Tips from the clinical experts

Edited by Daniel M. Baer, MD

Answering your questions

High iron saturation, normal ferritin

Q What would cause a woman to have 100% iron saturation with a low normal ferritin? She was diagnosed with hemochromatosis 10 to 15 years ago and had numerous phlebotomies until her iron and ferritin were down in the normal range. (Ferritin was initially >1,000.) She has not had phlebotomies for several years, and her ferritin has remained low normal, but her iron has climbed up to 100% saturation for several repeated tests. The hematologist recommended continuing the phlebotomies indefinitely, but her hemoglobin stays about 11, and she feels fatigued.

A Hemochromatosis denotes iron-induced injury to cells of various organs. In this disorder, excessive tissue accumulation of iron occurs as a result of an increased rate of iron absorption. Hemochromatosis is an insidious disease, and evidence of tissue injury may not appear until the fifth decade of life or later. Overt disease occurs more commonly in males than in females by a ratio of 3:1. Women may be somewhat protected from iron accumulation during the reproductive years because of iron loss during menstruation and pregnancy.

Screening tests for hemochromatosis include measurement of serum iron, total iron-binding capacity (TIBC), and transferrin saturation. Serum ferritin is usually normal early in the course of the disease, becoming elevated only when iron overload has developed. In patients with genetically proven hemochromatosis, however, serum ferritin has been found to be a better predictor of iron stores as compared with serum iron, TIBC, and transferrin saturation.

Early identification of iron overload is important since removal of excess iron can prevent organ damage. Thus, in hereditary hemochromatosis, regular phlebotomy instituted before development of symptomatic disease can restore life expectancy to normal.

Treatment usually consists of removal of 500 mL of blood once weekly. Each phlebotomy removes approximately 175 mg to 225 mg of iron. Since these patients may have total iron stores of 30 to 40 grams, weekly phlebotomy may be necessary for up to three years. There is an initial decline in blood hemoglobin concentrations that return to normal within a few weeks. A persistently falling blood hemoglobin concentration, after many months of phlebotomy therapy, is the best indicator that treatment has been adequate. Serum ferritin concentrations are usually below 10 ng/mL by this time.

Re-accumulation of iron can be prevented by phlebotomy every few months. In some patients that re-accumulate iron slowly, annual monitoring of serum ferritin concentrations may be sufficient for determining when additional phlebotomies are required. In many adequately treated patients, serum iron and transferrin saturation become abnormally increased long before there is a sufficient increase in iron stores to justify repeat phlebotomy. Thus, following the completion of phlebotomy therapy, serum ferritin concentration is a better guide to determining the need for additional phlebotomy. It must be noted, however, that in patients with substantial iron overload, the correlation between serum ferritin and individual iron stores is poor.

The patient in question has a low normal ferritin and a transferrin saturation of 100%. The serum iron concentration is not given, but is presumably increased given the high transferrin saturation. A couple of scenarios might explain the results in this patient. First, given the fact that this patient has not undergone any therapeutic phlebotomy for several years, it is possible that this patient's iron stores are abnormally increased, despite her low normal ferritin concentration. Another explanation for this patient's seemingly discrepant results may be that this patient is taking vitamins fortified with iron. Iron-fortified vitamins can increase transferrin saturation to 100%. Another scenario, although less likely, that can result in increased transferrin saturation is iron contamination of the syringe or vacutainer tube used to collect the sample.

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References

Culture after antibiotic

Q Our physicians and nurses are adamant about obtaining culture specimens prior to administration of antibiotics. How long does it take from the time an antibiotic is started until the pathogen is altered? I am not asking about many hours or days after antibiotics, but up to one or two hours at the most. Sputum specimens tend to cause the most anxiety.

A I cannot give you a definitive answer to this question, partly be-

—MLO’s Tips from the Clinical Experts—

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cause it has not been subjected to scientific study. There are many variables that would affect how soon antibiotic administration would reduce the number of recoverable bacteria for a valid culture. The major variables are:

- the identity of the bacterium;
- its susceptibility to the antibiotic;
- and the speed with which the antibiotic reaches bacteriocidal concentrations in the blood and tissues.

There are many variables that would affect how soon antibiotic administration would reduce the number of recoverable bacteria for a valid culture.

The latter variable is dependent on the pharmacokinetics of the drug and its route of administration, and whether the drug is given orally or intravenously, with or without a bolus to quickly raise the blood concentration.

In short, I do not think it is a safe practice to attempt to obtain the culture after an antibiotic is started.

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Checking for platelet-poor plasma

According to the NCCLS [now known as the Clinical and Laboratory Standards Institute], coagulation samples should be platelet-poor (<10 x 10⁹/L). What is the best procedure for determining this? How many samples should be tested? What level of platelet counts should be tested? Are hematology analyzers capable of accurately counting platelets at this level?

The criteria for acceptable samples for coagulation testing include plasmas that are "platelet-poor" and free from visible hemolysis. These criteria are based on the premise that both platelets and/or red cell stroma may initiate coagulation-factor activation and result in spurious clotting test times.

First, check whether your laboratory's centrifuge complies with the NCCLS document which recommends that specimens for coagulation testing be centrifuged at 1500 x g for no less than 15 minutes at room temperature. Alternatively, high-speed centrifuges can be used. A recent study showed that a five-minute centrifugation was adequate. The study used a broad range of specimens with platelet counts ranging up to 300-800 x 10⁹/L. Acceptable post-centrifugation platelet counts were obtained using an automated hematology analyzer. Since this study used a specified cell processor, you should validate your own equipment to confirm acceptable results; in that case, between 20 and 30 specimens should be studied. A check of most currently marketed hematology analyzers indicates they can accurately count platelets at the very low levels required by NCCLS.

The partial thromboplastin time is the most sensitive indicator for any significant differences in preparation methods. This was the case in the above referenced study. A general reference of tips on coagulation testing is also listed.

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References
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