Iron Supplementation For Athletes

Heather Hynes, MSc, RD

Adapted presentation from: Nicole Springle, MAN, RD, Sport dietitian, Nutrition Lead-CSI Ontario

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Outline

- Iron overview
- Assessment
- Indications for Supplementation
  - Cut off values??
- Iron Supplements Protocols
- Recommendations and Best Practices

Iron: Physiological Function

- Iron is an essential element with many important roles in the body:
  - Transporting oxygen in the blood and in the muscles
  - Involved in the electron transport system
  - Required for red blood cell production
  - Required for a healthy immune system
- Functional component of hemoglobin and myoglobin
- **Inadequate iron can impair aerobic metabolism and hinder training adaptations**
- Adequate iron stores are a necessity for haematological adaptation to hypoxia (Berglund 1992)

Suedekum and Dimeff 2005

Iron Pathway: Absorption to Storage

A quick review…

- Iron is absorbed in the intestine (duodenum) - then bound to transferrin (maintains iron as soluble and non-toxic) and carried through the blood stream
- Released into cells via 2 specific cell surface receptors
  - Transferrin receptor 1 (RBC, hepatocytes, monocytes)
  - Transferrin receptor 2 (liver)
- Once inside cell iron is incorporated into iron-containing proteins with excess intracellular iron converted to ferritin

Iron Deficiency and the Athlete

- Anemia is most commonly due to iron deficiency

Risk factors for athletes include:

- Poor nutritional intake/dietary choices
- Hemolysis caused by repeated foot strikes
- Blood & iron losses through menstruation
- Urinary tract losses (hematuria)
- GI bleeds via increased usage of NSAIDS
- Fe losses via sweating
- Helicobactor Pylori (H. Pylori)- infection cause of iron deficiency
- "sport anemia"
- Altered intestinal absorption- inflammation from training

Poor Nutritional Intake:

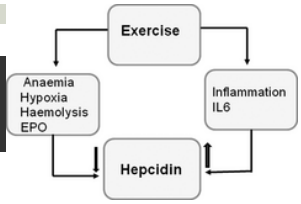
- Many factors at play….
  - Overall poor intake of heme iron sources (take a look at food sources and portions needed)
  - Increased consumption of dietary factors that inhibit iron absorption (phosphates, phytates, calcium, tannins, vit/min supplements with high calcium load)
    - Links with decreased Fe absorption with high dairy intake
    - Supplements that contain calcium inhibit absorption of Fe by 40% and all other divalent metals are in competition (Zn, Cu, Mg)
  - Low intake of dietary sources that enhance absorption (vitamin C, meat products, copper sources)

(Makrides et al., 2003 & Malczewska et al., 2000)

Iron Deficiency and the Athlete

- Mechanism is typically related to mismatch where there are **enhanced losses and inadequate dietary intake** leading to reduction in iron stores
  - Increased physical activity may increase the demand for iron (Malczewska et al., 2000)
  - Increased need during periods of growth
  - Increased workload (especially in initial training phases)= increased muscle mass and increased blood volume = increased demand for oxygen
  - Physical exercise **may IMPAIR iron absorption** and **increase iron losses**

Inflammation



- Roecker et al. (2005) discovered a new iron-regulatory hormone called hepcidin that may have an impact on iron metabolism at the conclusion of exercise
- Hepcidin has been shown to degrade iron channels responsible for absorption of iron from the gut
- **Increased hepcidin = reduction in serum iron (it puts the body in iron lockdown- Jeannie Callum, BA, MD, 2015 presentation at CSI Ontario)**
- Infection and inflammation cause upregulation of hepcidin via IL-6 leading to decreased absorption and eventually anemia
- Research has found that hepcidin response is less pronounced in females with ferritin levels <35ug/L (Peeling et al. 2006)

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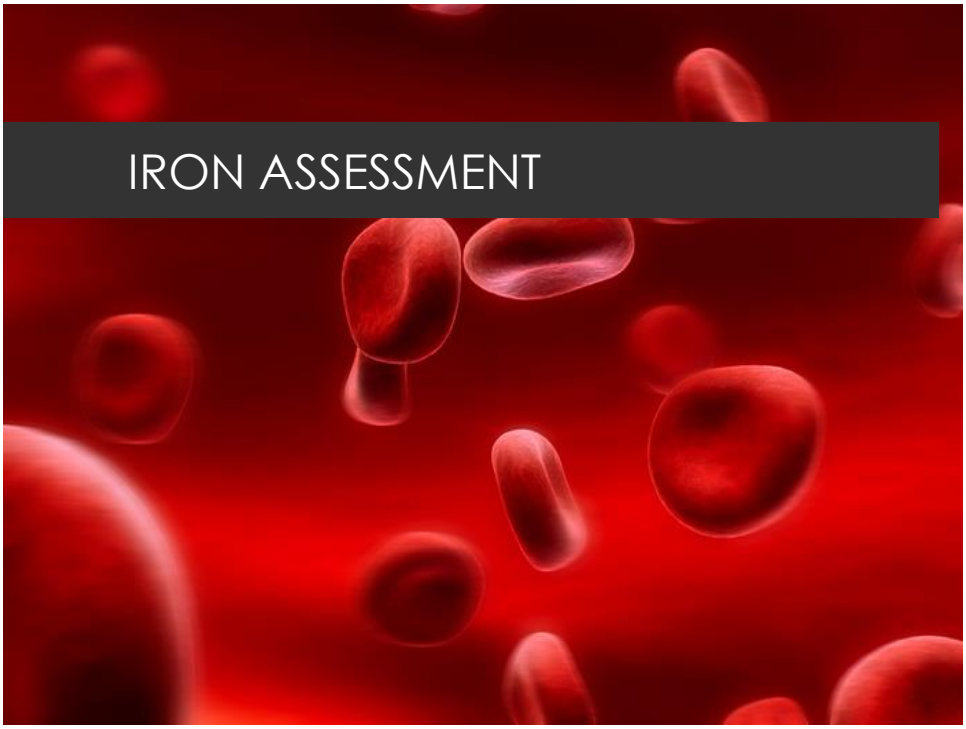
Inflammation

- IL-6 mediated hepcidin up-regulation may affect the absorption of iron from post-exercise feedings
- Endurance exercise has been shown to evoke an acute phase response that increases IL-6 and urinary hepcidin (Newlin et al. 2012, Peeling et al. 2009)
- Longer exercise durations result in greater increases in hepcidin (Newlin et al. 2012, Roecker et al. 2005)
- **Thus, exercise-induced, inflammatory up-regulation of hepcidin activity might potentially be a new mechanism for iron deficiency in athletes**
- Note: appears to be responders and non-responders to hepcidin
  - Maintenance of an elevated concentration of IL-6 may contribute to the higher hepcidin concentrations in the responders group (Newlin et al. 2012)



Screening

- IOC Consensus Statement on Periodic Health Evaluation of Elite Athletes recommends routine hematological screening during the Periodic Health Evaluation (PHE) for anemia and decreased iron stores (IOC 2009)
- ACSM – no specific recommendations on iron deficiency and anemia screening in Pre-Participation Physical Exam (PPE) form
- CASEM – no position statement on iron deficiency and anemia screening in athletes (only statement to ensure 'appropriate' serum ferritin prior to altitude camps/competitions)

Are you screening your athletes?

Iron Status

- Most common assessment for iron status - measuring serum ferritin
- Currently available testing:
  - Complete blood count
  - Serum ferritin level
  - Serum iron level
  - Serum transferrin level
  - Total iron binding capacity
  - Percent transferrin saturation
  - Soluble transferrin receptor concentration

Interpretation of Serum Ferritin

Serum Ferritin (ug/L)	Interpretation
<15 (<12 kids)	Diagnostic of iron deficiency
15-50	Depletion of stored iron, probable iron deficiency
51-100*	Reduced iron stores, possible iron deficiency
101-300	Iron deficiency unlikely (in the absence of inflammation)
>300	May reflect inflammation or iron overload
>800	Probable iron overload (in the absence of inflammation)

***Inflammation is common and in its presence ferritin may be elevated** and give seemingly normal results, even in the presence of iron deficiency. Therefore, a serum ferritin result within the normal range for the patient's age but less than 100 ug/L , does not exclude depleted or reduced iron stores

BC Medical Association, 2015

Interpretation of Serum Ferritin

- Ferritin is an Acute-phase reactant…nonspecifically elevated in a wide variety of inflammatory states including infection, malignancy, and autoimmune diseases
- Increased immediately after exercise
- Increase mainly due to hemoconcentration, cell destruction and inflammatory-like reactions post-exercise
- Type and duration of exercise is not related to extent of ferritin increase

Suedekum and Dimeff 2005

Indications for Supplementation

Iron Deficiency Classification

- In research studies on iron deficiency in athletes, the cutoff has varied from Serum Ferritin (SF)< 12-40 ug/L
- IOC consensus statement (2012) for altitude training/competition- SF >30 ug/L for females and >40 ug/L for males
- Peeling et al. (2007) suggested that iron deficiency can be classified into 3 stages of severity:
  - **Stage 1 – Iron depletion**
    - SF<35 ug/L, Hemoglobin (Hb)>115 g/L, transferrin saturation (Sat) > 16%
  - **Stage 2 – Iron deficient erythropoiesis**
    - SF<20 ug/L, Hb>115 g/L, Sat<16%
  - **Stage 3 – Iron deficient anemia (IDA)**
    - SF<12 ug/L, Hb<115 g/L, Sat<16%

Iron Deficiency without anemia (IDNA)

- IDNA affects approximately 30% of active females
- IDNA is 5–7 times more prevalent than iron deficiency with anemia
- Individuals with IDNA (SF< 20.0 ug/L, Hb > 120 g/L) are expected to have adequate O2-carrying Hb but impaired O_2 utilization

DellaValle and Haas 2011

IDNA and Athletic Performance

- Untrained women
  - IDNA has been shown to compromise aerobic performance and hinder adaptations to training (Brownlie, Utermohlen, Hinton, Giordano, & Haas, 2002; Jensen et al., 1992)
  - IDNA impaired 15-km cycling time-trial performance in nonathletic women (Hinton et al., 2000; Zhu & Haas, 1998)
- **But what about in athletes…**

IDNA and Athletic Performance

- Freidmann et al (2001):
  - Double-blind, placebo-controlled trial
  - Investigated the effect of iron supplementation (100 mg, bid) in 40 young elite athletes with iron depletion (serum ferritin < 20 ug/L) and normal hemoglobin
  - Serum ferritin levels increased to normal with no other significant changes to hematologic variables (i.e. Mean corpuscular volume (MCV)unchanged)
  - Iron supplementation group demonstrated significant changes in VO_2 max and in oxygen consumption in a maximal accumulated oxygen test

IDNA and Athletic Performance

- Dellavalle and Haas 2011
  - 165 collegiate level female rowers
  - Objective was to investigate the impact of iron depletion without anemia (IDNA) on performance indicators
    - Research group used a cut off of 20ug/L for serum ferritin
    - 27% (n = 44) IDNA (serum ferritin < 20.0 ug/L)
    - 10% (n = 16) IDA (hemoglobin <120 g/L)
  - IDNA female iron-depleted rowers reported 2-km times that were approximately 21 s slower (P < 0.004) compared to rowers with normal iron status
  - 30% reported regular or intermittent use of a multivitamin/multimineral supplement
  - Study recommendation- screening of all athletes at the start of he season

Athlete Screening:

Landahl et al., 2005

- IDA and IDNA within elite female soccer, N= 28 Swedish national team athletes
  - Objective was to determine the prevalence of IDA and IDNA on the team (timeline was 6 months out from FIFA world cup soccer)
  - 57% had IDNA and 27% had IDA
  - Cut off values used:
    - <120g/L Hemoglobin = absolute anemia
    - <16 ug/L serum ferritin = certain iron deficiency
  - Supplementation given: players with iron deficiency were given 37mg iron/tablets 2 x per day- follow up in 3 months
  - Athletes with IDA on Fe supplementation saw an increase from 114g/L to 133g/L for hemoglobin concentration (in 3 months)

IRON SUPPLEMENTS

Iron in the Diet

- Primary source is dietary - 2 types
  - Heme iron = myoglobin in flesh foods (meat)
  - Nonheme iron = vegetables and grains
- Healthy adults absorb about 10-15 % of dietary iron but individual absorption is influenced by several factors, including the chemical form of iron (heme or nonheme), and the body's storage levels of iron
- Absorption is improved by meat proteins and ascorbic acid (vitamin C)
- Tannins (tea), calcium, polyphenols and phytates (legumes/grains) can decrease absorption of nonheme iron

Iron Supplements: Type/dosage

- Typically ferrous iron salts
  - Ferrous fumarate (Palafer™) 300 mg = 100 mg Fe
  - Ferrous sulfate (generic) 300 mg = 60 mg Fe
  - Ferrous gluconate (generic) 300 mg = 35 mg Fe
- New formulations with fewer reported side effects ($$$)
  - Heme-iron polypeptide (Proferrin™) = 11 mg Fe
  - Polysaccharide-iron complex (Feramax150™) = 150 mg elemental iron

What type are you using?

Iron Supplements: Type

- Ferrous salts (in particular prolonged release FS preparations) remain the treatment of choice given their high effectiveness, acceptable tolerability, and low cost (Santiago 2012)
- IM injections vs oral supplementation – greater improvement in ferritin and faster rate of rise (Dawson 2006)
  - Implications when improvements needed for imminent competition

Iron Supplements: Dose

- Increased likelihood of GI side effects above 45 mg/d of elemental iron supplementation
- Guidelines for treatment of IDA: (Stotzfus and Deryfuss 1998)
  - 60 to 120mg of elemental iron of ferrous sulphate
  - 3 months in adolescents and adults, including pregnant women

What dose are you using?

Iron Supplements: Dose

- Guidelines by Nielsen and Nachtigall (1998) for iron supplementation in athletes:
  - Use of a pharmaceutical iron preparation with known high bioavailability
  - Dosage of ferrous (Fe++) iron 100 mg/day
  - Taken on an empty stomach/no other food/with no other divalent metals
  - Include vitamin C
  - Follow up 2-3 months
- Sufficient arguments to support controlled iron supplementation in all athletes with low serum ferritin levels (cut off values ???)
  - Prevent iron deficiency & nonspecific upregulation of intestinal metal ion absorption

Iron Supplements: Concerns

- Numerous studies have shown that there is no objective improvement in performance in a nondeficient state
- Indiscriminant iron supplementation carries risk of iron overload or inducing hemochromatosis
- Gastrointestinal effects (constipation, cramping)
- Can theoretically interfere with absorption of other minerals, such as zinc and copper
- Care not taken to improve diet when primary intervention is supplementation (Springle 2013 ☺)

Any other concerns with supplementation vs dietary intervention?

Suedekum and Dimeff 2005

Recommendations and Best Practices

National Sport Science and Medicine Committee (NSSMAC):

- March 2014 working group Guidelines:
  - Blood work target = SF >35ug/L
  - Initial screening- annually
  - Monitoring every 6-12 weeks if SF is < 35ug/L (otherwise annual monitoring)
  - Recommended modified training program until SF values >35ug/L
  - Supplementation: minimum of 100mg elemental Fe/day
    - Form: as iron salts (ferrous, ferrous fumarate, ferrous sulfate) or alternative supplements (heme iron, iron polysaccharides)
  - In the absence of blood work- do not supplement
  - Altitude- special protocol required

Screening

- At present, screening of athletes for iron deficiency and anemia is not routinely recommended by any major sport organizations except the IOC
- May be warranted with:
  - Elite-level female and male athletes
  - Team sports and endurance athletes (athletes dependant on aerobic capacity)
  - Athletes with performance declines
  - Vegetarians or athletes with restrictive diets
  - Competitors with a previous history of iron deficiency
  - Athletes training at altitude

Conclusions

- Iron is critical to athletic performance
- Athletes may be iron deficient due to mechanisms of loss due to training and possibly inflammation
- Iron deficiency without anemia in athletes remains a questionable indication for therapeutic iron supplementation, but evidence is growing to support this practice
- Athletes should primarily be encouraged to ensure adequate dietary intake of iron to prevent inadequate iron stores

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