

## **MSHSAA POSITION STATEMENT: IRON DEFICIENCY IN ENDURANCE ATHLETES (Dr. Kim Colter, MSHSAA Sports Medicine Advisory Committee)**

Iron deficiency is common in female distance runners and endurance athletes and occurs in male endurance athletes occasionally. Iron deficiency impairs the performance of endurance athletes even if not severe enough to cause iron deficiency anemia. Anemia is the last manifestation of iron deficiency. The impairment in distance running performance in iron deficient runners who are not anemic occurs because iron deficient athletes cannot properly metabolize the lactic acid created during exertion (Finch et al, 1979.) Iron deficient athletes are at increased risk of collapse during intense exertion because of the impaired ability to metabolize lactic acid.

Testing for iron deficiency in distance runners and correction of iron deficiency in runners can prevent decline in performance. Runners have been shown to have an increased loss of iron in the stool due to transient ischemia of the lining of the colon and rectum that develops with hard running. Menstrual blood loss increases the frequency of iron deficiency in female endurance athletes. There are many other factors that can contribute to iron deficiency in endurance athletes. The following conditions have all been seen as causes for iron deficiency in runners:

- 1) Gastritis, esophagitis, and duodenitis caused by taking non-steroidal anti-inflammatory drugs such as ibuprofen and naproxen.
- 2) Telangiectasias in the GI tract that leak blood. Telangiectasias are often seen on the lips of runners who have telangiectasias in the GI tract.
- 3) Meckel's diverticulum
- 4) Rectal prolapse during running
- 5) Inflammatory bowel disease caused by the acne medicine, Accutane
- 6) Esophagitis caused by swallowing tablets without liquid
- 7) Celiac disease
- 8) Colonization of the GI tract with the bacterium H Pylori that predisposes to ulcers and blocks iron absorption.

Iron supplementation to correct deficiency in distance runners and prevent recurrence should always be guided by the athlete's personal physician. It is essential that athletes taking iron supplementation be monitored with serum ferritin testing to be certain that replenishment of iron stores is adequate and that iron excess is not occurring. Iron is potentially toxic in excess. Athletes who are unwilling or unable to monitor ferritin as directed by their personal physicians while taking iron supplementation should probably not take iron supplementation at all.

Serum ferritin is the best test for iron deficiency. A serum ferritin less than 30 micrograms per liter constitutes iron deficiency and is an indication for replacement therapy (Camaschella, NEJM). While some clinical laboratories have updated the normal range for ferritin on lab reports, many clinical laboratories are still issuing reports stating that the lower limit of normal for ferritin assays is as low as 6 mcg/liter. Parents, coaches, and athletes should ask for the actual numerical value for serum ferritin on their lab reports. A serum ferritin of 6, 12, or 18 is never "normal." The amount of iron storage in the body can be rather accurately estimated in milligrams by multiplying serum ferritin times 10. The goal for iron storage in female athletes would be a total of 500mg, and in smaller adolescents and young adult females should be at least 5mg/kg, which would correspond to 250mg for a 50kg (110 pounds)

female runner, and that runner would be expected to have a ferritin of 25 mcg/dl. Many males have 1000mg of iron storage and would have serum ferritin values in the 100 mcg/dl range.

There are two sources of dietary iron which are absorbed through separate channels in the gut. Heme iron is found in meat and blood based supplements such as ProFerrin. Heme iron is 30% absorbed. Non heme iron is found in vegetable sources of iron and in iron supplements such as iron sulfate. Non-heme iron is 5 to 10% absorbed. In many individuals, constipation and other GI side effects of non heme iron supplements such as iron sulfate limit the number of doses that can be taken per day, slowing the correction of a deficit in total body iron stores. The use of non heme iron supplements, that are more easily tolerated in the gut, may allow for quicker correction of large total body iron deficits. Rarely, intravenous iron infusion may be necessary to correct refractory iron deficiency. Oral iron regimens to correct iron deficiency and prevent recurrence of iron deficiency should be directed by the athlete's personal physician.

Recent information from a study in Polish rowers (reference 3 below, Skarpanska-Stejnborn) reveals one more way in which iron absorption can be blocked in endurance athletes. During intense exertion, some red blood cells burst inside blood vessels and release the iron that is present in hemoglobin into the blood stream. The liver detects the presence of this iron, and releases hepcidin, the hormone that blocks absorption of oral iron from the intestinal tract. This hepcidin effect lasts for five or six hours after intense exertion. If rowers burst red blood cells and release iron from hemoglobin into the circulation it is certain that the footstrike hemolysis of runners does this as well. We know from another study that urinary hepcidin levels are higher in runners than they are in cyclists, and this is felt to be due to the footstrike hemolysis in runners. Hepcidin will stop the oral absorption of any form or orally ingested iron, whether it is heme iron (Proferrin, meat) or non heme iron (iron sulfate, iron gluconate).

There are a couple of important implications of this information about red cell hemolysis causing hepcidin release and blocking iron absorption. The timing of oral iron administration should be such that iron is present in the duodenum when hepcidin is not present in the circulation inhibiting iron absorption. Runners who run in the afternoon should take their iron the next morning. Runners who run in the morning should take iron late in the day. This phenomenon helps explain why some runners have difficulty with replenishing iron stores orally, and athlete's refractory to correction of iron deficiency by oral replenishment will require iron infusions to overcome iron deficiency. In the author's clinical experience, it is difficult to get hepcidin levels done because many labs do not offer them and insurance is often reluctant to cover doing hepcidin levels. In my opinion it is rarely necessary to do hepcidin levels outside research studies.

Athletes who have a positive family history of the iron storage disease, hemochromatosis, should not take iron supplements until they have been tested for the presence of the two gene markers associated with hemochromatosis, C282Y and H63D, and been cleared to take supplementation by their personal physician. Any male athlete with ferritin greater than 300 or iron saturation greater than 50% should stop iron supplementation and be tested by their physician for these two gene markers. Any female athlete with ferritin greater than 200 or iron saturation greater than 45% should stop iron supplementation and be tested by their physician for the two gene markers for hemochromatosis.

Total body iron stores are known to fall during the arduous training and racing that occurs towards the end of the autumn cross country season and the spring outdoor track season. It is advantageous if endurance athletes have serum ferritin values in the 40 to 50 range at the start of cross country and outdoor track in order to have ferritin values greater than 30 during the championship competition

weeks at the end of their seasons. Testing the athlete's serum ferritin at the end of cross country and the end of outdoor track is one suggested regimen. An athlete's personal physician may prefer a different schedule of testing.

- 1) Camaschella, Cara MD NEJM 2015;372:1832-1843 May 2015 "Serum ferritin level is most sensitive and specific test used for the identification of iron deficiency (indicated by a level of <30 micrograms per liter)"
- 2) Finch, Clement J Clin Invest. 1979 Jul; 64(1): 129–137. Rats who were iron deficient but not anemic collapsed during treadmill running more rapidly than iron replete rats, had higher lactate levels during exertion, and had lower levels of an iron dependent enzyme in muscle mitochondria that is involved in lactate metabolism.
- 3) [Anna Skarpańska-Stejnborn](#) et al, Effect of intense physical exercise on hepcidin levels and selected parameters of iron metabolism in rowing athletes, [Eur J Appl Physiol](#). 2015; 115: 345–351.