Iron deficiency anemia in CKD

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- Importance of iron metabolism
- Definition anemia in CKD

- Prevalence of IDA
- Evaluation IDA
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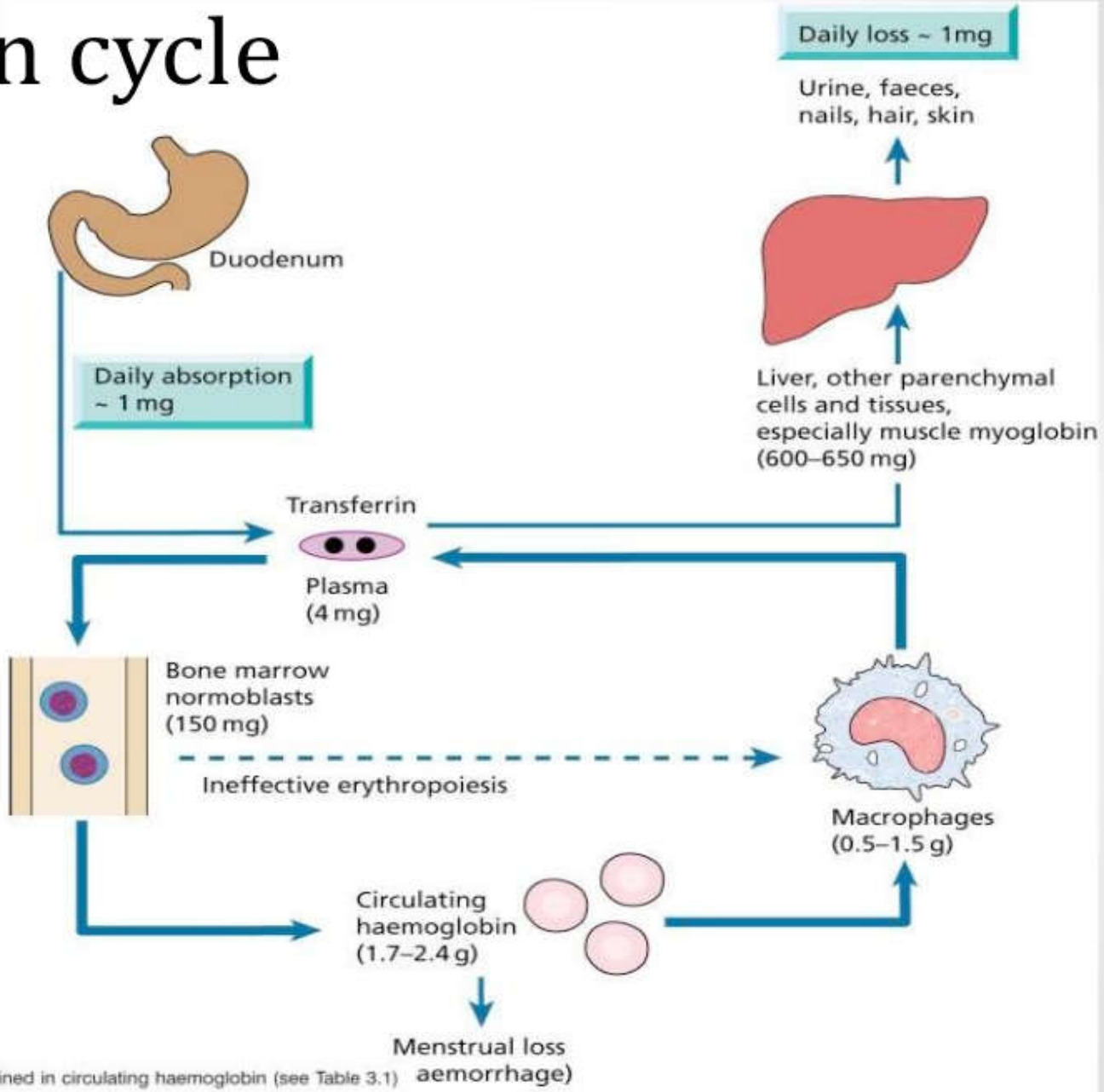
Normal Iron cycle

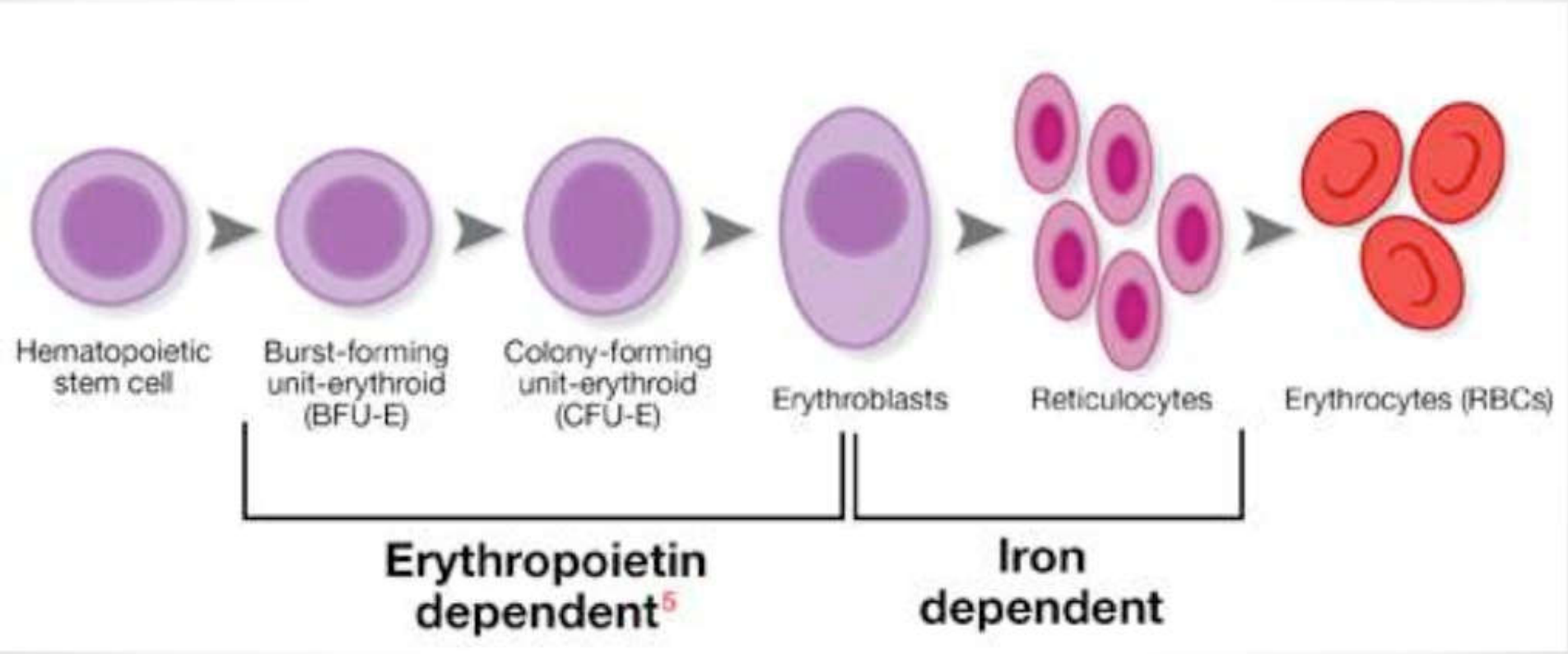


ure 3.2 Daily iron cycle. Most of the iron in the body is contained in circulating haemoglobin (see Table 3.1) is reutilized for haemoglobin synthesis after the red cells die. Iron is transferred from macrophages to ma transferrin and so to bone marrow erythroblasts. Iron absorption is normally just sufficient to make up for loss. The dashed line indicates ineffective erythropoiesis.

Importance of iron metabolism

- Iron affect
  - ✓ adequate Hb synthesis,
  - ✓ DNA synthesis,
  - ✓ immune response,
  - ✓ oxidative metabolism and mitochondrial electron transport.
- Iron deficiency has been linked to
  - ✓ decreased muscle function
  - ✓ cognitive impairment
  - ✓ fatigue in non-anemic women.

Normal erythropoiesis



Anemia definition

Definition WHO:

Hg <13 g/dl for adult males and postmenopausal women

<12 g/dl for premenopausal women

Anemia definition in CKD

NICE 2015[1] (National institute for the clinical Excellent)	Hb≤11
KDIGO 2012[2]	Female: Hb<12g/dl Male: Hb<13g/dl
CSN (Canadian Society of Nephrology)[3]	Female: Hb<12g/dl Male: Hb<13.5g/dl
ERBP (European renal Best practice)[4]	Female: Hb<12g/dl Male: ≤70y Hb<13.5 >70y Hb<13.2g/dl

minimum frequency Hb measurement

- Hb concentration should be measured with the following minimum frequency:

- **Annually** in CKD Stage 3
- **Twice yearly** in CKD Stage 4-5ND
- **Monthly** in patients with CKD 5HD
- Iron therapy and ESAs are administered to achieve target hemoglobin levels between 10 and 11.5 g/dL

Investigation into the cause of anemia

- CBC
- Absolute retic count
- serum iron , TIBC, TSAT, Ferritin
- Serum B_{12} and Folate
- Stool guaiac (in IDA if its possible)

Diagnostic role of GFR

- **eGFR< 60 ml/min/1.73m2** ➔should trigger investigation into whether **anemia is due to CKD.**
- **eGFR ≥60 ml/min/1.73m2** ➔ anaemia is more likely to be related to **other causes**.

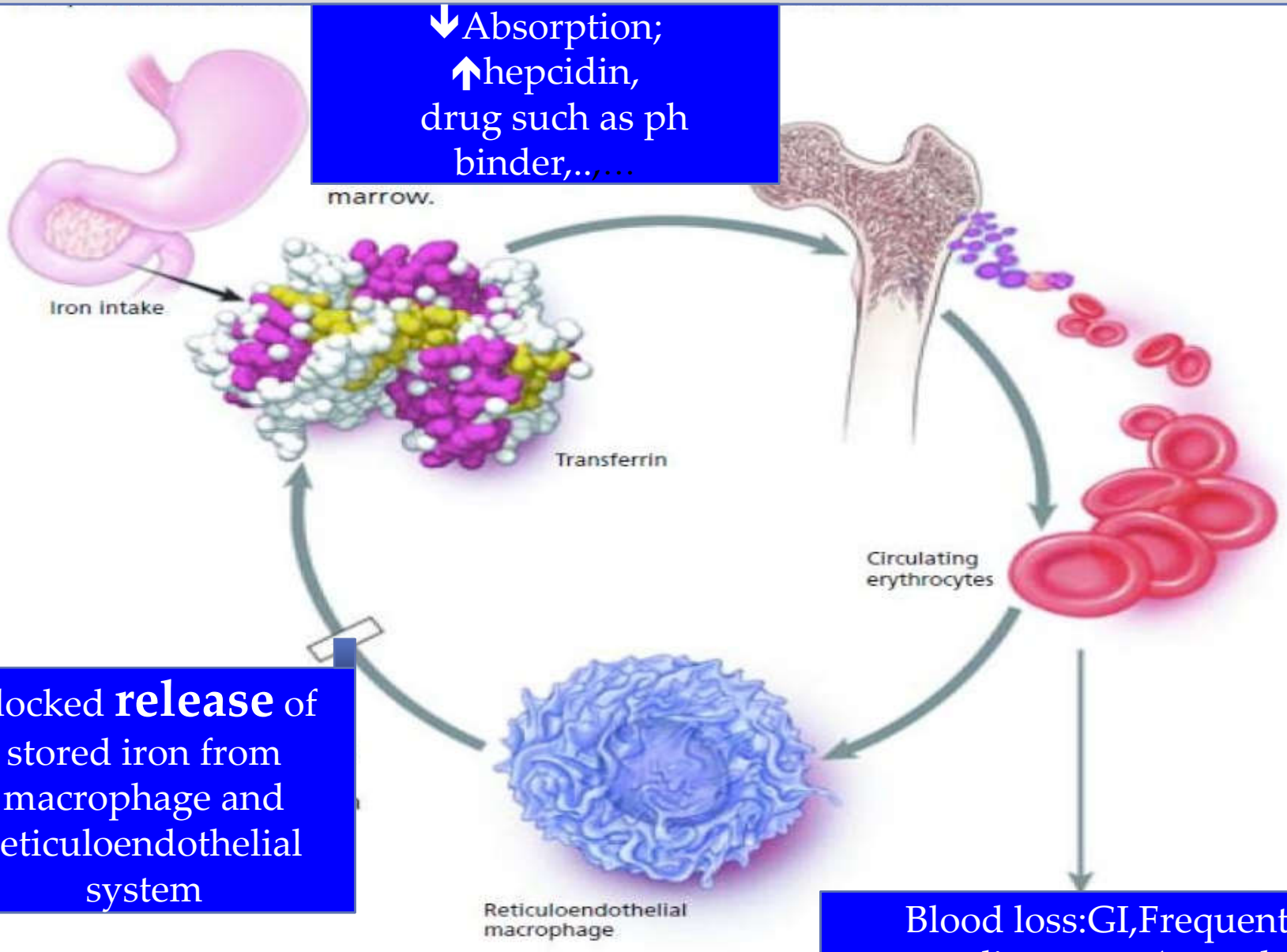
Prevalence IDA

- Iron deficiency anemia is common in CKD patients **(20-40%)**
- **Iron deficiency is related to**
  - ✓ **stage of CKD**
  - ✓ **Sex**
  - ✓ **Diabetes mellitus**
  - ✓ **erythropoietin therapy and dialysis therapy**.
- There was inconsistent relationship with **age, hypertension, and type of iron therapy.**

- **Mortality** :not related to iron deficiency in CKD patients.

Causes of IDA

↓Absorption;
↑hepcidin,
drug such as ph binder,..,…



Blocked **release** of stored iron from macrophage and reticuloendothelial system

Blood loss:GI,Frequent sampling,surgy(vascular

Markers of iron status in CKD

Current clinical standard	Available but not routinely used for iron monitoring in ESRD	Novel
• Serum ferritin • TSat • Serum iron	• Mean cellular Hb • Red cell volume distribution width • LIC • Reticulocyte Hb content	• sTfR1 • Hepcidin • NTBI • Labile plasma iron

Assessing Iron status

- Absolute iron deficiency – ferritin<100ug/l, TSAT<20%

Assessing Iron status

- Functional iron deficiency – ferritin>100ug/l, TSAT<20%

Assessing Iron status

neither TSAT nor ferritin predicts with accuracy which patients will have an improved response to ESAs after iron , except that the likelihood of a response is small in patients whose TSAT>30 percent and Ferritin> 500 ng/mL.

Assessing Iron status

Hypochromic Red cell>10%

Assessing Iron status

Reticulocyte Hb content <29Pg

Assessing Iron status

Mean cellular Hb

A randomized trial of iron deficiency testing strategies in hemodialysis patients[1]

Steven Fishbane, Warren Shapiro, Paula Dutka, Osvaldo F. Valenzuela, and Jessy Faubert

Winthrop-University Hospital, Mineola, and Brookdale Medical Center, Brooklyn, New York, USA

Reticulocyte Hb content <29pg vs ferritin<100ng/ml:

CHr is

- **simple and practical**
- significantly **reduced need for intravenous iron**, **without any decrease in hematocrit or increase in epoetin dose** requirements
- **lower level of test variability** compared to serum ferritin and transferrin saturation.

- **Liver iron concentration(LIC)** : **reference standard** to estimate body **iron stores**. LIC levels > 15– 20 mg/g dry weight cause hepatic dysfunction, hepatic fi brosis and worse prognosis .
- **Super-conducting quantum interference device biomagnetic liver susceptometry (SQUID-BLS) and MRI** (**Noninvasive methods for measuring LIC**):very **accurate** and well-validated noninvasive method ,restricted in **high costs** of the machine and the requirement of dedicated trained staff. MRI, on the other hand, is widely available and less expensive.
- **Myocardial T2* MRI** :accurate assessment of cardiac iron status

AVAILABLE NOVEL METHODS TO ASSESS IRON STATUS

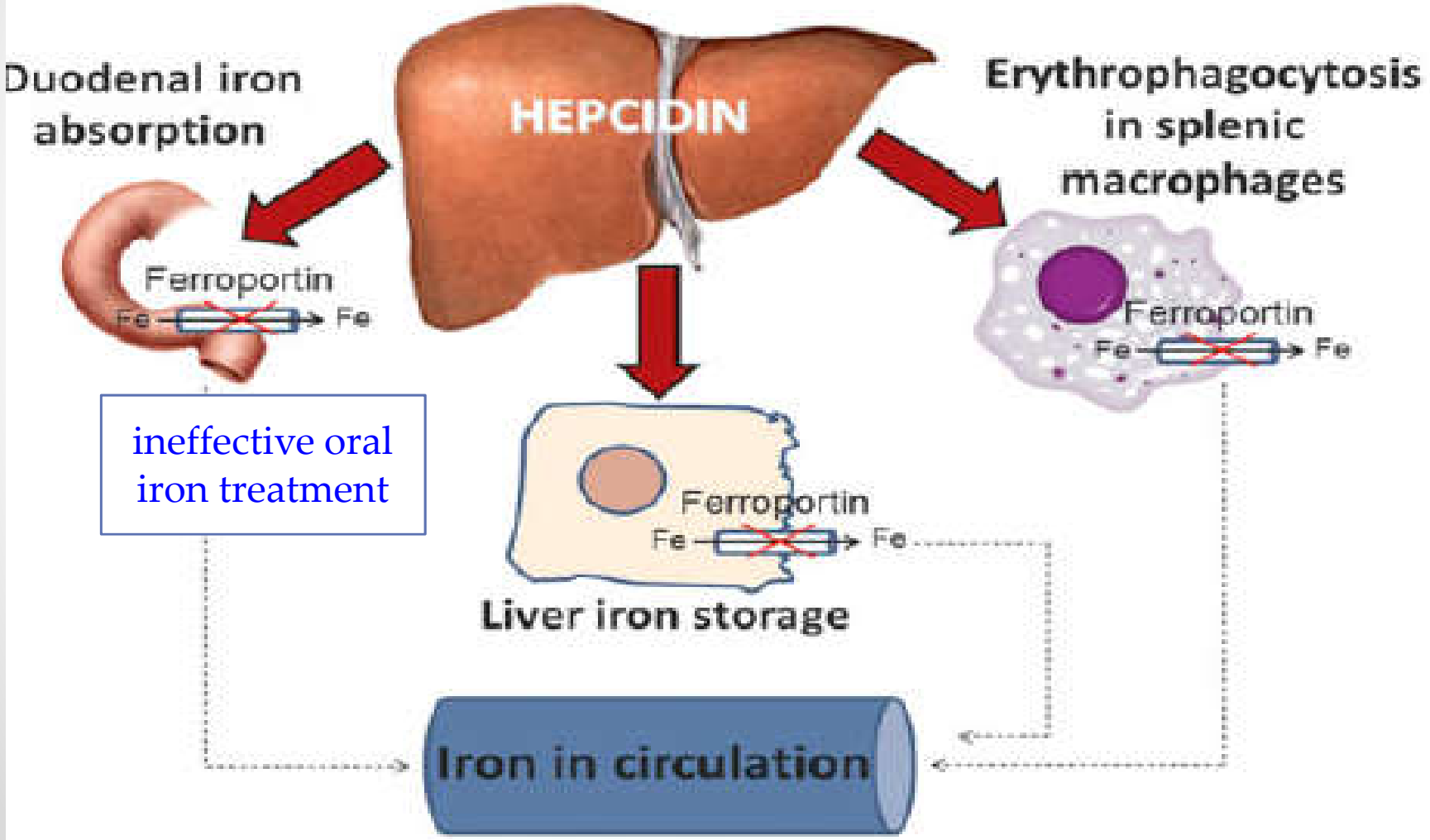
- **Soluble transferrin receptor 1 (sTfR1) concentration and sTfR1/log ferritin** :
- ↑under two conditions, (↑iron absorption):

✓IDA,

✓↑erythropoiesis.

- sTfR1 concentration is **proportional to** cellular expression of the **membrane associated TfR1** and **increases with increased cellular iron requirements and cellular proliferation** .

a peptide hormone that regulates **absorption of dietary iron** and **iron recycled** from senescent RBCs. Hepcidin exerts its function by binding to ferroportin (FPN-1), found on all cells involved in iron homeostasis. Hepcidin binds FPN-1, causes its **internalization and degradation** and results in impaired iron release .



hepcidin

- Increase Hepcidin:
  - Inflammation
  - Iron overload
- Decrease Hepcidin:
  - Hypoxia
  - erythropoiesis
  - IDA
- **Elevated levels in CKD patients may due to** :
  - CKD-related inflammation
  - lower hepcidin clearance

↑ Hepcidin cause anemia with :

- **iron deficiency**
  - decrease in iron absorption,
  - availability of recycled iron from macrophages and ultimately (functional IDA)
- **direct effect on erythropoiesis** by inhibiting erythroid colony formation when erythropoietin is low
- **Impairing RBC survival**

Classification IDA in CKD:

- 1)**Absolute:** results from depleted body **iron stores**, frequently a result of blood loss
- 2**) functional**: is caused by insufficient iron **availability** at the site of erythroblast production, despite **adequate body iron stores**

Treatment

TRATENT GUIDLINES

NICE 2015	**Anemic-CKD patients (Not on ESA)** TSAT<%20 AND Ferritin< 100ng/ml **Anemic CKD-patients (on ESA)** TSAT<%20, Ferritin< 800ng/ml	Review dose of iron when ferritin reach 500 ng/mL; do not exceed 800
KDIGO[2,9] 2012	**NOT ON ESA OR On ESA (Not on Iron)** TSAT is ≤30% and ferritin ≤500 ng/mL	ferritin >500 ng/mL: based upon patient's clinical status, Hb,TSAT, and ESA responsiveness,
CSN [3] 2008	Target: TAST>%20 and Ferritin>100µg/L (ND-CKD) Ferritin>200µg/L (HD)	
ERBP [4]	There should for Iron overload: Ferritin>500ng/ml and TSAT>%30	

IV or Oral Iron

FIND-CKD: a randomized trial of intravenous ferric carboxymaltose versus oral iron in patients with chronic kidney disease and iron deficiency anaemia

Nephrol Dial Transplant (2014)

- FIND-CKD was a 56-week, open-label multicentre, prospective, randomized and three-arm study . Patients were randomized at 193 nephrology centres in 20 countries.

Randomized (n=626) Hg=9-11g/dl,ferritin<100 or ferritin<200with TSAT<20% And eGFR<60 ml/min/1.73m2

During the first 8 weeks after randomization, patients were not to receive ESAs, blood transfusion or any anaemia therapy other than study drug . Subsequently ESAs and other therapies were permitted according to local practice if the Hb was <10 g/dL.

Allocated to high ferritin FCM(n=155) Ferritin:400-600 µg/L

Allocated to low ferritin FCM(n=154) Ferritin:100-200 µg/L

Allocated to oral iron (n=317)

Day 0: 1000 mg FCM During Weeks 4– 48, every 4 weeks 500 mg iron if ferritin 200 to <400 µg/L, and 1000 mg if ferritin <200 µg/L

200 mg iron as FCM During Weeks 4– 48, every 4 weeks 200 mg iron if ferritin was <100 µg/L. In

200 mg elemental Iron

Result FIND-CKD

- Both IV and oral iron therapy were effective in increasing Hb, ferritin and TSAT levels
- **FCM therapy with a higher ferritin target was shown to be superior to oral iron in**:
- **delaying and/or reducing** the requirement for **other anaemia management**
- occurrence of an **Hb trigger during the 12-month study**, as well as producing a **faster haematological response**. (These results were achieved with relatively few FCM injections).
- **well tolerated**, **fewer** treatment-related **adverse events** and study **discontinuations** versus oral iron
- **no renal toxicity** and **no increases in cardiovascular or infectious events.**

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Kidney Int. 2015 October ; 88(4): 905–914. doi:10.1038/ki.2015.163.

A randomized trial of intravenous and oral iron in chronic kidney disease

Rajiv Agarwal, MD[1], John W. Kusek, PhD[2], and Maria K. Pappas, BA[1]

REVOKE(N=136)CKD Stage3-4 with IDA

Oral Iron 200mg 8W elemental iron)

N=67 IV iron sucrose (200 mg every 2 weeks, total 1 g

primary end point :change in the slopes of measured GFR over 2 years

Termination early on the basis of little chance of finding differences in mGFR slopes, but a higher risk of serious adverse including cardiovascular events and hospitalization requiring infections events in IV iron
no difference in achieved hemoglobin levels

AJKD

A 12-Week, Double-Blind, Placebo-Controlled Trial of Ferric Citrate for the Treatment of Iron Deficiency Anemia and Reduction of Serum Phosphate in Patients With CKD Stages 3-5

N=149, eGFR<60 mL/min/1.73 m2, IDA without IV Iron OR ESA usage
Ph ;4-7 mg/dl

Ferric citrate(N=75) 1-g ferric citrate containing 210 mg of ferric iron.

Placebo(n=74)

12 Week

Short-term use of ferric citrate repletes **iron stores**, increases **hemoglobin** levels, and reduces levels of **serum phosphate, urinary phosphate excretion, and FGF-23** in patients with chronic kidney disease stages

Study	Type of patients enrolled	No. of people Enrolled	Duration of Ferric Citrate Treatment	Primary Endpoint(s)	Secondary Endpoints	Results
Phase 2	NDD*-CKD with elevated serum phosphorus and IDA**	149 at 20 sites	12-weeks	*Co-primary endpoints* Mean changes in serum phosphorus and transferrin saturation (TSAT) from baseline to the end of 12-week treatment period versus placebo	Mean changes in ferritin (iron), hemoglobin and FGF-23 from baseline to the end of the 12-week treatment period versus placebo	Met all primary and pre-specified secondary endpoints[1]
Phase 3[2]	NDD*, stage 3-5 CKD with IDA	234*** at 32 sites	16-weeks	Proportion of patients achieving a 1 g/dL or greater increase in hemoglobin at any point during the 16-week randomized period	From baseline to end of 16-week randomized efficacy period: - Mean change in hemoglobin (carries blood through the body) - Mean change in TSAT (bloods ability to bind iron) - Mean change in ferritin (stores iron until use) - Proportion of patients with a durable response on hgb (during 16-week efficacy period) - Mean change in serum phosphate	Met all primary and pre-specified secondary endpoints

*NDD is non-dialysis dependent, or pre-dialysis

** IDA or iron deficiency anemia is one of the most common complications of CKD. Approximately 1.6M adults in the U.S. with CKD suffer from IDA

***Patients enrolled had not adequately responded to or tolerated treatment with current oral iron supplements

[1] Results published December 2014 American Journal of Kidney Disease (Am J Kidney Dis. 2015;65(5):728-736)

[2] Keryx Phase 3 IDA study initiation announcement; September 2014; JPMorgan 2016 presentation deck, Phase 3 topline results release, March 2016

Effect of a Ferric Citrate Formulation, a Phosphate Binder, on Oxidative Stress in Chronic Kidney Diseases-Mineral and Bone Disorder Patients Receiving Hemodialysis: A Pilot Study

Fifteen patients (HD) were orally administered a ferric citrate formulation for 6 months:

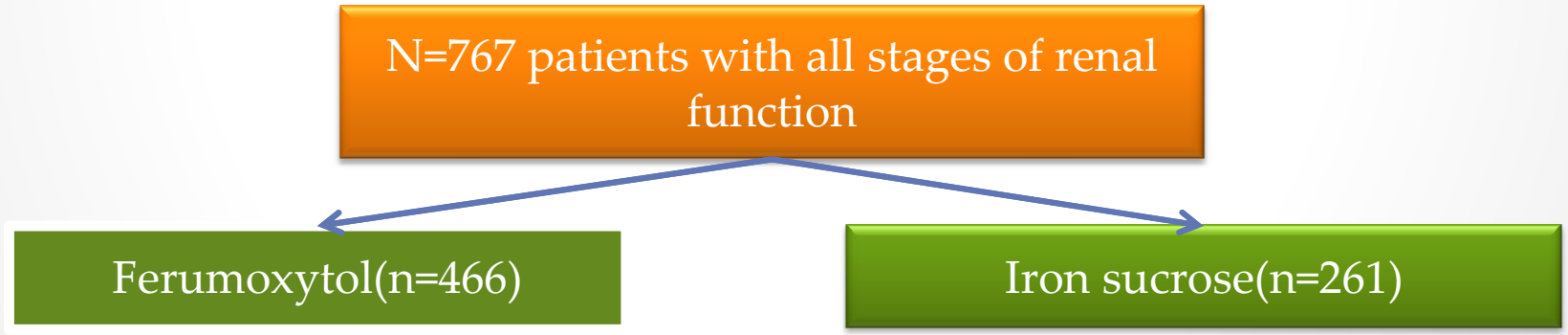
- Phosphorus unchanged (with switch from other phosphorus adsorbents to the ferric citrate)
- ↓Dose of ESA
- ↑ferritin (not exceed 100 ng/mL)
- **not increase oxidative stress** markers significantly, and **not significantly decreased anti-oxidative** capacity

Strauss et al. BMC Hematology (2016) 16:20
DOI 10.1186/s12878-016-0060-x

BMC Hematology

Ferumoxytol versus iron sucrose treatment: a post-hoc analysis of randomized controlled trials in patients with varying renal function and iron deficiency anemia

William E. Strauss*, Naomi V. Dahl, Zhu Li, Gloria Lau and Lee F. Allen



adverse events (hypotension, hypersensitivity)was numerically lower .The efficacy and safety of ferumoxytol is at least comparable to iron sucrose in patients with varying degrees of renal function.

IV or Oral?

KDIGO: a clearly defined benefit of IV iron therapy was not supported by evidence at this time.

The 2012 KDIGO guidelines have recommended that either oral iron therapy or intravenous iron therapy can be given in nondialysis patients

intravenous iron therapy.

1. not tolerate oral iron
2. After 1-2months of therapy,If the TSAT<30%, Hb not increase to the target level, and ferritin <500 ng/mL

- Oral iron is typically prescribed to provide approximately 200 mg of elemental iron daily

(for instance ferrous sulfate 325 mg three times daily; each pill provides 65 mg elemental iron).

200mg elemental=600 mg ferrous fumarate ,1.8g ferrous gluconate,1g ferrous sulfate

	Iron Dextran	Ferric gluconate	Iron sucrose (venofer)	Ferumoxytol	Ferric carboxymaltose(ferrinject)
Replacement theraphy TSAT<20% OR Ferritine <100	500-1000mg in 250 cc NS single infusion(1h)	250 mg once weekly for 3-4 dose	300-400mg once Weekly for 3-4 dose	510 mg initial dose ,3-8 day after first dose,secend dose base on weight and Hb	Doses base on weight
Maintenance: If TSAT<%30 و Ferritin<500	25-100mg /W 10 W	25-100mg /W 10 W	25-100mg /W 10 W	NA	200mg q3-12m
Test dose , saftey	Yes; 25mg once time significant risk of anaphylaxia	NO	NO	NO	NO

دوزFerrinjectبرمبنای وزن

وزن / Dose	<40kg	40-44kg	45-44kg	50-70kg	>70kg
دوز اول	500mg	800mg	900mg	1000mg	1000mg
دوز دوم	Not required	700mg	600mg	500mg	1000mg

Monitoring therapy

Markers of Iron Status in CKD Patients	
Test	**Recommended Range**
Serum ferritin	100–500 µg/L (CKD) 200–500 µg/L (HD)
Transferrin saturation	20%–40%
Hypochromic red cells	<10%
Reticulocyte hemoglobin content (CHr)	>29 pg/cell
Serum transferrin receptor	Not established
Erythrocyte zinc protoporphyrin	Not established

Figure 79.8 Markers of iron status and the recommended target ranges in chronic kidney disease (CKD).

Thanks for attention

- Parenteral:

	Iron Dextran	Ferric Gluconate	Iron Sucrose	Ferumoxytol
Replacement therapy %TSAT < 20% and ferritin < 100–200 mg/dL	IVP: 100 mg IV 3 times/week during HD for 10 doses (1 g) IVPB: 500–1000 mg in 250 mL of NSS infused for at least 1 hour (option for non-HD patients)	125 mg IV 3 times/ week during HD for 8 doses (1 g)	100 mg IV 3 times/ week during HD for 10 doses (1 g) For nondialysis CKD, 200 mg IV × 5 doses	510 mg at up to 30 mg/second followed by a second 510 mg IV 3–8 days later (all CKD)
Maintenance therapy (iron stores in goal)	25–100 mg/week IV × 10 weeks	31.25–125 mg/ week IV × 10 weeks	25–100 mg/week IV × 10 weeks	N/A
Iron overload %TSAT > 50% and/ or ferritin > 500	Hold therapy	Hold therapy	Hold therapy	Hold therapy
Initial test dose	Yes; 25-mg one-time test dose	No	No	No

CKD = chronic kidney disease; HD = hemodialysis; IV = intravenous; IVP = IV push; IVPB = IV piggyback; N/A = not applicable; NSS = normal saline solution; TSAT = transferrin saturation.

- Oral: 200mg elemental iron per day **(= 600 mg Ferrous fumarate,1.8g ferrus gluconate or 1gm ferrous sulphate).**

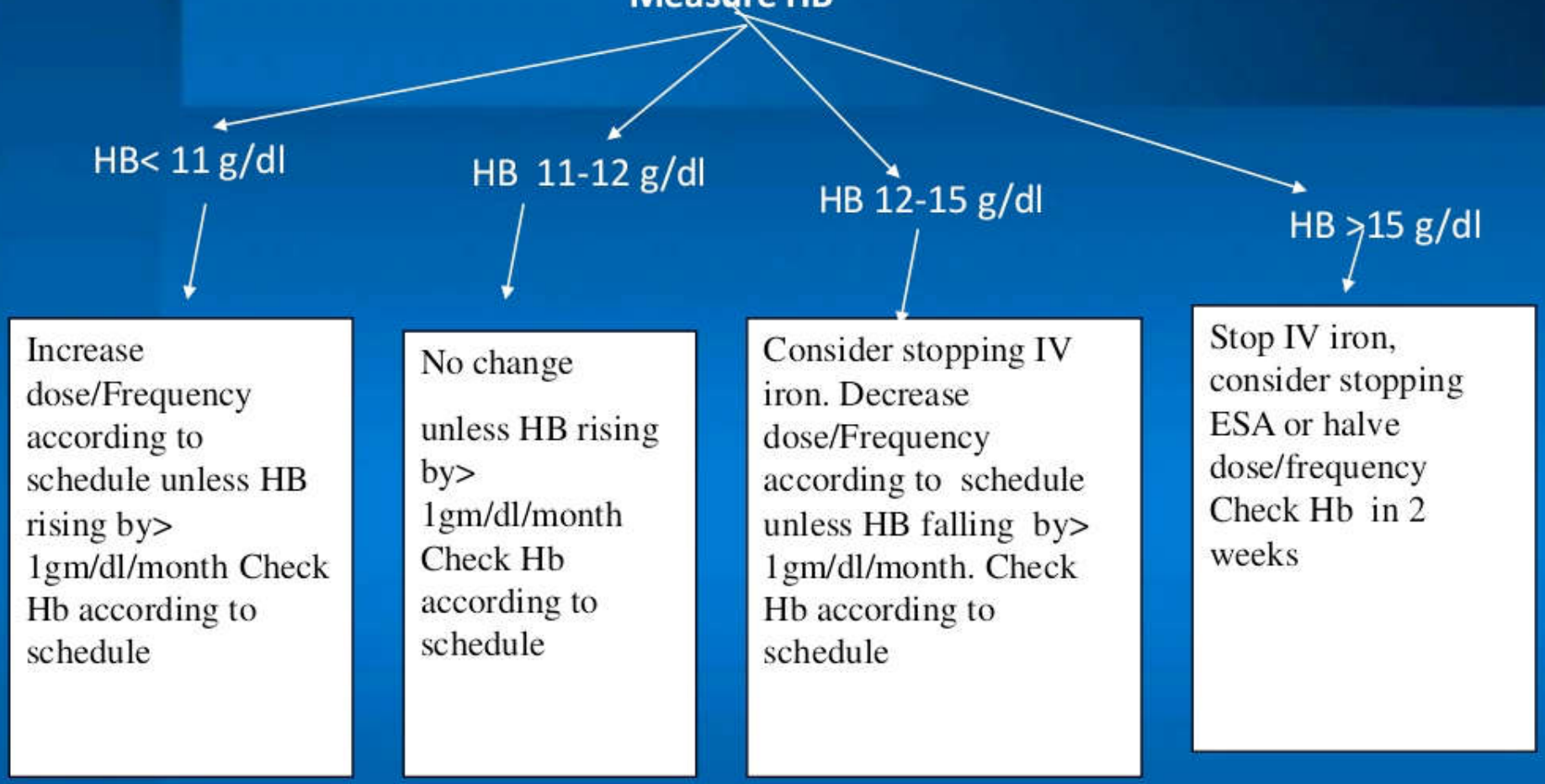
600 mg ferrous fumarate ,1.8g ferrus gluconate,1g ferrous sulfate

Absolute iron deficiency should be treated, except in patients who become polycythaemic when iron replete. Functional iron deficiency in non-HD patients who are not on ESAs should be treated only the Hb is less than 11g/dl.

CKD 4/5 patients on ESAs or with an Hb<11g/dl should be given iron supplements to keep their:

- Serum ferritin between 200 and 500 mcg/l in HD patients
- Serum ferritin between 100 and 500 mcg/l in non-HD patients
- The TSAT level above 20%

Iron supplements should be discontinued when the ferritin is greater than 800 mcg/l irrespective of the TSAT.


Measure HB
HB< 11 g/dl
HB 11-12 g/dl
HB 12-15 g/dl
HB >15 g/dl
Increase dose/Frequency according to schedule unless HB rising by> 1gm/dl/month Check Hb according to schedule
No change
unless HB rising by> 1gm/dl/month Check Hb according to schedule
Consider stopping IV iron. Decrease dose/Frequency according to schedule unless HB falling by> 1gm/dl/month. Check Hb according to schedule
Stop IV iron, consider stopping ESA or halve dose/frequency Check Hb in 2 weeks

Non-HD patients

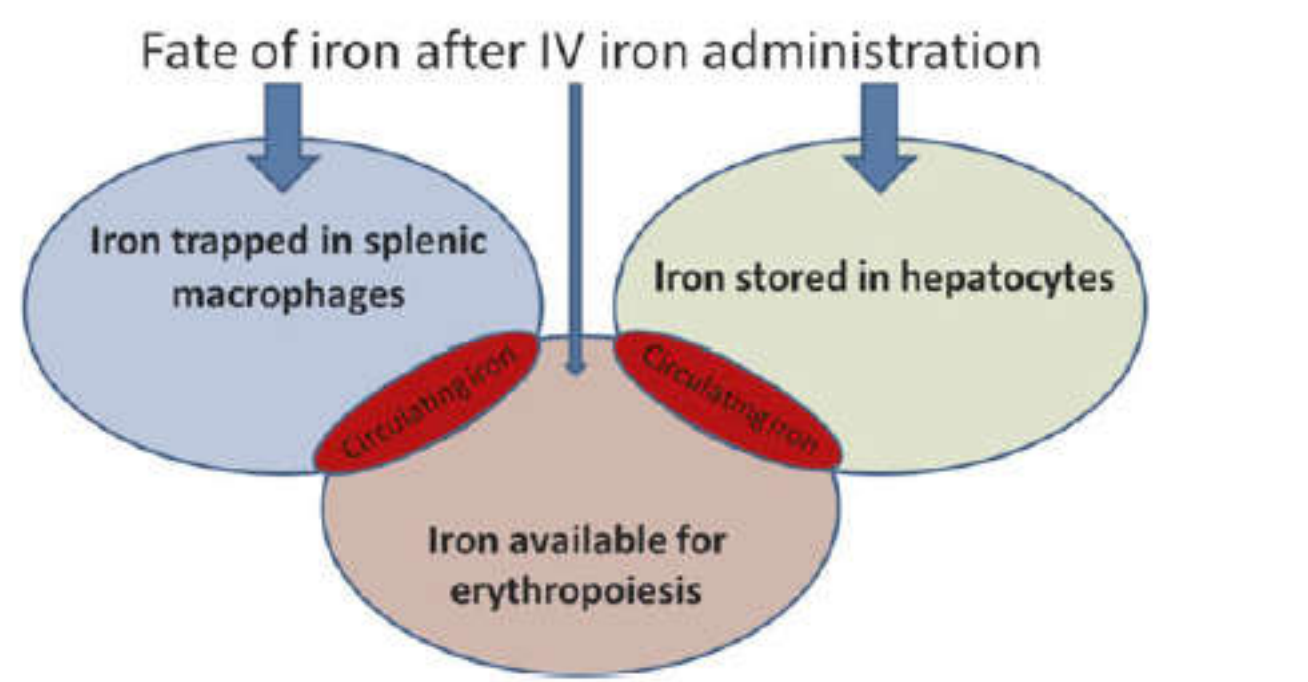
Iron sucrose is given intermittently in cycles of 3-5 doses as required to maintain the targets specified, (monitored at least 3 monthly). A single dose of iron sucrose may be given to patients with a serum ferritin <500 in the absence of a TSAT measurement but the TSAT must be measured prior to subsequent doses.

Ferritin	TSAT	Iron sucrose regime
<100	ANY	5 doses 200mg over 6-10 weeks
100-500	<20%	3 doses 200mg over 3-6 weeks
100-500	>20%	Withhold
501-800	<20%	3 doses 200mg over 3-6 weeks
501-800	>20%	Withhold
>800	Any	Withhold

Recently the Ferinject is used for Non HD patients in the following method

Ferritin	TSAT	Ferinject® (ferric Carboxymaltose)	Amount of sterile 0.9% sodium chloride for dilution	Administration Time 15min infusion 200mls per hour
<100	ANY	1000mg** (in 20mls)	30mls	**15 minutes**
100-500	<20%	1000mg (in 20mls)	30mls	**15 minutes**
100-500	>20%	500mgs (in 10mls)	40mls	**15 minutes**
501-800	<20%	500mg (in 10mls)	40mls	**15 minutes**
501-800	>20%	Withhold	Withhold	
>800	Any	Withhold	Withhold	

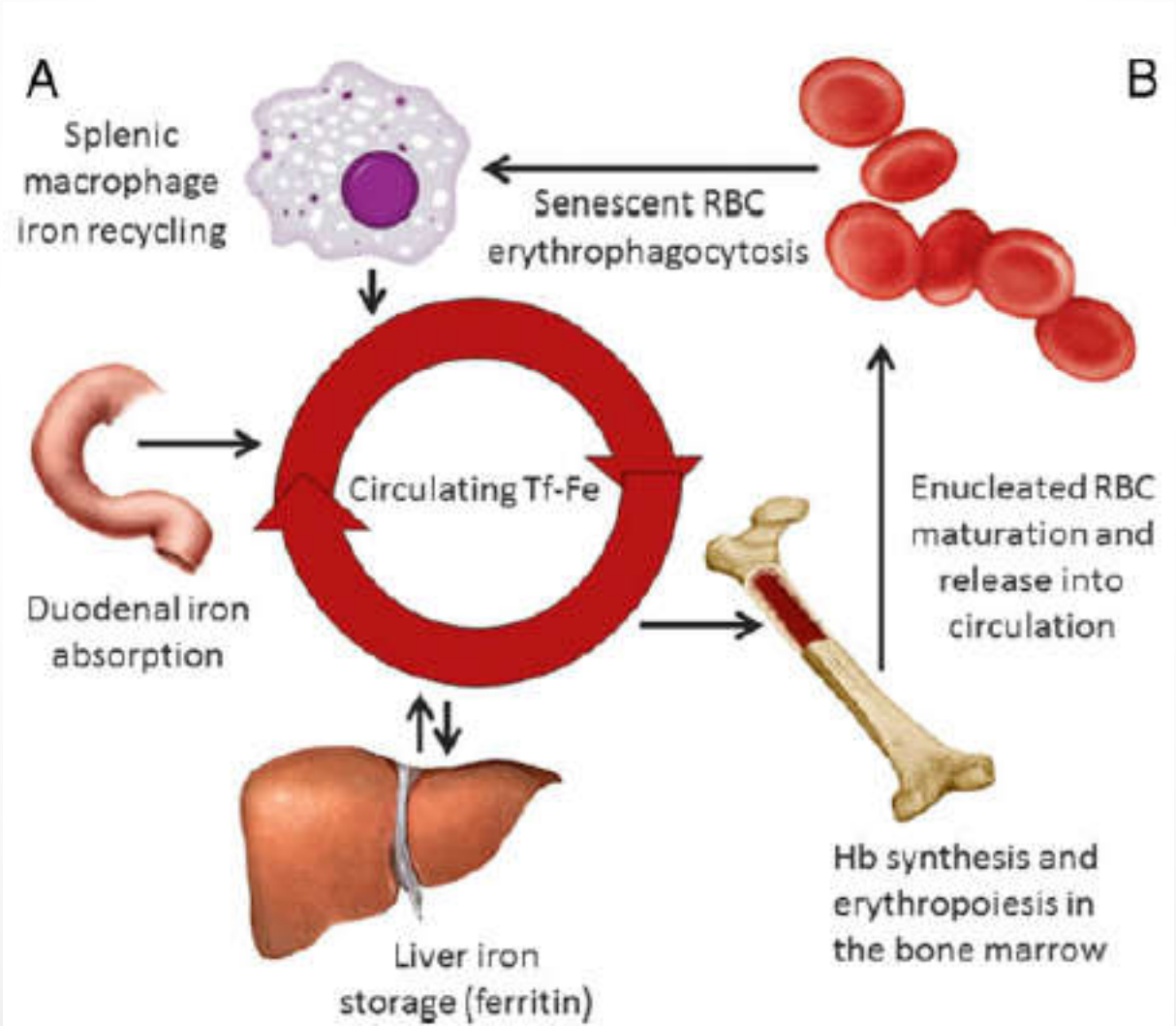
administered to patients is unavailable for erythropoiesis.



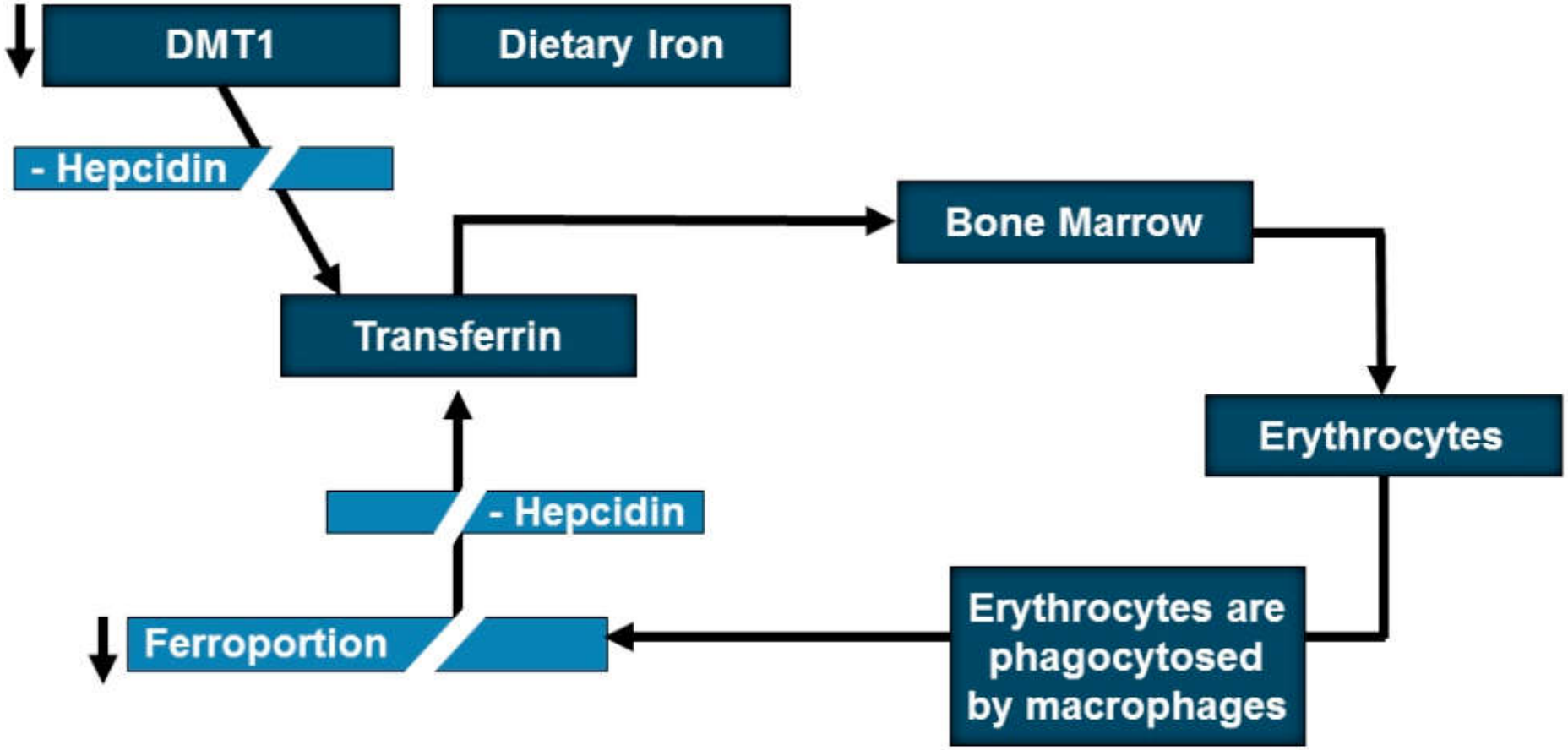
Schedule for the tests

- A FBC and iron studies to be measured at least 3 monthly for all CKD 4/5 patients.
- In practice, this will be at every clinic visit for non-HD patients.
- Hospital HD patients are tested monthly by default.
- Ferritin and iron profile measurements should be at least one week after the last dose of IV iron sucrose.
- All testing should be pre-HD.
- After initiation of ESA, monthly FBC monitoring is required until a stable Hb 11-12g/dl is achieved.
- Thereafter three-monthly monitoring is acceptable for non-HD patients.

Interaction between iron homeostatic and erythropoietic systems



Iron Cycle



DMT = divalent metal transport

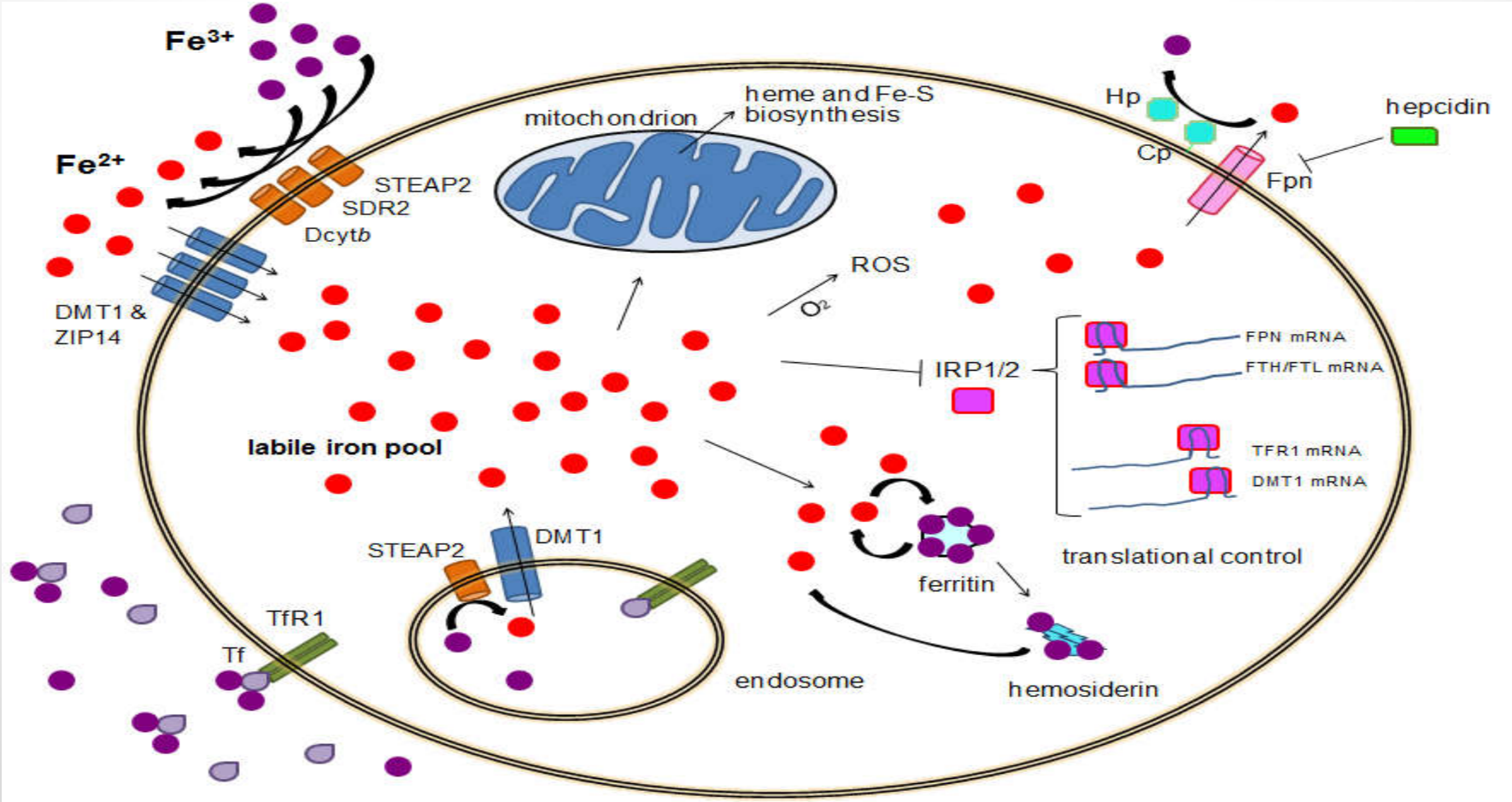
Hörl WH. *J Am Soc Nephrol*. 2007;18:382-393.

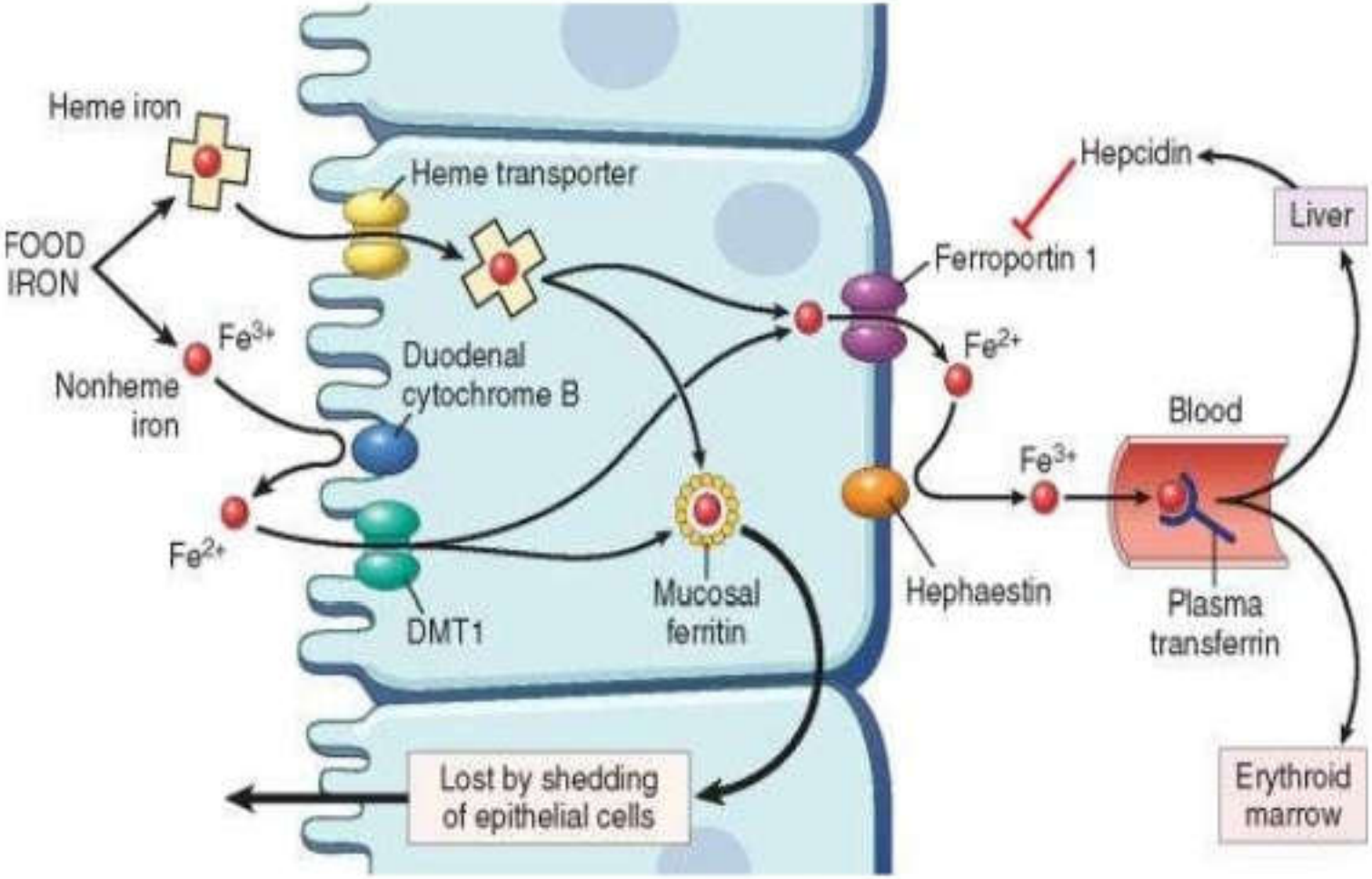
Anaemia of chronic disease
Diagnosis

Laboratory Measure	Anaemia of Chronic Disease	Iron-Deficiency Anaemia
Plasma iron concentration	**Reduced** to normal	Reduced
Plasma transferrin concentration	**Reduced** to normal	Increased
Transferrin saturation	**Reduced** to normal	Reduced
Plasma ferritin	Normal to **increased**	Reduced
Plasma Transferrin Receptor	Normal	Increased
Transferrin receptor/log ferritin	Low (<1)*	high (>4)

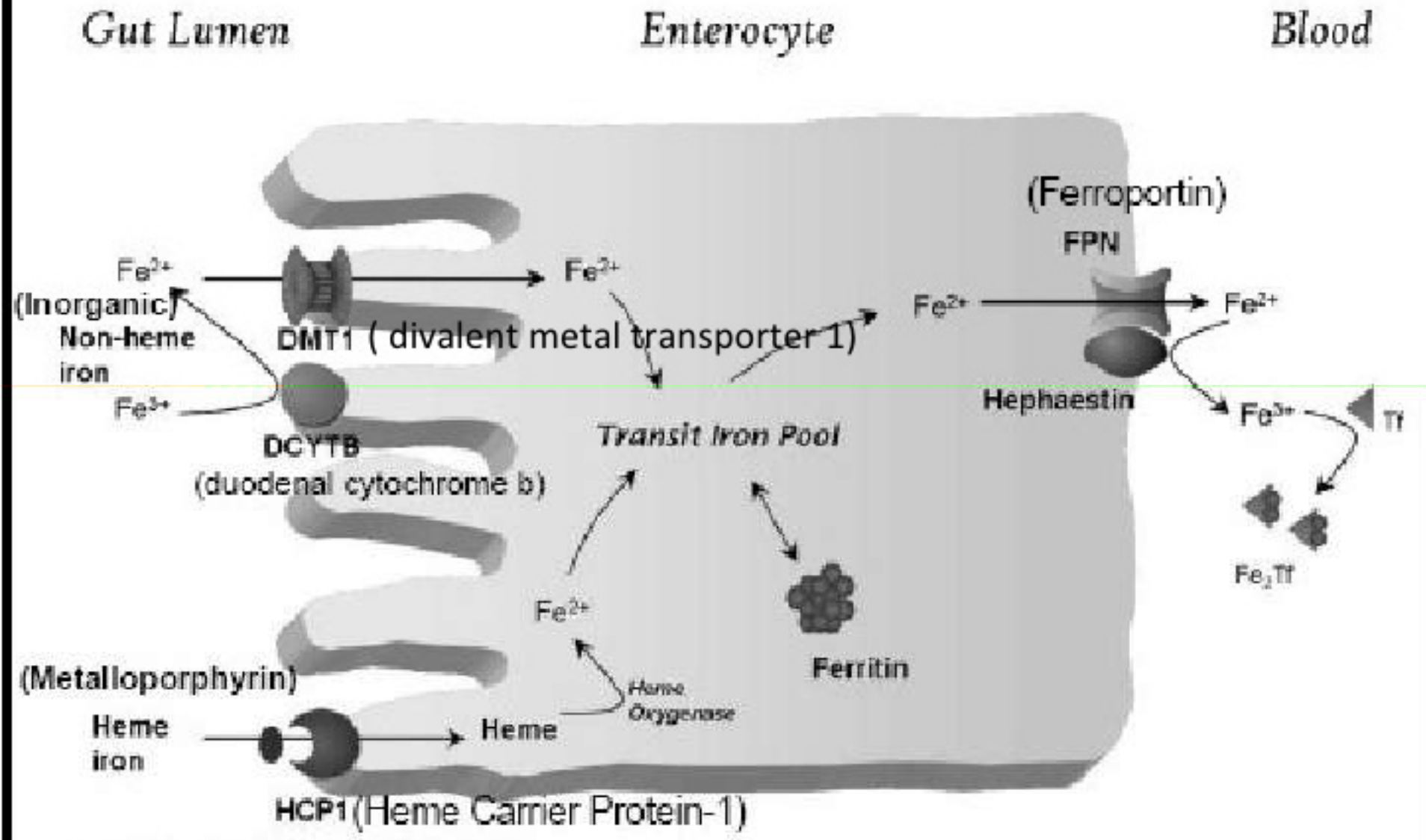
ransferrin receptor protein 1 (TfR1)

- TfR1 is required for iron import from transferrin into cells by endocytosis





DUODENAL EPITHELIAL CELL UPTAKE OF HEME AND NONHEME IRON.

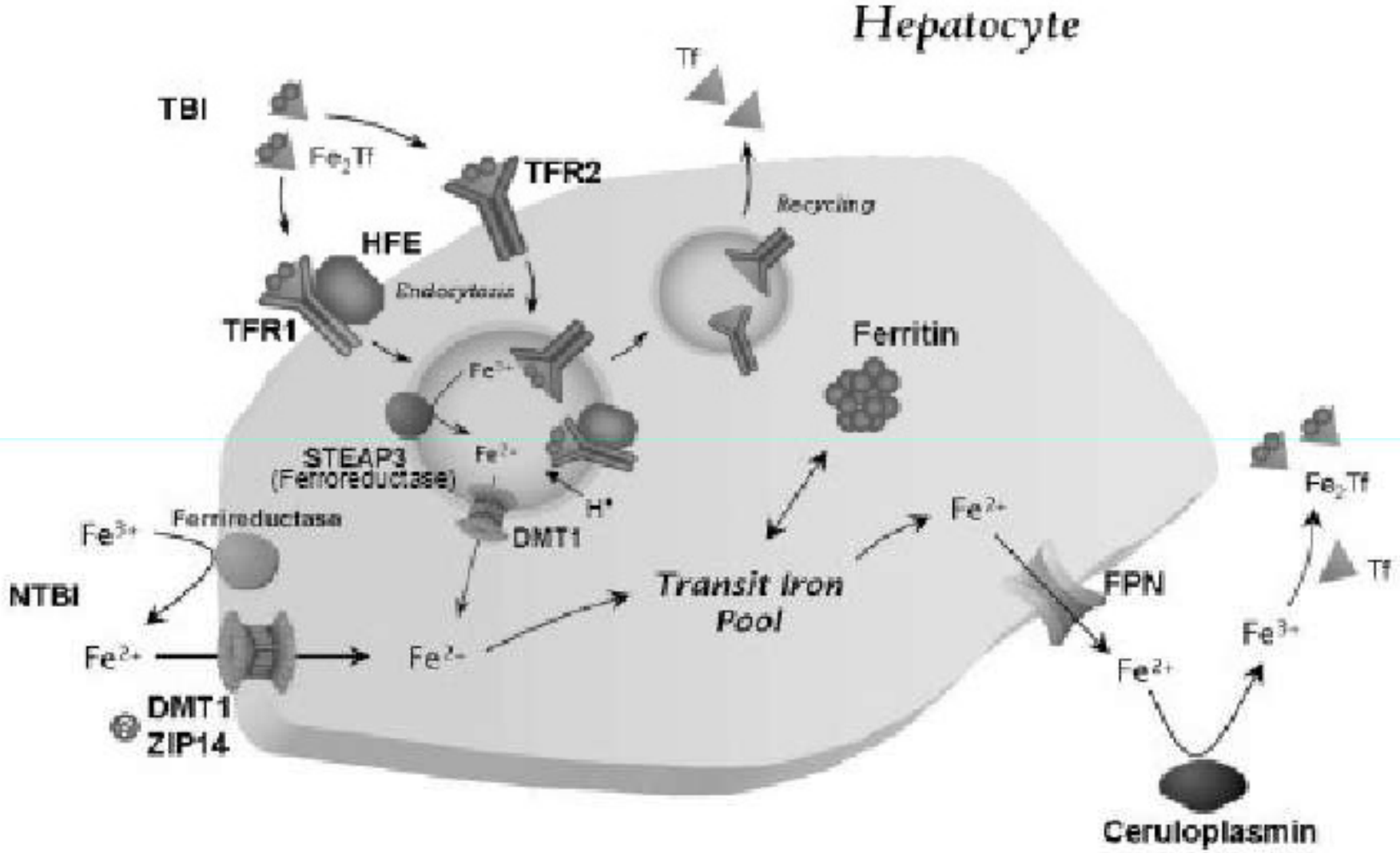


Crit Rev Clin Lab Sci 2007, 44(5-6):413-459

Iron exists in 2 forms:

- Inorganic/non-heme iron (90%) Fe^{3+} (less soluble)
- Organic/heme iron (10%) Fe^{2+} (more soluble)

- To be soluble, Ferric (Fe^{3+}) needs to be reduced to Ferrous (Fe^{2+}).
- The enzyme that does this is called **Duodenal cytochrome b** (Dcytb)
- This enzyme is **Vitamin C dependent**.



Crit Rev Clin Lab Sci 2007, 44(5-6):413-459

Hepcidin

- Hepatic Bactericidal Protein.
- Negative regulator of iron metabolism.

Actions:

- It inhibits intestinal transport.
- Blocks Fe transport across placenta.
- Induces Fe sequestration in macrophages.

- If **low iron stores** = hepcidin expression **reduced**.

- If **high iron stores** = hepcidin expression **increased.**

- **Molecular target** of Hepcidin is **Ferroportin.**

Serum soluble transferrin receptor

High transferrin receptor= high Erythroid mass.

Causes for **low transferrin receptor**: erythroid **hypo**plasia.

- Aplastic anemia
- CRF

Causes for **raised transferrin receptor**: erythroid hyperplasia.

- Chronic hemolysis
- Thalassemia
- Iron deficiency (absence of erythroid hyperplasia)

- **Not elevated** in anemia of chronic disease.

Hepcidin **decreased** in:

- Hypoxia
- Anemia
- Iron deficiency.

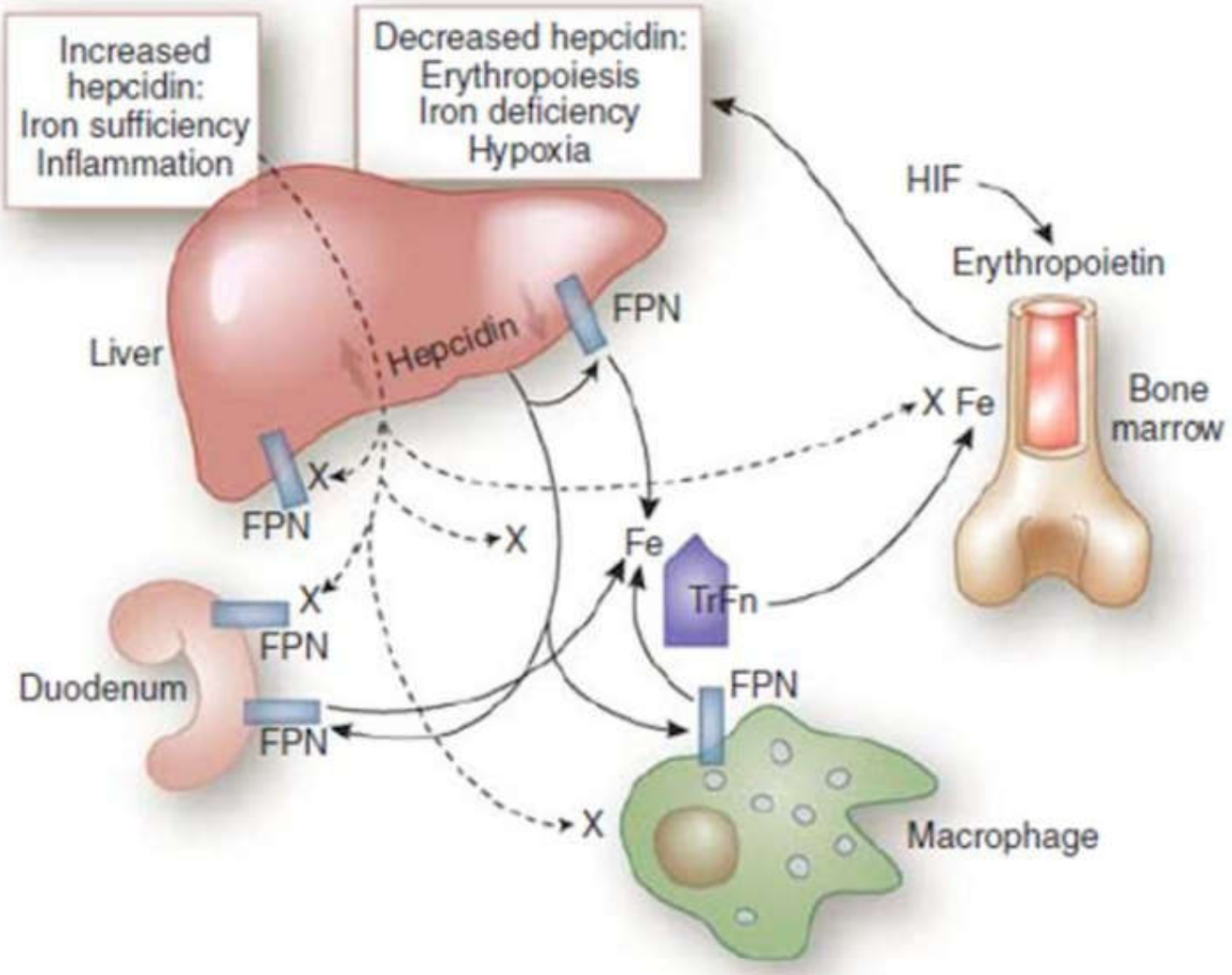
Hepcidin **increased** in: Inflammation

leading to:

- low transferrin Sat (low iron saturation)
- increased ferritin (storage of iron)
- anemia.

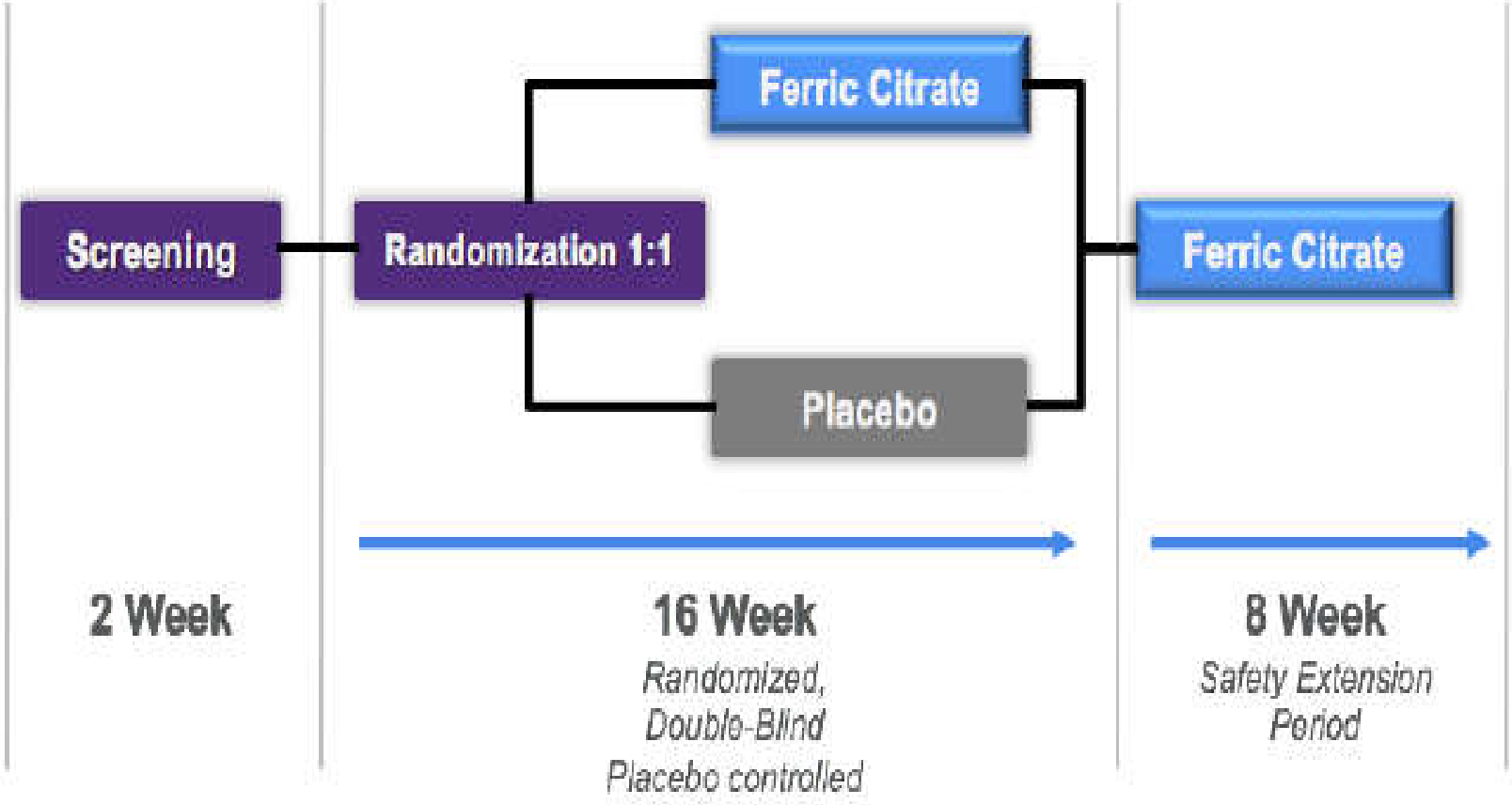
Inappropriately decreased in chronic hemolytic anemia and thalassemias.

Iron and Hepcidin



From Coyne DW. Hepcidin: clinical utility as a diagnostic tool and therapeutic target. *Kidney Int.* 2011;80:240-244. Republished with permission.

- In ESRD patients treated with a combination of ESAs and IV iron, a signifi cant portion of the IV iron dose administered deposits in organs [102]. Furthermore, because a high dose of IV iron is given rapidly, the binding capacity of transferrin is easily exceeded, resulting in the generation of NTBI and labile plasma iron [94]. Because only transferrin-bound iron can deliver iron for erythropoiesis, most of IV iron may be unavailable for erythropoiesis and may be directly shuttled to iron stores in parenchymal cells where it accumulates and is expected to cause cellular injury (Figure 3)



Ferric citrate is approved in the U.S. and indicated for the treatment of elevated serum phosphorus levels in patients with chronic kidney disease on dialysis and
marketed under the brand name, Auryxia™

- The overall incidence of adverse events was numerically lower in ferumoxytol-treated patients compared to those treated with iron sucrose (42.4 vs. 50.2 %, respectively); the incidence of treatment-related adverse events was generally similar between the two treatment groups (13.6 vs. 16.0 %, respectively). Adverse events of Special Interest (i.e., hypotension, hypersensitivity) occurred at lower rates in those treated with ferumoxytol compared to those treated with iron sucrose (2.5 vs. 5.3 %, respectively). Overall, mean hemoglobin increased in both treatment groups, regardless of degree of renal insufficiency, although greater increases were seen among those with less severe kidney damage. Mean increases in hemoglobin from Baseline to Week 5 were significantly greater with ferumoxytol than with iron sucrose treatment in the subgroup with an estimated glomerular filtration rate ≥ 90 mL/min (Least Squares mean difference = 0.53 g/dL; $p < 0.001$). There were no other consistent, significant differences in hemoglobin levels between treatment groups for the other chronic kidney disease categories except for isolated instances favoring ferumoxytol. Conclusions: The efficacy and safety of ferumoxytol is at least comparable to iron sucrose in patients with varying degrees of renal function.

Auryxia™ (ferric citrate)

- Patients with Gastrointestinal Bleeding or Inflammation: Safety has not been established for these patients.
- Adverse Events: The most common adverse events with Auryxia were diarrhea (21%), nausea (11%), constipation (8%), vomiting (7%) and cough
- (6%). Gastrointestinal adverse reactions were the most common reason for discontinuing Auryxia (14%). Auryxia contains iron and may cause dark stools, which
- is considered normal with oral medications containing iron.
- Drug Interactions: Doxycycline should be taken at least 1 hour before Auryxia. Ciprofloxacin shouldbe taken at least 2 hourshours before or after Auryxia

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Changes in Echocardiographic Parameters in Iron Deficiency Patients with Heart Failure and Chronic Kidney Disease Treated with Intravenous Iron

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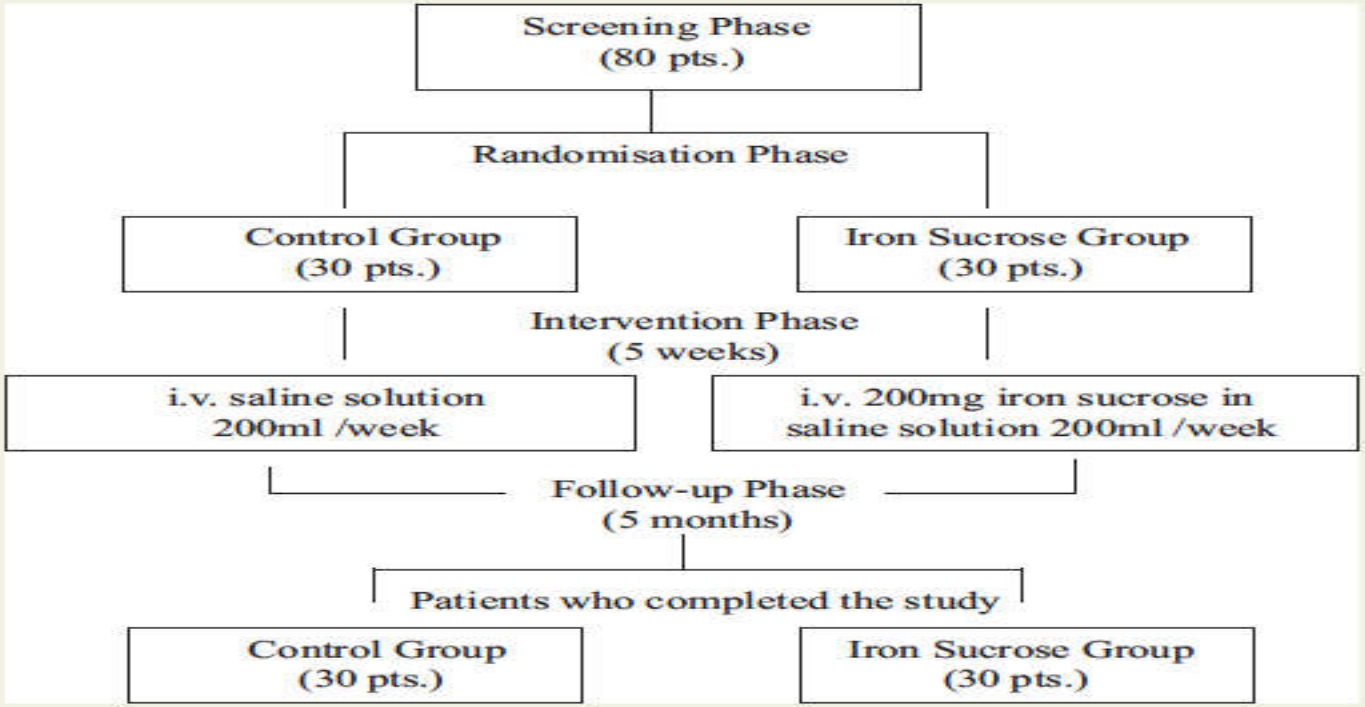

At six months after treatment initiation, intravenous iron was associated with reduced severity of th symptoms of chronic heart failure and improved renal function (both $p<0.001$ versus control). Also, ferriti and transferrin saturation levels were increased, as were haemoglobin levels, whereas inflammatory markers were reduced (all $p<0.001$ versus control). Left ventricular systolic and diastolic diameters wer increased and improved left ventricular function correlated with iron status in patients receiving intravenou iron but not patients in the control group.

Conclusions Intravenous iron treatment was associated with improved myocardial functional parameters and cardia dimensions in patients with anaemia and chronic kidney disease.