Laboratory Evaluation of Microcytic Anemia
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Anemias can be classified according to the mean corpuscular volume (MCV) into microcytic, normocytic and macrocytic anemias. A microcytic anemia is defined by a MCV of <80fL. The differential diagnosis of a microcytic anemia includes iron deficiency anemia (IDA), thalassemias, anemia of chronic disease (ACD) and sideroblastic anemias, including lead poisoning. A useful diagnostic algorithm has been recently published in the *Mayo Clinic Proceedings*.1
Initial evaluation begins with interpretation of the complete blood count (CBC) and peripheral smear examination. The red blood cell count is usually decreased in IDA and may be normal or increased in thalassemias. The red cell distribution width, an indicator of variation in cell size, is increased in IDA and usually normal in thalassemias and ACD. IDA cases will commonly have an associated thrombocytosis. On peripheral blood smear examination, patients with IDA have prominent anisopoikilocytosis (variation in size and shape) and occasional pencil cells. The peripheral blood of patients with thalassemia and lead poisoning may show basophilic stippling.

Following a review of the CBC and peripheral blood smear, the proposed diagnostic algorithm advises obtaining a serum ferritin level. Low serum ferritin levels are seen in IDA. Ferritin has a high sensitivity and specificity for IDA when a cut-off of $\leq 30$ µg/L is used. Though ferritin is an acute phase reactant, studies
have demonstrated that the majority of patients with concomitant IDA and a chronic inflammatory or liver disease will be classified as iron deficient employing these criteria.\textsuperscript{2,3} In the small subset of IDA patients with normal serum ferritin levels, it has been suggested that serum transferrin receptor, a more recently developed iron study, may be helpful. Serum transferrin receptor levels are increased in IDA and normal in ACD. (\textit{For more information on serum transferrin receptor, see NewsPath® Archives Spring 2004: “The diagnostic role of soluble transferrin receptor in patients with anemia”}.) Many authors no longer recommend obtaining other iron studies, such as serum iron and total iron binding capacity (TIBC), for the diagnosis of IDA.\textsuperscript{1}

If IDA is ruled out with a normal or elevated serum ferritin level, it is important to establish the duration of the anemia.\textsuperscript{1} Patients with life-long microcytic anemia should be evaluated with hemoglobin electrophoresis for microcytic hemoglobinopathies, including β- and α-thalassemia. β-Thalassemia trait is diagnosed with an elevated hemoglobin A\textsubscript{2} level of >3.5%.\textsuperscript{4} As quantification with electrophoresis is inherently imprecise, it is recommended that hemoglobin A\textsubscript{2} levels be confirmed with high performance liquid chromatography or microcolumn chromatography.\textsuperscript{4} Patients with α-thalassemia trait will have a normal electrophoretic pattern; thus the diagnosis is made based on family history and exclusion of other entities. Genetic testing is available for confirming deletions in the α-globin chains.

The diagnosis of ACD should be considered in patients with acquired microcytic anemia, in whom IDA has been ruled out.\textsuperscript{1} ACD is diagnosed with normal to elevated serum ferritin and normal to decreased serum iron levels. In the appropriate clinical setting, especially the pediatric population, lead poisoning should also be considered as a cause of an acquired microcytic anemia.

In summary, the evaluation of a microcytic anemia begins with a CBC and peripheral blood review as well as a serum ferritin level to rule out IDA. Hemoglobin electrophoresis and lead levels may be clinically warranted.

Bibliography