

Chelating agent in treatment of  
Iron overload

Iron overload during iron deposition in multiple organs is along with serum ferritin value over than 1000  $\mu\text{g/L}$  ,Iron overload, either ,genetically or acquired

### **Genetically :**

- hereditary hemochromatosis
- sickle cell disease,
- major beta-thalassemia,
- sideroblastic anemia,
- enzyme deficiency (pyruvate kinase, G6PD)
- Atransferrinemia (rare)

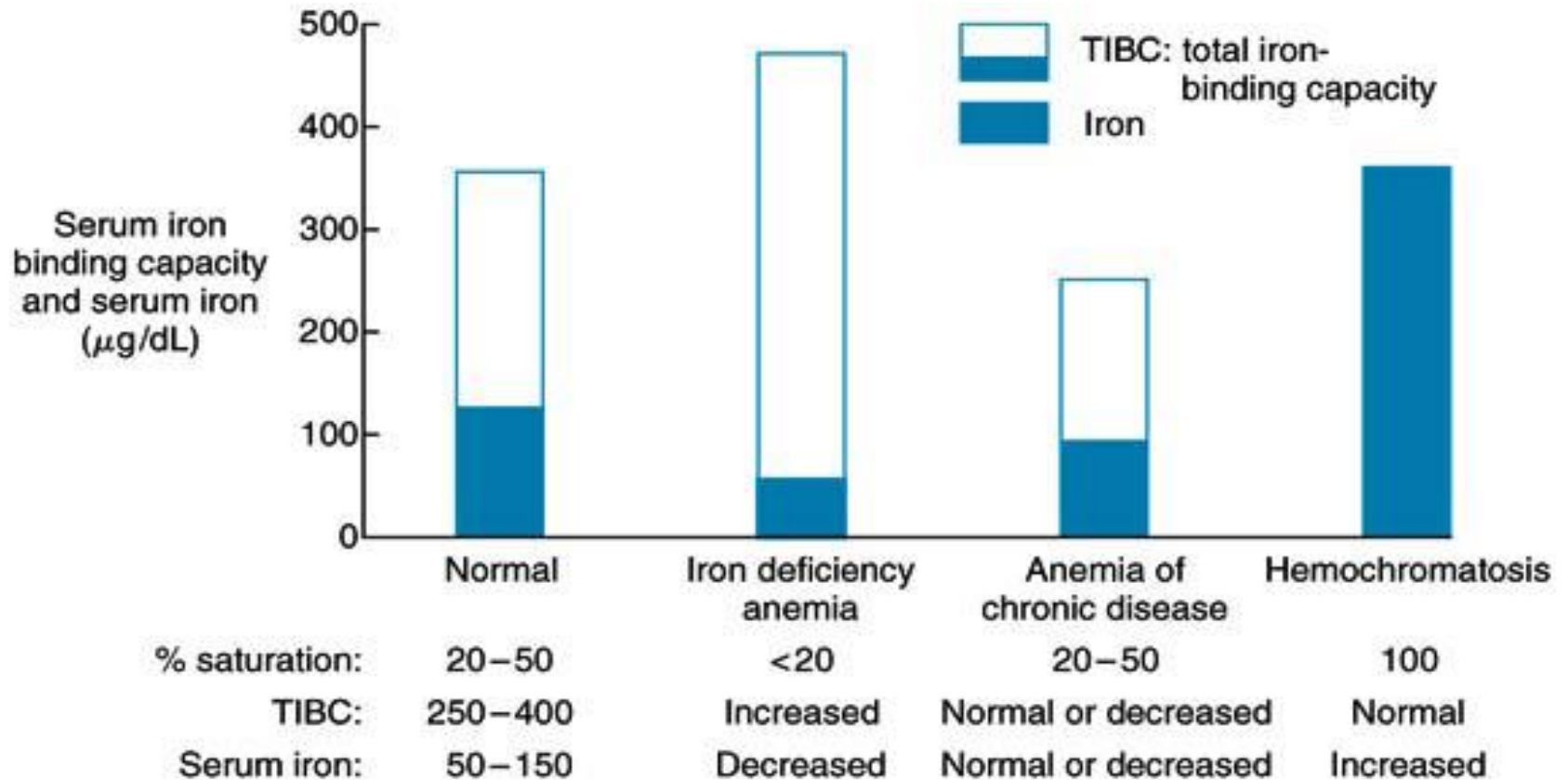
## acquired

- frequent transfusions
- abuse consumption of iron (often as supplement)
- chronic hepatitis have potential to cause acquired iron overload. *The exact mechanism of how chronic hepatitis causes iron overload is not yet fully understood. However, it is believed that the inflammation caused by chronic hepatitis leads to increased absorption of iron from the gut and increased release of iron from macrophages in the liver*

# Blood tests

The two key tests to detect iron overload are:

**Serum transferrin saturation.** Transferrin saturation values greater than 50% are considered too high.



# Serum ferritin

- measures amount of iron stored in body



# High serum ferritin levels can be caused by:

1. Chronic disease and inflammation
2. Chronic alcohol consumption
3. Liver disease
4. Renal failure
5. Metabolic syndrome
6. Malignancy
7. Rheumatoid arthritis
8. Acute infections

# High TIBC saturation levels

High transferrin saturation levels can be caused by a variety of conditions, including:

1. Cirrhosis
2. Liver cancer

**Liver function tests.** These tests can help identify liver damage: elevated SGPT, SGOT

**MRI.** An MRI is a fast and noninvasive way to measure the degree of iron overload in liver

**Testing for gene mutations.** Testing your DNA for mutations in the HFE gene is recommended if you have high levels of iron in your blood

**liver biopsy** If liver damage is suspected, may have a sample of tissue from liver, using a thin needle



# Complications of Iron Overload

- Cardiac iron overload
  - Heart failure and arrhythmias
- Endocrine failure
  - Growth hormone deficiency
  - Delayed puberty, hypogonadism, infertility
  - Diabetes Mellitus
  - Hypothyroidism
  - Hypoparathyroidism
- Liver fibrosis or tumors

# Phlebotomy

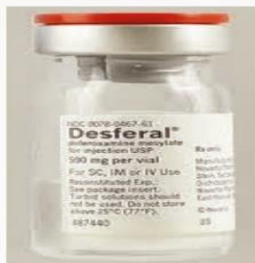
## CAN BE USED TO TREAT

in hemolytic anemia phlebotomy is impossible because patients are anemic.

### TWO WAY OF TREATMENT

**AISHA**  
WELFARE SOCIETY

#### Desferal Injections



#### Asunra Tablets



# Approaches to Chelation

## Maintenance Therapy

- Serum ferritin and liver iron are in optimal range
- Chelation is needed only to remove iron that is added with each transfusion

## Reduction Therapy

- Serum ferritin and liver iron are elevated and/or mild cardiac iron overload is detected
- Chelation is needed to reduce iron burden + remove iron that is added with each transfusion

## Rescue Therapy

- Critical organs are failing or are at imminent risk of failure (heart or pancreas)
- High-dose chelation is needed to rapidly lower iron burden + remove iron added with each transfusion + provide continuous protection of the organs from labile plasma iron

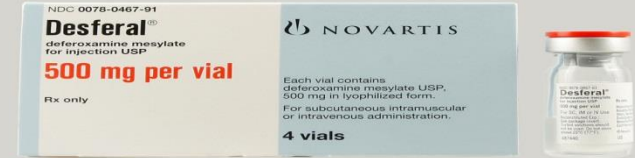
# Different types of Iron Chelators

## 1. DEFEROXAMINE

(DFO or Desferal) is a non-toxic iron chelator

pharmacokinetics

- intravenous or subcutaneous infusion should be recommended.
- it is not used orally or IM



The main mechanisms of iron deposition by DFO are as follows:

- Non-bonded DFO will be enter liver parenchymal cells and attached to excess hepatic iron and excreted via bile.
- DFO can directly absorb iron accumulation in cardiac muscle cells and other tissues and then excreted in urine



- Due to DFO short plasma half-life, continuous injection is required for patient with iron overload until iron level disposal reaches to 15 mg daily.



# 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

hypotension.

most toxicity is reversible when DFO treatment is withdrawn.

Deferoxamine therapy increases the risk of infection of mucormycosis, vibrio and yersinia. it cannot be seen with other iron chelators such as Deferasirox and Deferiprone because they do not work as siderophores.



## **2. DEFERIPRONE**

-Oral iron chelator which is proper choice for patients who showed an inadequate response to prior chelation therapy such as Deferasirox and Deferoxamin.

The most typical side effects include elevated liver enzymes, gastrointestinal disorders and arthralgia. The most serious adverse effects associated with DFP is agranulocytosis reversible after stopping therapy.

The primary recommended oral dose of Deferiprone is 25 mg/kg 3 times a day (daily consumption: 75 mg/kg) and a maximum recommended daily use is 100 mg/kg.

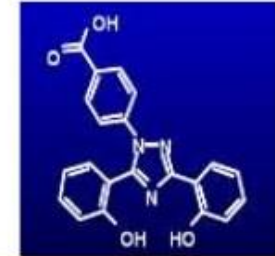
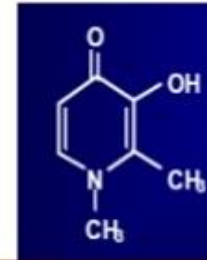
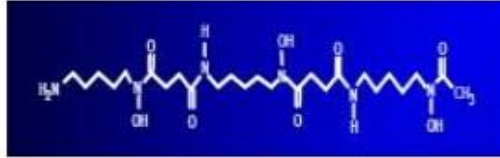
For agranulocytosis monitoring during therapy, neutrophil absolute count should be performed regularly

Basically, in iron overload condition such as hereditary hemochromatosis, deferiprone therapy would be intolerable. Also, transfusion dependent patients with cardiac failure require more serious chelation therapy than regular patients with chelation therapy. In such cases, combination therapy with subcutaneous or intravenous deferoxamine and oral deferiprone is recommended.

### **3. DEFERASIROX**

- The most common side effects of DFX are abdominal pain, nausea, vomiting, diarrhea, skin rashes and ophthalmic complication.
- These reactions frequently occur in older patients with predisposition to renal or hepatic disease and patients with low platelet counts.
- Serum creatinine level, serum transaminases, bilirubin and CBC should be regularly monitored.

# Iron Chelators



	<b>Deferoxamine</b>	<b>Deferiprone</b>	<b>Deferasirox</b>
<b>Brand Name</b>	<b>Desferal</b>	<b>Ferriprox</b>	<b>Exjade</b>
<b>Half-life</b>	20 minutes	2-3 hours	8-16 hours
<b>Route</b>	SQ, IV infusion	PO	PO
<b>Dose (mg/Kg/d)</b>	20-60	75-100	20-40
<b>Frequency</b>	5-7 days/week	3 times daily	Once daily
<b>Iron Excretion</b>	Urine/Stool	Urine	Stool
<b>Side Effects</b>	Vision, Hearing, Growth, Local Reactions, Allergy	Gastro-intestinal symptoms, Kidney dysfunction, Hepatitis	Gastrointestinal symptoms, agranulocytosis/neutropenia, Arthralgia

# Formulation of Chelators and their consumption dosage

**Deferiprone** is presented as 500 mg tablets and oral solution (100 mg in 0.4 ml).

**Deferasirox** is available in different tablet sizes such as 125 mg, 250 mg and 500 mg.

can be taken with an empty stomach. The recommended dosage is 20 mg/kg up to a maximum of 30 mg/kg/day in a single dose. Ferritin level monitoring will prescribe the further dosage.

Thank you