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Iron Deficiency in Athletes: An Update

Abstract: *Adequate body stores of iron are necessary for optimal endurance exercise performance. Severe iron depletion resulting in overt iron-deficiency anemia clearly depresses endurance fitness, but it is not clear if milder degrees of iron deficiency (low serum ferritin with normal hemoglobin levels) impair physical capacity. The question is an important one for athletes, particularly females, who are particularly prone to iron deficiency without anemia. This review examines research data, in both animals and humans, which have addressed this issue. Constructing guidelines based on this often-conflicting body of information is difficult. Routine screening is advocated for at-risk athletes, particularly elite-level female competitors in distance sports, and, although controversial, many authorities recommend iron treatment for athletes with hypoferritemia (ferritin <12-20 ng/mL), even without overt anemia. However, "blind" supplementation with oral iron by athletes is not recommended.*

Keywords: iron deficiency; physical fitness; anemia; ferritin

The amount of iron in the human body is not large—approximately 4.0 g in a typical adult male—but adequate stores of this element are critical for health as well as the capacity to perform physical work.[1] A deficit of body iron resulting from inadequate dietary intake and/or excessive losses can negatively affect immune function, temperature regulation, cognitive abilities, efficiency of energy metabolism, and sports performance. Such reductions in iron are readily detected through standard blood tests (hemoglobin and ferritin levels), and iron deficiency is usually easily treated (either through increased dietary intake or supplementary oral iron).

The importance of maintaining adequate body iron stores has not been lost on the competitive athlete. Many factors influencing success in sports lie outside the individual athlete's control (skill of the opponent, weather, referees' judgments). However, maintaining appropriate levels of body iron is a variable that he or she can usually control. Competitive athletes therefore have considerable interest in assuring proper iron stores, recognizing that levels of iron in the body can be readily assessed and that a deficiency that would affect negatively on sports performance can be promptly managed.

These observations notwithstanding, there currently exists considerable controversy surrounding (*a*) the clinical definition of significant iron deficiency in athletes (ie, the level of iron deficit that will negatively affect exercise performance), (*b*) the appropriate strategies for screening athletes for iron deficiency, and (*c*) the indications for iron treatment. It has long been recognized that iron is critical in the formation of hemoglobin and that iron-deficiency anemia—a decline in blood hemoglobin concentration as a late manifestation of diminished body stores—clearly impairs physical

> . . . iron-deficiency anemia—a decline in blood hemoglobin concentration as a late manifestation of diminished body stores—clearly impairs physical performance by limiting oxygen transport to exercising muscles.

performance by limiting oxygen transport to exercising muscles. More controversial is the issue of whether lesser degrees of iron deficiency, characterized by depressed levels of serum ferritin (a marker of iron stores) but preserved hemoglobin concentration, will also diminish endurance performance. This question bears considerable importance, since survey studies consistently indicate that a state of iron deficiency without anemia is evident in a quarter to a third of all female athletes. This review will examine this controversy and attempt to place decision making regarding identification and treatment of iron deficiency by physicians, coaches, and athletes into a practical perspective.

Body Iron: Distribution and Measurement

The recommended daily allowance for dietary iron in the adult male is 8 mg per day, whereas that for menstruating, nonpregnant females is higher (18 mg) to account for increased basal iron losses via menstruation.[2] The bioavailability of iron in food depends on its source. Absorption of iron in the gastrointestinal tract is greatest for *heme* iron contained in red meats (15% to 35%), as compared with 2% to 20% of *nonheme* iron present in vegetables and grains.

Once absorbed in the small intestine, iron is transported in the blood bound to transferrin. Approximately 60% to 70% of iron is used in the formation of hemoglobin in the bone marrow, whereas 5% is incorporated in intracellular myoglobin (for oxygen utilization and storage). Small but essential amounts of iron are critical for enzyme function in oxidative metabolic pathways and as components of the cytochromes in the oxidative phosphorylation chain.

The remainder, about 20% to 30%, is stored in the liver and reticuloendothelial system principally in the form of ferritin. Ferritin circulating in the blood stream accurately reflects body iron stores and serving as a reliable marker of iron deficiency.[3] A value of 1 ng/mL of ferritin corresponds to about 5 to 9 mg of stored iron.[4] Other biomarkers may be useful

for accurately gauging adequacy of body iron stores, including transferrin, transferrin saturation, and soluble transferrin receptor.[5] These are neither commonly used in clinical settings nor in routine screening of iron status in athletes, however, and will not be addressed in this review. Serum iron levels demonstrate a great deal of variability over time (both circadian and rate of release from the reticuloendothelial system), bear no reliable relationship to ferritin concentration, and cannot be expected to accurately reflect body iron status.[6]

Among general population studies of healthy individuals, normal plasma ferritin values vary widely. The mean value in postpubertal males is approximately 90 ng/mL and in females 25 to 30 ng/mL during their reproductive period.[4] In the face of a negative balance between iron intake and losses, body iron stores are progressively depleted, and serum ferritin levels fall. In most studies a ferritin concentration of <12 to 20 ng/mL has been considered an indicator of significant iron deficiency.[7,8]

A number of different methods are used for determination of plasma ferritin levels, including immunorachiometric assay and enzyme-linked immunosorbent assay, as well as immunochemiluscent and immunoflurometric techniques. Different reference norms have been defined for each. For this reason, it is generally recommended that normal values be established for each testing laboratory.[9(p1703)]

It is important to recognize that plasma ferritin is an acute phase reactant, and levels will be consequently elevated following vigorous physical activity or in an individual with an inflammatory illness. Thus, determination of ferritin levels should be postponed in athletes in an inflammatory state (ie, those who have recently completed an acute bout of exercise training or in those with acute febrile illness).

Hemoglobin synthesis is jeopardized when body iron stores become seriously reduced, resulting in *iron-deficiency anemia*. This is indicated by a hemoglobin concentration of <12 g/dL in females and <13 g/dL in males. In earlier stages of

iron depletion, hemoglobin levels remain normal in the face of depressed serum ferritin concentrations, defined as *iron deficiency without anemia*. To summarize

- Normal body iron stores
  [Hb] >12 g/dL females, >13 g/dL males
  Ferritin >12 to 20 ng/mL
- Nonanemic iron deficiency
  [Hb] >12 g/dL females, >13 g/dL males
  Ferritin <12 to 20 ng/mL
- Iron-deficiency anemia
  [Hb] <12 g/dL females, <13 g/dL males
  Ferritin <12 to 20 ng/mL

The Role of Iron in Defining Exercise Capacity

Iron serves as a critical factor for specific biochemical–physiologic processes that are important for endurance exercise performance. The formation of hemoglobin, the central transporter of oxygen for aerobic metabolism, and the activity of intracellular metabolism (oxidative enzymes) depend on iron for their function. In addition, iron is important for optimal mental function and might serve to influence exercise motivation. Identifying which among these processes might be responsible for decrements in the iron-deficient athlete is not always clear cut.

Hemoglobin Formation

Iron is an essential component of the heme molecule, which binds with globulins in the bone marrow to form hemoglobin. An adequate quantity of circulating hemoglobin is critical for transport of oxygen from the inhaled air to exercising muscle. There it is utilized in the metabolic machinery as an energy source for oxidation of substrate (principally carbohydrates and fats). The Fick equation expresses this oxygen utilization (V_{O_2}) as the product of the circulatory blood flow (or cardiac output) and the extraction of oxygen by the peripheral cells. The latter is calculated as $C_a - C_v$, or the difference between the oxygen content in the capillaries approaching the cell and that of the venous efflux leaving it. The component in this scenario that is dependent on blood hemoglobin

concentration—and therefore, adequate iron stores—is C_a, and a close correlation is observed between arterial oxygen content and the maximal ability of the contracting skeletal muscle to utilize oxygen (Vo_{2max}).[10]

Such oxidative metabolism is typically considered to be contributory to sustained forms of exercise (distance running, cycling), but even short burst, sprint activities rely to some extent on oxygen-dependent energy systems. Thus, a depletion of iron stores can be expected to generally impair endurance exercise performance.

Even small reductions in hemoglobin concentration can negatively affect exercise capacity. Gardner et al[11] found a direct relationship between hemoglobin concentration and treadmill endurance time, demonstrating a 20% decrease in endurance in those with a hemoglobin concentration of 11.0 to 11.9 g/dL compared with those with a level of >13.0 g/dL. Similar findings have been reported in subjects undergoing progressive phlebotomies to create anemia.[12] When iron-deficiency anemia is corrected in these studies, normal endurance times are restored.[13]

Impairment of exercise capacity in anemic individuals may reflect more than reduced oxygen transport. Subjects with low hemoglobin concentrations also manifest a decrease in blood viscosity and reduction in systemic vascular resistance, effects that increase cardiac work and strain circulatory function.

Intracellular Metabolic Function

Iron is an important component of a number of enzymatic functions within the cell that are essential for providing energy for muscular contraction during exercise.[14] Iron is a component of the heme-containing cytochromes of the oxidative phosphorylation chain. Activity of enzymes such as succinate dehydrogenase and NADH dehydrogenase, which contain iron, are reduced in conditions of iron deficiency. Evidence exists that the synthesis of heme, which depends on adequate iron stores, may be a limiting factor for the assembly of muscle cell mitochondria.

Unfortunately, as opposed to the ready determination of blood hemoglobin concentration to identify anemia, there exists no convenient biomarker of these iron-dependent intracellular metabolic functions. Tissue studies in animals (reviewed later in this article) clearly indicate that iron deficiency without anemia depresses endurance performance, and this is linked to depression of intracellular aerobic enzyme activity. Little such data are available in humans. Thus, the question as to whether iron deficiency without anemia can limit sports performance in human athletes, and, if so, whether this is a consequence of depressed cellular metabolic functions, current remains unanswered.

Mental Function

High levels of exercise performance demand mental fortitude and motivation. Evidence has accumulated to indicate that iron deficiency negatively affects emotional health and cognitive function.[1,15,16] It is reasonable to speculate, then, that iron deficient athletes might lack the psychological tools necessary for sustained high levels of work.

This evidence for a negative effect of iron deficiency on mental capacities originally arose as reports of developmental delay and behavioral changes in infants and small children with iron-deficiency anemia.[1] Such conclusions did not go uncontested, as some felt that iron deficiency might simply serve as a surrogate marker for a poor nutritional and psychosocial environment. However, animal studies have indicated that reduced body iron stores decrease brain iron content and can interfere with normal neurotransmitter function within the central nervous system.[1]

Such clinical findings have now been extended to individuals in older age groups (ie, adolescents) who exhibit iron deficiency without anemia. For example, in a randomized controlled study by Bruner et al,[15] 81 adolescent girls with normal hemoglobin levels and ferritin <12 ng/mL improved performance on tests of verbal learning and memory (but not mood or attention) after iron treatment. Murray-Kolb and Beard[16] reported

that after iron treatment, a significant increase in ferritin level was accompanied by a 5- to 7-fold improvement in cognitive performance in 18- to 35-year-old nonathletic women.

Furthermore, it is commonly observed that patients treated for iron-deficiency anemia frequently report increased memory, energy, and mood.[17] The possibility that this effect of diminished iron stores might improve tolerance to extended exercise is intriguing but the question remains to be addressed.

Frequency of Iron Deficiency in Athletes

Overt iron-deficiency anemia is highly uncommon in populations of athletes. Most survey studies indicate a frequency of no more than 0% to 2%, the higher numbers being reported in female competitors.[18] However, values in groups of female athletes as high as 10% to 15% have been described.[19,20] The expected number of individuals with iron-deficiency anemia among any group of athletes is probably little different from that observed in the general population.[18] Because of its rarity, athletes found to have iron-deficiency anemia, particularly males, should be considered for evaluation of disease processes than accelerate iron losses.

Borderline low hemoglobin concentrations with normal ferritin concentrations are sometimes observed in athletes, particularly during the initial phases of a vigorous training program. This so-called "sports anemia" does not reflect a true anemia and does not affect sports performance. Rather, it represents a relative decrease in hemoglobin concentration from the dilution effects of increased plasma volume at the onset of endurance training.[21] Augmented red cell volume typically rises later as training continues, normalizing hemoglobin concentration.[22]

A high frequency of iron deficiency without anemia, on the other hand, has been consistently observed in trained athletes, particularly female runners. Table 1 presents a representative (but not comprehensive) list of studies that have assessed the frequency of low ferritin levels in male and female athletes.[19,20,23-31]

Table 1.

Sample of Studies Assessing Frequency of Nonanemic ([Hb] > 12 g/dL in Females, >13 g/dL in Males) Iron Deficiency as Indicated by Hypoferritinemia in Young Athletes

Study	Athletes	Hypoferritinemia Definition (ng/mL)	Frequency (%)	
			Females	Males
Ostojic and Ahmetovic[19]	Mixed	<12	25-35	
Sinclair and Hinton[20]	Endurance	<16	29	4
Fallon[23]	Elite	<12	30	5
Mettler and Zimmermann[24]	Marathoners	<15	28	2
Di Santolo et al[25]	Non-professional	<12	27	
Gropper et al[26]	Mixed	<15	24	
Dubnov and Constantini[27]	Basketball	<20	35	15
Rowland et al[28]	Runners	<12	45	17
Nickerson et al[29]	Runners	<20	40	
Brown et al[30]	Runners	<12	44	
Rowland and Kelleher[31]	Swimmers	<12	47	0

From these data, a number of observations can be offered. Nonanemic iron deficiency is a common finding among female athletes, particularly adolescent distance runners. In any group of training endurance athletes, 1 out of every 3 or 4 females can be expected to satisfy criteria for nonanemic iron deficiency. However, hypoferritinemia is not frequently detected in males.

This gender difference has traditionally been attributed to the influence of iron losses through menstrual flow in females. Supporting this, Fallon[23] and Mettler and Zimmermann[24] demonstrated a negative relationship between estimates of menstrual loss and serum ferritin levels in high school distance runners. Sex differences in dietary iron intake may also play a role, as female athletes appear to consume less iron than their male counterparts. Using 5-day diet records, Nickerson et al[32] reported average daily iron intakes of 8.5 mg and 12.9 mg in female and male cross-country runners, respectively. Similarly, Rowland and Kelleher[31] found that female swimmers consumed an average of 7.8 mg of iron daily compared with 12.1 mg in males, representing 43% and 67%, respectively, of the recommended daily allowance in this age-group.

Despite the significant variation in cutoff point of ferritin level to define iron deficiency in the different studies, the frequency of reported cases is similar. This supports the implication that such variations reflect different normal ranges depending on method of analysis.

Causes of Iron Deficiency in Athletes

As noted above, the etiology of nonanemic iron deficiency in athletes—and the explanation for its strong predominance in females—lies in a combination of inadequate dietary iron intake and exaggerated losses via menstrual flow. Some studies have indicated that the high frequency observed in athletes is no different from that seen in the general adolescent population.[25,33,34] For example, Braun et al[33] found no significant difference in mean ferritin level in training female collegiate swimmers (20 ± 9 ng/mL) and sedentary subjects (17 ± 11 ng/mL). Similar findings were reported by Rowland et al,[34] who found similar average ferritin levels of 18 ± 15, 22 ± 13, and 22 ± 11 ng/mL, respectively, in female adolescent swimmers, cross-country runners, and nonathletic control subjects at the beginning of a competitive high school season. In the swimmers, no significant change was observed in ferritin levels at the end of a 10-week season

$(20 \pm 14$ ng/mL).[31] DiSantolo et al[25] found no difference in frequency of nonanemic iron deficiency (ferritin <12 ng/mL) in female athletes and sedentary controls. Such findings indicate that survey studies may indicate a large number of young female athletes with iron deficiency without anemia simply because of the high frequency of this state among menstruating females of this age in the general population.

At the same time, there is convincing evidence that sports participation, per se, can engender iron loss and contribute to hypoferritinemia. Serum ferritin levels have been documented to fall with sports training, particularly during the early phases.[35-37] For example, Rowland et al[28] found that 40% and 3% of a group of female and male high school runners, respectively, had nonanemic iron deficiency at the beginning of a competitive season. At the end of the season these numbers rose to 45% and 17%. In another study, a group of untreated female runners identified as having nonanemic iron deficiency at the start of a running season experienced a fall of average serum ferritin from 14 ± 4 to 9 ± 4 ng/mL by the end of the season.[37]

Negative correlations between training volume and serum ferritin levels have been reported by some[38-40] but not others.[19] Also, certain investigators have failed to discover alterations in ferritin levels with training by swimmers[31,41] figure skaters, and gymnasts.[42]

Several processes have been considered to possibly contribute to progressive iron losses induced by athletic training (see Chatard et al[6] for review and references). Occult blood loss from the gastrointestinal tract is not uncommon among distance runners, with frequencies ranging from 8% to 83%. The most likely explanation for this gastrointestinal blood loss is the transient ischemia experienced by the gut when circulating blood flow is diverted to the skeletal muscles during exercise. Such bleeding appears to be reversible and benign.

Similarly, blood appears in the urine in runners following vigorous competition, usually in microscopic quantities. This phenomenon has been described in up to 90% after a marathon race, with resolution within 24 to 72 hours. Although renal ischemia might be responsible, bleeding from direct trauma of the bladder to anterior pelvic structures may be a more likely explanation.

Iron is present in sweat, but it is unlikely that losses via this route, even with profuse sweating, contribute significantly to exaggerated iron losses in athletes. Studies examining this question are confounded by the contamination of sweat by iron present in superficial skin cells as well as the large interindividual variability in sweat iron content.

Some studies have indicated significant hemolysis of red blood cells in runners and swimmers, but others have failed to substantiate these findings. The model here is the "foot strike hemolysis" that can occur in military recruits after prolonged marches. In athletes, it has been suggested that similar red cell breakdown might also occur as erythrocytes become squeezed by muscular contractions. Hemolysis will not necessarily produce iron deficiency, since iron released as erythrocytes break down can be reused for the formation of new red cells. However, with brisk hemolysis, iron can be lost in the urine.

In summary, the high frequency of nonanemic iron deficiency among female athletes appears to reflect (*a*) a similar incidence in the general population, (*b*) the influence of menstrual blood loss and low dietary iron, and (*c*) exacerbated losses of iron triggered by sports training. The latter effect may be particularly important in distance runners.

Effect of Iron Deficiency Without Anemia on Exercise Performance

There is no disagreement that athletes found to have iron-deficiency anemia deserve treatment with oral iron supplementation. Depressed hemoglobin levels clearly diminish performance, and iron supplementation can be expected to reverse this decrement. On the other hand, whether iron deficiency without anemia decreases performance in humans is debatable, leading to uncertainty regarding indications for treatment.

The research evidence in animals (at least those in which the question has been addressed) is clear cut: Depletion of body iron stores without fall in hemoglobin diminishes endurance performance, the fall in exercise capacity is related to diminished intracellular metabolic capacity, and hemoglobin and metabolic functions of iron appear to contribute to separate aspects of endurance performance (Vo_{2max} and endurance time, respectively).

Research in humans has failed to indicate such a clear picture. Indeed, many have regarded the research data in athletes as providing insufficient evidence that this detrimental effect of nonanemic iron deficiency observed in animals can be transferred to humans.

Animal Studies

Using a model of treadmill run time to exhaustion, Finch et al[43] reported decreased endurance times in nonanemic iron-deficient rats, which improved with iron treatment. In this study, blood hemoglobin levels were maintained in 4 groups of animals at normal concentrations by removal or addition of blood via a venous catheter. The rats in group A were fed an iron-deficient diet for 4 weeks prior to exercise testing, whereas group B animals consumed a normal diet. Those in group C ate an iron-deficient diet during the 4 weeks supplemented by iron. Group D animals were fed an iron-deficient diet but were supplemented with iron only at the start of the exercise testing. The rats in groups B and C, who had normal hemoglobin concentrations as well as iron stores, could exercise for 15 to 20 minutes, whereas the nonanemic, iron-deficient animals in groups A and D endured for only 4 minutes. After 4 days of iron treatment, those in group D improved their performance to match those of groups B and C. Muscle concentrations of cytochromes, myoglobin, succinic dehydrogenase, and α-glycerophosphate were depressed in the iron-deficient animals.

Davies et al[44] demonstrated that rats with severe iron-deficiency anemia improved hemoglobin concentration and Vo_{2max} when given iron treatment. However, increases in muscle

Table 2.

Studies Assessing the Effect of Nonanemic Iron Deficiency on Endurance Performance in Human Beings

Study	Subjects	Ferritin (ng/mL)		Duration (Weeks)	Daily Iron Rx (mg Elemental)	Testing Mode
		Pre	Post			
Studies showing endurance performance improvement						
Rowland et al[37]	Female runners	13.9	26.7	4	295	Progressive treadmill duration
LaManca and Haymes[46]	Female athletes	10.8	22.5	8	100	Submaximal treadmill duration
Hinton et al[47]	Untrained women	10.4	14.5	6	20	15-km cycling time trial
Yoshida et al[48]	Runners	13.7	21.2	8	60	3-km run speed
Studies showing no endurance performance improvement						
Klingshirn et al[49]	Female runners	11.6	23.4	8	100	Treadmill endurance
Zhu and Haas[50]	Untrained women	14.3	29.0	8	135	15-km cycling time trial
Peeling et al[51]	Female athletes	19	57	4	Intramuscular iron injections	Treadmill endurance
Blee et al[52]	Female netballers			2	Intramuscular iron injections	Shuttle run

oxidative function and treadmill endurance time were delayed until 2 days later. In another study, these investigators found that Vo_{2max} could be improved by blood transfusion in rats with iron-deficiency anemia without a parallel effect on endurance time.[45] These studies in rats imply that (a) depletion of iron stores with normal hemoglobin concentrations impairs endurance performance via decreased intracellular aerobic metabolism and (b) iron-deficiency anemia negatively affects work capacity by impairing oxygen delivery to muscle (Vo_{2max}).

Human Subject Studies

A number of studies have attempted to determine if nonanemic iron deficiency negatively affects endurance performance in humans. In general, these have failed to provide convincing evidence that the results cited above in animal experiments can be translated into similar conclusions regarding human athletes. However, it must be recognized that these studies, which have provided conflicting results, suffer from a number of methodological difficulties. It is challenging to study influences on endurance sports performance, given the large number of variables involved (weather, motivation, nutrition, etc), and therefore most investigations have examined physical endurance in respect to iron status in the exercise testing laboratory where such factors can be more tightly controlled.

The most typical design has been to identify a group of subjects with nonanemic iron deficiency, randomly divide them into iron treatment and control groups, and assess group differences in exercise performance. The latter has been most commonly examined by endurance time during treadmill running with a submaximal protocol. In such a test, end-points of fatigue cannot be neatly identified, and it has been argued that such procedures do not truly mimic actual endurance competition.[18] Moreover, one is confronted with the difficulty of distinguishing differences, which may have competitive but not statistical significance. That is, a 5-second difference between 2 endurance tests times might not satisfy criteria for statistical significance but might bear importance in actual competitions.

Table 2 outlines studies that have supported or refuted the importance of nonanemic iron deficiency in humans using this experimental approach.[37,46-52] Clearly, the findings are conflicting. It should also be noted that subject populations

differ in nature and are small in number. Moreover, these investigations vary considerably in terms of initial ferritin concentration, dose of iron, and study duration.

Other outcome variables have been examined using this randomized, controlled assessment of iron versus placebo treatment of subjects identified with nonanemic iron deficiency. With rare exception,[53] such iron treatment has not been demonstrated to improve Vo_{2max}.[54-58] Reduced lactate level during exercise following iron treatment was reported by Schoene et al,[58] but others have failed to duplicate this finding.[54-56] Improved energy efficiency during submaximal exercise in response to iron supplementation has been described.[50,59]

Efforts have been made to duplicate in human subjects the transfusion-based experiments used in the animal studies reported above. Celsing et al[60] performed serial phlebotomies on human volunteers over a 9-week period to create iron-deficiency anemia, which predictably diminished treadmill exercise performance. The subjects were then transfused to create normal hemoglobin concentrations but were left with low ferritin levels (mean 9.1 ng/mL). In this nonanemic iron-deficient state, the running endurance times returned to normal.

Lukaski et al[61] induced a state of non-anemic iron deficiency via a low-iron diet and phlebotomy in adult female volunteers, with a drop in average ferritin concentration from 26 to 6 ng/mL and final mean hemoglobin of 12.0 g/dL. No impairment of exercise duration or Vo_{2max} was observed. However, other markers of improved metabolic function were seen after iron treatment, including reduction in rate of oxygen utilization.

In summary, this research literature in human subjects suffers from numerous methodological weaknesses, and among the many studies cited, no 2 studies have used the same investigative approach. Confident conclusions consequently are problematic. Nonetheless, it is difficult to mount a compelling argument from these data that nonanemic iron deficiency impairs endurance performance in athletes.[62]

Assessment and Management of Iron Deficiency in Athletes

Given the uncertainty of the impact of nonanemic iron deficiency on exercise performance, it is not surprising that appropriate guidelines for screening of iron status in athletes, particularly females, as well as indications for iron treatment are not entirely clear. Nonetheless, certain recommendations have been offered.[6,63-67]

Routine Screening

A blood sample for determination of hemoglobin concentration and ferritin level constitutes an appropriate means of screening athletes for iron status. It should be reemphasized that ferritin is an acute phase reactant, and blood levels will be elevated following vigorous exercise or in inflammatory conditions.

Routine screening has been recommended for high-risk populations, including male endurance athletes and female athletes in general.[65] Such regular screening might be most appropriately restricted to elite and highly competitive athletes, however. In general populations of high school athletes, for example, the costs of routinely measuring ferritin levels might be prohibitive, particularly since determinations would need to be repeated later during the competitive season.[67] However, certain athletes participating even at this level of competition should undergo regular assessment of iron status, specifically (*a*) all those who are experiencing an unexplained decrement in performance, (*b*) individuals consuming a vegetarian diet, and (*c*) athletes with a previous history of iron deficiency.

Indications for Iron Treatment

There is no dispute that all athletes with iron-deficiency anemia should be treated with appropriate doses of oral iron. Too, although disagreement exists, most authorities suggest iron supplementation for athletes who have been documented to have hypoferritinemia without anemia. Although the influence of this state on performance has not been well defined, this recommendation is supported by arguments that (*a*) this

condition predisposes athletes to overt anemia, (*b*) iron supplementation will provoke a rise in hemoglobin in those individuals who have a subtle degree of anemia, and (*c*) nonanemic iron deficiency may have a negative impact on general health, including impaired cognitive performance as well as increased susceptibility to infection.[64]

The ferritin level that signals a need for treatment depends on the normal values for the laboratory in which the determinations are made. In most cases, a threshold level of 12 to 18 ng/mL has been considered indicative for iron supplementation.

Certain potential risks of iron supplementation have been emphasized.[64,66] Oral iron may cause gastrointestinal effects (diarrhea, cramping) and can theoretically interfere with absorption of other minerals, such as zinc and copper. Increased oral iron may pose a risk for athletes with hemochromatosis, a genetic disorder of abnormal accumulation of body iron.

Expert opinion is in agreement that, considering these possible risks, athletes with normal ferritin levels should not take iron supplements. Nonetheless, information suggests that highly competitive athletes *do* frequently take oral iron. Petroczi et al[69] sent surveys to highly competitive athletes in the United Kingdom requesting information regarding supplement use. Of the 874 respondents (out of 2995), 30% reported routine oral iron supplementation. Among professional cyclists, Zotter et al[70] found that 45% had a serum ferritin level >300 ng/mL and one fourth had a value exceeding 500 ng/mL.[70] These findings would imply that high doses of oral iron were regularly used by these competitors.

Anecdotally, such elite athletes would seem to base this practice on their sense that (*a*) iron deficiency at all levels depresses endurance performance in animals, (*b*) the definitive study to determine if early stages of iron deficiency (ie, nonanemic iron deficiency) affects performance in human athletes has not been done, and (*c*) the risks of iron supplementation are neither substantial nor well documented.

Treatment Regimens

To optimize dietary iron intake, athletes should be encouraged to consume a diet that includes regular portions of lean red meat as well as iron-fortified cereals and other foods. However, it has been demonstrated that it is difficult to increase body iron content by dietary means in an athlete who already demonstrates low iron stores.[32,71] Thus, a period of oral iron supplementation is indicated. As demonstrated in Table 2, a daily dose of 100 mg of elemental iron is a reasonable starting dose for substantially increasing serum ferritin levels, administered for 2 to 3 months during a training season, with follow-up ferritin determinations (two 325-mg ferrous sulfate tablets contain 130 mg elemental iron). Nickerson et al reported that this amount prevented a fall in ferritin levels in high school girls during a cross-country seasons,[32] whereas 60 mg failed to prevent such a decrease.[29] Vitamin tablets with iron generally do not contain sufficient iron (usually 18 mg) for this purpose.

Given these recommendations, the report of Cowell et al[72] regarding current practices among college athletic programs is illuminating.[72] These authors surveyed policies regarding screening female athletes among 55 National Collegiate Athletic Association Division I-A schools. Routine screening was reported by 44%, and among those institutions, approximately one half described screening of all female athletes. The most common definitions for iron deficiency were serum ferritin <20 and <12 ng/mL. All responding schools that performed screening reported treating athletes who were found to have nonanemic iron deficiency. Various treatment regimens were described, most commonly with ferrous sulfate in does of >300 mg per day (37%) and 50 to 100 mg per day (26%).

Summary

Iron is important for optimal sports performance, and assuring adequate body stores is a critical issue for athletes. Severe iron deficiency with anemia is uncommon, but low ferritin concentrations with normal hemoglobin levels are frequent, particularly in female distance competitors. At least a quarter of any group of such athletes can be expected to demonstrate hypoferritinemia, a consequence of menstrual losses, low dietary iron intake, and the training process itself (gastrointestinal bleeding, hemolysis). Uncertainty surrounds the performance implications of these athletes with nonanemic iron deficiency. Routine screening is indicated for certain high-risk groups, such as elite-level female athletes, those with performance declines, vegetarians, and competitors with a previous history of iron deficiency. Many authorities recommend iron treatment with those found to have hypoferritinemia. Unmonitored (ie, "blind") supplementation with oral iron by athletes is felt to be inappropriate. AJLM

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