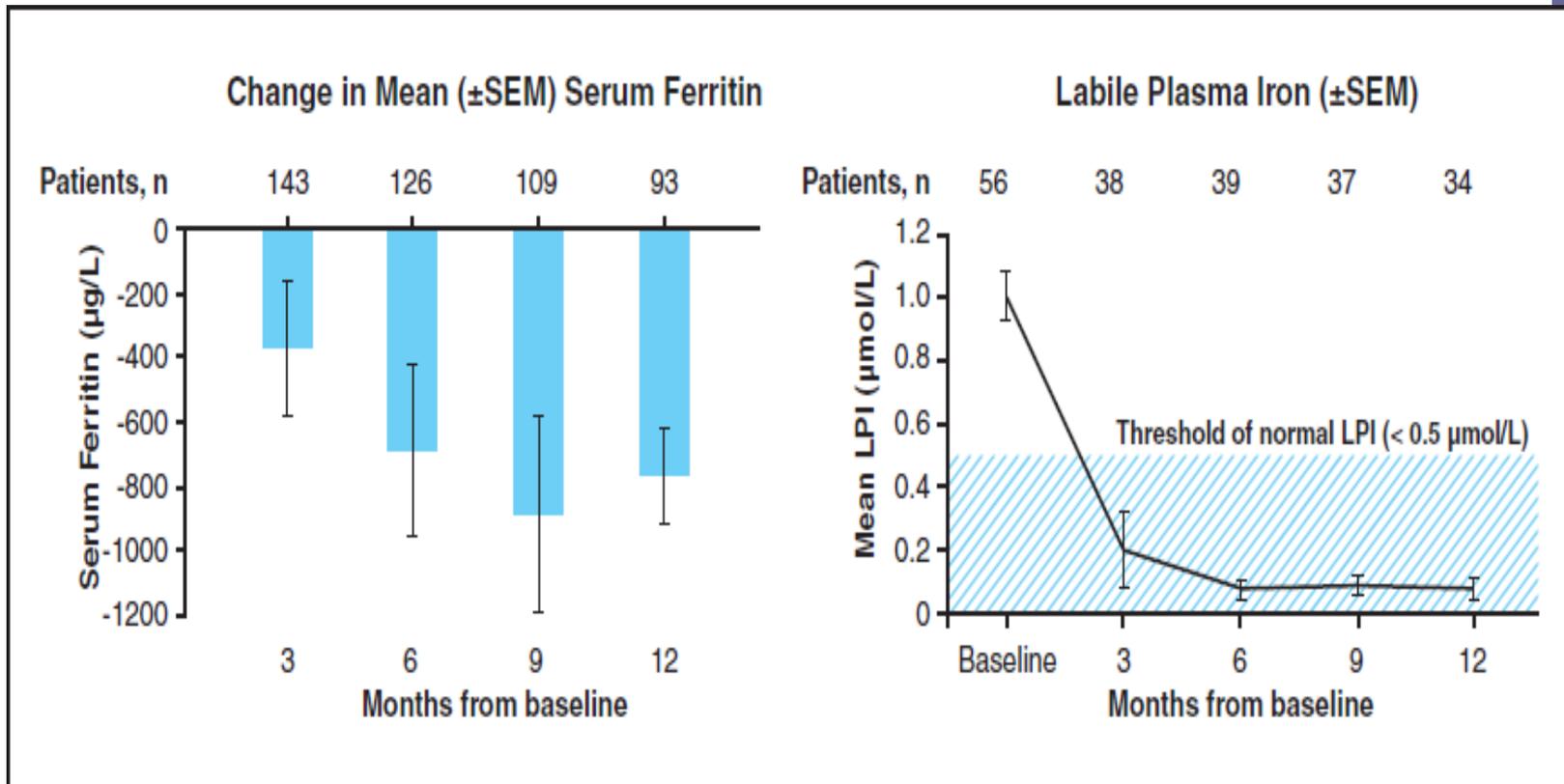


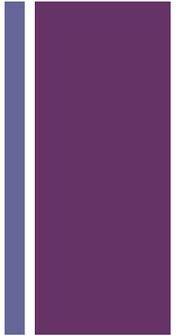
Fig 3. — Serum ferritin and labile plasma iron change with deferasirox. This research was originally published in *Blood*. From List AF, Baer MR, Steensma D, et al. Iron chelation with deferasirox (Exjade®) improves iron burden in patients with myelodysplastic syndromes (MDS). *Blood (ASH Annual Meeting Abstracts)* 2008;112:634. Abstract © 2008 American Society of Hematology. Reprinted with permission.

+ Canadian Guidelines;

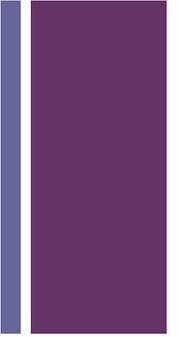
- Why: to prevent end-organ complications of iron overload and extend lifespan.
- Whom: transfusion-dependent patients with expected survival >1 year or BMT candidates.
- When: ferritin >1000, TfSat>0.5.
- How: DSX 20 mg/kg/day or DFO 50 mg/kg/day 5/7; target ferritin <1000.



Summary



- Iron overload is an inevitable consequence of Chronic RBC transfusion.
- Iron toxicity affects the function of the liver, heart, and endocrine organs.
- Chelation therapy should be offered to iron overloaded patients with life expectancy > 1 year.
- Desferal and Exjade are both effective.



Thanks, Questions?