What is the appropriate management for a 1-year-old infant with anemia?

Evidence-based answer
Iron deficiency is the most common cause of anemia in an asymptomatic 1-year-old infant, so either further laboratory evaluation (eg, serum ferritin [SF] or reticulocyte hemoglobin concentration [CHr]) or empiric treatment with oral iron are appropriate (SOR: B, cohort studies and expert opinion).

Evidence summary
In 2010 the American Academy of Pediatrics (AAP) committee on nutrition published recommendations for the diagnosis and treatment of iron deficiency anemia (IDA) in infants and young children. They defined anemia as a hemoglobin (Hgb) concentration of >2 standard deviations below the mean for age and sex. For toddlers (children between the ages of 12 and 35 months), this value is <11.0 g/dL.

The AAP noted, based on data from the 1999–2000 National Health and Nutrition Examination Survey (NHANES), that anemia was present in 5.1% of US toddlers, with IDA present in 2.1%. NHANES defined IDA as anemia plus abnormal values for at least 2 of the following 3 factors: SF <10 mcg/L, erythrocyte protoporphyrin (EP) >1.4 micromol/L red blood cells, or transferrin saturation (SAT) <10%. The committee suggested clinicians test anemic infants using either SF plus C-reactive protein (CRP), or CHr alone.

Accuracy of CHr versus SF for diagnosing IDA
The committee noted that CHr might be more accurate than SF for diagnosing IDA, citing a 1999 retrospective laboratory analysis of blood samples from 210 children (mean age, 2.9 years), of whom 11% had IDA, defined as a serum SAT of <20% (used as the gold standard). Compared with nonanemic children, children with IDA had a significantly lower mean CHr level (24 vs 27 pg; P<.001) and no significant difference was found in SF levels between the groups (32 vs 34 mcg/L; P=.7). When plotted as a receiver operating characteristic (ROC), the area under the curve for CHr was 0.78 compared with 0.57 for SF (P=.04). (A test with 100% sensitivity and 100% specificity has an ROC area of 1, whereas a test that is 50% sensitive and 50% specific has an ROC area of 0.5.) Using a cutoff of 26 pg, CHr was 83% sensitive and 75% specific for diagnosing IDA.
In another prospective cohort trial of 344 children aged 2 to 16 years, researchers examined the effectiveness of various measures of iron nutrition in predicting response to iron therapy. Patients received iron (3 mg/kg per day) for 8 to 12 weeks and the investigators measured pre- and posttreatment SAT, SF, and EP. Due to a high dropout rate, only 277 completed the study.

Response rates were 43% (Hgb increase >1.0 g/dL), 26% (Hgb increase 0.5–1.0 g/dL), and 31% (Hgb increase <0.5 g/dL; no response). Before treatment, 25% of patients had Hgb values more than 2 SD below the mean. After treatment, this number was only 5%. All 3 tests performed poorly in predicting response to iron therapy (TABLE). 5

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR–</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF &lt;10 mcg/L</td>
<td>63%</td>
<td>45%</td>
<td>1.1</td>
<td>0.8</td>
</tr>
<tr>
<td>SAT &lt;16%</td>
<td>39%</td>
<td>65%</td>
<td>1.1</td>
<td>0.9</td>
</tr>
<tr>
<td>EP &gt;3 mcg/g Hgb</td>
<td>42%</td>
<td>61%</td>
<td>1.1</td>
<td>1</td>
</tr>
</tbody>
</table>

EP = erythrocyte protoporphyrin; Hgb = hemoglobin; LR+ = likelihood ratio of a positive test; LR– = likelihood ratio of a negative test; SAT = transferrin saturation; SF = serum ferritin.

Nevertheless, the AAP committee noted that SF might be more available than CHr and an SF concentration of <10 mcg/L could be used to diagnose IDA. For SF values >10 mcg/L, the committee recommended checking serum CRP level, as SF could be falsely elevated in patients with an inflammatory disorder. As an alternative for patients with mild anemia (Hgb 10–11 g/dL), the AAP committee suggested clinicians could treat presumptively with oral iron and monitor the response after 1 month. An increase of Hgb of >1 g/dL over 1 month suggests IDA.

Empiric treatment
Evidence supporting empiric treatment comes mainly from studies done in the 1980s. A prospective cohort trial screened 1,128 1-year-old infants for anemia and identified 278 with an Hgb concentration of <11.5 g/dL. These infants received oral iron 3 mg/kg per day (as ferrous sulfate) and then had their Hgb retested after 3 months.

Of the 188 infants who completed the trial, 75 had an initial Hgb less than 11 g/dL and, of these, 34 (45%) responded to iron (defined as an increase in Hgb concentration of ≥1 g/dL after iron treatment). A total of 113 infants had an initial Hgb between 11 and 11.5 g/dL and, of these, 32 (28%) responded to iron.

In a related cohort study of the same patients above, the investigators evaluated the effectiveness of 4 laboratory tests—mean corpuscular volume (MCV), EP, SAT, and SF—for diagnosing IDA. No single test helped predict iron response. The authors did not report sensitivity and specificity, but noted that for iron responders, the percent who had abnormal values was 33% for MCV <70 fl, 42% for EP >3 mcg/g Hgb, 52% for SAT <10%, and 29% for SF <10 mcg/L. Among patients with at least 1 abnormal test, 45% responded to iron. Among patients with abnormal findings in all 4 tests, 83% responded to iron. Conversely, 90% of iron responders had at least 1 abnormal test, and only 25% had 4 of 4 abnormal.

REFERENCES