Iron metabolism

And

Anemia in chronic kidney disease

Chittima Sirijerachai
Iron distribution

Intracellular iron

- Intracellular ferrous iron
  - Heme iron compound: Hb, myoglobin
  - Iron containing enzyme

- Intracellular ferric iron
  - RE cell, heart, epithelial cell of small intestine

Extracellular iron

- Ferric-transferrin
Dietary iron 1-2 mg/day

Liver 1000 mg

Plasma transferrin 3 mg

Slough mucosal cell 1-2 mg/day

Spleen 600 mg

Myoglobin 300 mg

Bone marrow 300 mg

Erythrocyte 1800 mg
Iron absorption

Promote absorption
- Fructose
- Vitamin C
- Heme iron
- Amino acid

Inhibit absorption
- Phosphate
- Phytate
- Tannin
- Soil clay

Fe^{++} \rightarrow Fe^{++} \text{ ferritin} \rightarrow Fe^{+++} - \text{ transferrin}
Iron absorption

Apical surface

Fe$^{3+}$ → Fe$^{2+}$

Ferric reductase → DMT1

Ferritin

Basolateral transporter

Fe$^{2+}$ → Fe$^{3+}$

Hephaestin
Regulation of iron absorption

- Dietary iron – mucosal block
- Iron stores – store regulator
- Erythropoietic regulator
Iron utilization
Dietary iron
1-2 mg/day

Liver
1000 mg

Spleen
600 mg

Plasma transferrin
3 mg

Sl
1-2 mg/day

Myoglobin
300 mg

Bone marrow
300 mg

Erythrocyte
1800 mg

Iron deficiency anemia

utilization

utilization

utilization

utilization

utilization

utilization

utilization

utilization
Anemia of chronic disease

Liver

Liver

hepcidin

hepcidin

Plasma

Fe-Tf

rbc

Bone marrow

spleen

inflammation
Iron study

- Serum iron
- Total iron binding capacity (TIBC)
- Transferrin saturation (Tf sat)
- Ferritin
Iron depletion

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Functional</th>
<th>Absolute</th>
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<tbody>
<tr>
<td>Erythrocyte</td>
<td>Normal</td>
<td>Functional</td>
<td>Absolute</td>
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<tr>
<td>Iron stores</td>
<td>Normal</td>
<td>Functional</td>
<td>Absolute</td>
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<tr>
<td>Serum ferritin (ng/ml)</td>
<td>&gt; 100</td>
<td>&gt; 100</td>
<td>&lt; 100</td>
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<tr>
<td>Tf sat %</td>
<td>&gt; 20</td>
<td>&lt; 20</td>
<td>&lt; 20</td>
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</table>
erythropoietin

Decreased production

- iron
- protein
- etc

Blood loss

Increased destruction
Causes of anemia in ESRD

- Decrease erythropoietin
- Iron deficiency
- Nutritional deficiency
- Decrease red cell survival
- Bone marrow suppression by uremia
- Osteitis fibrosa cystica
- Inflammation
- Aluminum toxicity
Work-up for a diagnosis of anemia in CKD

Hb

Adult male < 13.5 g/dl

Adult female < 12.5 g/dl
Diagnosis of renal anemia

- Significant impairment of renal function
  \[ \text{GFR} < 30 \text{ cc/min}, \ Cr > 2 \text{ mg/dl} \]
- No other causes of anemia
  - Iron deficiency anemia
  - Nutritional deficiency anemia
Diagnosis of renal anemia

History taking
- Dietary intake
- Chronic blood loss

Physical examination
Investigation

- CBC
- Red cell indices
- Iron study, ferritin
CBC and RBC indices

<table>
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<tr>
<th>CBC</th>
<th>RBC Indices</th>
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<tr>
<td>WBC</td>
<td>6.8 %</td>
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<tr>
<td></td>
<td>#</td>
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<tr>
<td>NE</td>
<td>52.6 %</td>
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<tr>
<td>LY</td>
<td>36.7 %</td>
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<tr>
<td>MO</td>
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<td>EO</td>
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<td>BA</td>
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<td>RDW</td>
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<td>PLT</td>
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<tr>
<td>MPV</td>
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80-96 fl.
27-33 pg.
33-36 g/dl
12.0-13.6%
Iron study, ferritin

TSAT $< 20\%$

Ferritin $< 100\ ng/ml$

Iron deficiency anemia
Treatment of renal anemia
Benefit of anemia control in ESRD

- Increased survival
- Decreased cardiac complication
- Improved quality of life
- Increased exercise capacity
- Decreased hospitalization
Target for anemia treatment

Hb > 11 g/dl  Hct > 33 %

Within 4 months

Ferritin 200-500 ng/ml

TSAT 30-40 %
Treatment of renal anemia

- Erythropoietin
- Iron therapy
- Adequate dialysis
- Nutritional support
Iron therapy

Improved response to EPO

Reduced dose of EPO
Iron therapy

Oral iron vs IV iron

Iron sucrose (venofer)
Iron therapy

- Ferrous sulfate 1 x 3

- Iron sucrose 25-150 mg/wk

Monitor:- serum ferritin, TSAT q 1-3 months
Iron therapy in CKD

**Serum ferritin**
- < 100 ng/ml - iron deficiency
- > 800 ng/ml - stop iron Rx

**Transferrin saturation**
- < 20 % - iron deficiency
- > 50 % - stop iron Rx
Side effects of iron therapy

**Oral iron**
- GI irritation
- Diarrhea
- Constipation

**IV iron**
- anaphylactoid
- hypotension
- muscle cramp
Erythropoietin

Erythropoietin $\alpha$

Erythropoietin $\beta$

Eprex
Eporon
Epokrine

Recormon
Erythropoietin

80-120 U/kg/wk SC

120-180 U/kg/wk IV

↑ Hb 1-2 g/dl/month
Erythropoietin

Side effects

- hypertension
- headache
- PRCA
- Thrombosis
Inadequate erythropoietin response

Patient fail to attain the target Hb while receiving:

- EPO 300 U/kg/wk SC
- EPO 450 U/kg/wk IV

4-6 months
Inadequate erythropoietin response

- Iron deficiency anemia
- Chronic blood loss
- Chronic inflammation
- Inadequate dialysis
- Hyperparathyroidism