"Healthy Running"

When the Labs Come Back Abnormal!

In last month's "Healthy Running" I discussed running with fatigue or labored effort and touched on the role of laboratory testing to evaluate these problems. This month, I'll expand on lab tests to review abnormal lab results in normal healthy runners.

OK, you're thinking, that's weird. Not really. In the past few months, I had several occasions to review a variety of abnormal test results in runners who had no apparent medical problems. A couple of these people were already undergoing further evaluation for these abnormal results, and all came back confirming good health. In the interim, frustration and anxiety levels were elevated. Could this have been avoided if we know that lab results may be different in runners? As early as the 1970's, it was observed that healthy endurance athletes can have laboratory values that might indicate myocardial ischemia (inadequate oxygen to heart muscle), liver disease, kidney disease, and anemia, and physicians were advised to inquire about a person's exercise habits. To discuss this further, I'll summarize information on 3 common blood tests: blood count, liver chemistries, and muscle chemistries.

The complete blood count (CBC) measures the number of white blood cells (WBC), red blood cells (RBC), hemoglobin and hematocrit (amount and concentration of the blood's oxygen carrying protein), the size and shape of red blood cells, and the number of platelets (which play a role in normal clotting). A low RBC count or low hemoglobin/hematocrit is an indicator of anemia. As previously noted, the most common cause of anemia in distance runners is iron deficiency, due to inadequate dietary iron intake, normal iron losses (menses), or abnormal iron losses due to disease. On the other hand, though, many runners have a mild anemia that is not due to iron deficiency. A normal response to endurance training is an expansion of blood volume that results in an increase in the delivery of oxygen to exercising muscles. Blood volume increases in 2 ways: an increased production of red blood cells and increased amount of plasma (fluid). When the fluid increase is proportionately greater than the increase in blood cells, the red blood cells are "diluted" and there is a mild drop in blood count as measured by concentration (hematocrit). This is termed dilutional pseudo-anemia, has no adverse effects on training or performance, and requires no treatment. According to some sources, testing for iron deficiency is undertaken if the hemoglobin level is under 12 in women or under 14 for men and when the blood count also shows a small red blood cell size (a sign of iron deficiency). (A future article will discuss iron deficiency in further detail.)

The white blood cell count is typically normal in most runners. However, there are several literature reports of mildly low white blood cell counts in endurance runners. These low WBC were not associated with impaired ability to fight infection. At the other extreme, several studies reported mildly elevated WBC and platelets after marathon races. The rise in WBC and platelets is temporary and ultimately returns to normal in under a week's time, and may be a transient inflammatory response to tissue injury in endurance running.

To discuss liver chemistry tests (AST, ALT, LDH, bilirubin) and muscle chemistry tests (CPK, sometimes referred to as CK), keep the following in mind. CPK comes from both skeletal and heart muscle. LDH, AST, and ALT are found in both liver and muscle cells. LDH is also found in blood cells. (There will not be a pop quiz!)

LDH and bilirubin can be briefly elevated due to a phenomenon called foot-strike hemolysis. This is also well known in military recruits as march hemolysis. In this situation, the force of repeated foot strikes results in a breakdown of red blood cells in the small capillaries of the feet. The result is an elevated LDH and, particularly in ultra events, elevated bilirubin. Though testing laboratories include these tests in what are called "liver panels", these results are not associated with damage to the liver.

Of note, in foot strike hemolysis, hemoglobin released from the blood cells can pass through the kidneys and impart a temporary pink tone to urine. The important point here is "temporary" and the urine color should clear quickly with hydration.

Members of the running community are aware of elevations in CPK with endurance efforts. CPK is a traditional marker for heart muscle damage of a heart attack. Several studies of runners, including marathon runners, have demonstrated normal cardiac testing in these participants and no evidence of myocardial ischemia (compromised blood and oxygen flow to heart muscle). A study of runners of the 2002 London Marathon observed this CPK elevation and concluded, "a full history is essential before interpreting any abnormality in these indices, in order to avoid the marathon runner being mistakenly confined to a hospital bed for spurious reasons." (A future article will discuss the current reports related to running and possible cardiac injury.)

The rise in CPK is known to come from the effects of endurance running on skeletal muscle. Some articles in the medical literature call this "tissue damage" or "transient muscle injury" though some use the explicit term "exertional rhabdomyolysis". Dr. Timothy Noakes, physiologist and author of *The Lore of Running*, found that the rise in CPK is in proportion to the intensity and duration of the preceding exercise. The 2002 London Marathon study observed that the rise in CPK was higher in less trained finishers despite their slower times. There is, though, uncertainty about what is a "normal" CPK level in the exercising population. Reports from the military, where formal efforts are in place to recognize and promptly treat "rhabdo", note that the treating physician must exercise caution in evaluating the recruit (in our case, the runner) with an elevated CPK who has NO symptoms. Some in military medicine suggest that the CPK elevation should be greater than 5 times the normal value before considering rhabdomyolysis, and even this suggestion is debated. Research in this field is ongoing. For our purposes, the important point is that knowledge of a runner's training, mileage, and intensity is essential when evaluating CPK elevation. (I'll review exertional rhabdomyolysis as well in a future article.)

Of the medical reports on marathon runners, a study of finishers of the 2001 Boston Marathon is very informative. Blood samples were drawn from 37 participants who were attending the pre-marathon science symposium of the American Medical Athletic Association. These racers ran an average of 25 training miles per week, completed 5 previous marathons, and ran a qualifying race of under 4 hours in the preceding year. Samples were taken from these runners the day before the marathon and then again at 4 hours and, for 11 of the runners, 24 hours after the race. The authors reported a statistically significant change in multiple laboratory parameters at the 4-hour and 24-hour sampling points. Of interest to this discussion are the results for AST, ALT, bilirubin, and CPK (the liver and muscle related tests). All remained significantly elevated at the 24-hour point and were outside of the standard lab reference ranges for "normal" in 30% of these runners. ALT was elevated over the pre-race level but was not outside normal laboratory reference values. The authors comment that CPK and AST elevations indicate "exertional rhabdomyolysis and leakage from skeletal muscle" while ALT, which is a more specific for liver injury, showed little change. These results are very similar to a 1999 report of a 1600K ultramarathon in Australia – that's 1600K, no typo!

The authors of the Boston Marathon note that the purpose of normal laboratory reference ranges is to compare a patient's results to similar control subjects. Unfortunately, that is not the case when evaluating lab results in runners. Reference ranges in most laboratories are statistically determined from the results on various volunteer populations that do not specifically include endurance athletes and runners. The authors of the Boston Marathon study proposed a table of normal results for marathon runners, and they encouraged further study on a larger sample of marathon participants.

So what should a runner do when faced with abnormal lab result? If the labs were obtained to evaluate specific symptoms, the focus should first and foremost remain on the symptoms. Lab results related to specific symptoms should not be attributed to the effects of running until further tests

demonstrate good health. On the other hand, what if the labs were drawn "as routine"? In this situation, the runner has no symptoms, and the assumption is that the labs will assist in the early detection of problems, referred to as screening. For the labs discussed here, there is no evidence that they are valid screening tests. In this instance, abnormal labs can be understood by reviewing running mileage, intensity, training, and recent race participation. This information will guide the physician in deciding if your labs are abnormal but you are fine. At times, repeat labs after a brief period of reduced running will demonstrate a return to normal values. This typically does not require a complete cessation of running to clarify this. If the labs remain elevated but come down to values closer to reference ranges, they are very likely "your normal". To repeat these periodically, for example every 6 months, for reassurance should be decided on a case-by-case basis.

If you are having lab work done, it's helpful to discuss what the tests will be looking for and what the results might reasonably reveal. It's also helpful, in advance of the results, to discuss what steps might be taken if unexpected abnormal results return. And above all, include information about your running to insure decisions that are most relevant to you.

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