

ADVANCES IN HEMATOLOGY

Current Developments in the Management of Hematologic Disorders

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Inherited and Acquired Hematologic Disorders in Athletes

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H&O How do you define “athletes” as a hematologist?

JD Most of the information for hematologists on recognizing abnormalities unique to athletes is aimed toward the elite athlete—professionals, Olympians, elite marathon runners, etc. These are athletes exercising at extreme levels. However, many of the hematologic abnormalities also occur in serious amateurs, who exercise many days per week.

H&O What are the inherited hematologic abnormalities of concern to athletes?

JD Inherited hematologic abnormalities are relatively common. Coagulation disorders are not particularly relevant to a discussion of athletes because it is likely that a person with a bleeding disorder learned early on that any activity involving contact would lead to bruising or bleeding. However, von Willebrand disease and some other coagulation disorders can be subtle and may not become apparent until an athlete is playing a contact sport. If someone has been diagnosed with such a disorder, it would be useful for a coach or trainer to be aware and informed of the presence of this disorder. Much more common are hemoglobinopathies. The greatest issue is with hemoglobin S, which is responsible for sickle cell disease and sickle cell trait. Patients with sickle cell disease are typically symptomatic from a young age and are less likely to become an elite athlete, but those with sickle cell trait have a relatively asymptomatic disorder. As these patients grow up and develop physically, they do not manifest problems that would inhibit them from participating in sports. Sickle cell trait has been recognized as an important issue for collegiate and competitive athletes

by the National Athletic Trainers’ Association, which has developed a consensus statement for athletes with sickle cell trait. There is a small but real risk of sudden death for people with sickle cell trait. Most of the early data on this association came from the military, which first noted in the 1980s that young men, primarily African Americans, had an increased incidence of sudden death during high-stress physical situations, such as long marches at high altitudes or under severe heat. Although red cells in patients with sickle cell trait do not sickle under normal conditions, they can sickle under conditions of hypoxemia and dehydration, leading to rhabdomyolysis and increased risk of death.

H&O What acquired hematologic abnormalities are common to athletes?

JD The most common acquired hematologic abnormality in athletes is anemia, either with or without iron deficiency. It is clear from a number of studies that strenuous athletic activity over a prolonged period of time causes a negative iron balance, meaning that athletes lose more iron than they ingest. This negative iron balance is thought to result from destruction of red blood cells during activity, as well as from small amounts lost in the gastrointestinal tract and potentially the urinary tract. This loss tends to be exaggerated in menstruating women. There is also a group of athletes who have borderline iron deficiency without anemia but have symptoms as if they are anemic, which has led to some controversy regarding treatment recommendations. Studies have been done to assess the changes in an athlete’s iron levels and changes in that athlete’s performance over the course of a season. It is clear that athletes with borderline anemia or iron deficiency are not able to maintain the same level of physical activity over that period of time, despite training. Such anemia has been noted most frequently in runners, where it is thought that the trauma of repeatedly striking the ground can cause destruction of red cells. However, this condition has been seen in swimmers, cyclists, and other athletes performing at significant levels of intensity.

H&O Are there specific risk factors for iron deficiency in athletes?

JD Other than being a premenopausal woman, there do not seem to be specific risk factors. There is an association between iron deficiency and celiac disease, which is an

autoimmune disease that affects the mucosa of the small intestine. Celiac disease is a relatively common cause of iron deficiency because it interferes with the body's ability to absorb iron. Furthermore, current studies are assessing whether the inflammation that results from intense physical activity could also indirectly decrease the absorption of iron. A diet low in iron would put a patient at risk, but it is very uncommon for elite or collegiate athletes not to follow a well-balanced diet with adequate sources of iron.

H&O Are there treatment strategies for anemia other than good nutrition or simply avoiding strenuous activity?

JD Overall, the answer is no. There are no data on trying to increase the blood count if a patient is anemic, other than ensuring that levels of iron, vitamin B-12, and folic acid are sufficient. Otherwise, education of coaches and athletes is very important. For example, keeping athletes hydrated is a simple but effective strategy. If patients are iron-deficient or borderline iron-deficient, one strategy is iron replacement. Improvements in both hematologic parameters and athletic performance have been observed with this strategy. In the case of hemoglobinopathies, monitoring is essential, as is maximizing rest and nutrition.

H&O Do athletes come to the attention of hematologists only after exhibiting symptoms?

JD Generally, athletes come to the attention of hematologists after they exhibit symptoms of hematologic disorders. But there have also been trials evaluating the utility of testing all athletes on a collegiate cross-country running team, for example. These trials have shown that many athletes can be identified as having anemia or borderline anemia. Routine testing has not been recommended, but my institution is currently running a small trial checking hematologic parameters in female athletes, whether they have symptoms or not. We are hoping to understand how common hematologic abnormalities are and whether it would be possible to prevent a decline in performance over the course of a season. Athletes train to be in the best physical shape at the end of the season, when championship events occur, but declining iron levels can lead to a decline in performance at the end of the season.

H&O Are there any particular concerns that an athlete with a hematologic abnormality could register a "false-positive" on a test for the use of a banned substance?

JD The main cause for suspicion that an athlete is using a banned substance is a high hematocrit. However, it is possible to raise one's hematocrit by training at a high altitude

(>10,000 feet above sea level). The lower level of oxygen at that altitude causes the body to produce greater quantities of red blood cells. This effect can also be achieved through the use of erythropoietin (EPO) or similar substances. The use of EPO causes the hematocrit to edge toward the upper limit of normal or surpass it. Hemoglobinopathies or acquired hematologic disorders, on the other hand, lead to a low hematocrit. Therefore, it is unlikely that such a disorder would lead to a "false-positive" in a test for the use of banned substances. Furthermore, the urinary test developed for recombinant EPO is able to distinguish between endogenous EPO and recombinant EPO that has been introduced into the system via injection. However, a recent study demonstrated that if urine is collected immediately after extensive strenuous activity, the likelihood of finding a "false-positive" is increased, whether the athlete has a hematologic abnormality or not.

H&O Does training at a high altitude increase the risk of developing a hematologic abnormality or other problems?

JD There is a potential risk of high-altitude training leading to problems in those with inherited hematologic abnormalities. An athlete with sickle cell trait who becomes dehydrated while training at a higher altitude is at some risk of sudden death. Other abnormalities are less likely to be caused by training at high altitudes. Many elite athletes, as part of a training regimen, sleep at low altitude in tents that mimic high altitude. The use of these tents raises the hematocrit, which could enhance performance. These tents are, thus far, considered safe and relatively effective for elite athletes.

H&O Do athletes who develop malignancies pose any special challenges?

JD In general, an athlete who develops cancer becomes a patient first and foremost and the primary focus is on treating the malignancy. However, there can be modifications of therapy based on the patient's status as an elite athlete. For example, Lance Armstrong did not receive bleomycin for treatment of his germ-cell cancer because of its potential long-term lung toxicity. Athletes should receive similar considerations, as applicable, but the primary focus is on treating the malignancy effectively.

Suggested Readings

Mercer KW, Densmore JJ. Hematologic disorders in the athlete. *Clin Sports Med.* 2005;24:599-621, ix.

Mitchell BL. Sickle cell trait and sudden death: bringing it home. *J Natl Med Assoc.* 2007;99:300-305.

National Athletic Trainers Association consensus statement for athletes with sickle cell trait. Available online: <http://www.nata.org/statements/consensus/sicklecell.pdf>.