

## **Do not order red blood cell folate levels at all. In adults, consider folate supplementation instead of serum folate testing in patients with macrocytic anemia**

Folate is a water-soluble B vitamin essential for the synthesis of DNA and for converting homocysteine to methionine.

In patients with inadequate folate intake, the earliest sign is a decline in serum folate levels, followed by a fall in RBC folate levels. Only weeks later do macrocytosis, megaloblastic bone marrow, and finally anemia occur.

The most common indication for folate testing is anemia, either with or without macrocytosis. Despite the link between folate deficiency and megaloblastic anemia, >85% of patients evaluated for folate deficiency have normocytic or microcytic anemia. In addition, a study found that 30% of all folate testing was performed not as part of an anemia workup but in the evaluation of other comorbidities (e.g., dementia and altered mental status) that are not causally linked to folate deficiency.

The lack of a gold standard limits the ability to fully quantify the sensitivity and specificity of either serum or RBC folate testing, though falsely low and high serum folate results can be seen.

Falsely low serum levels do not necessarily reflect tissue stores and do not represent true folate deficiency. There is no clear consensus on the level of serum folate that indicates deficiency. Serum folate measurement provides equivalent information to red cell measurement, routine red cell folate testing is not necessary.

Before the fortification era, a study has shown that only 1.9% of patients had low serum folate, and another one showed a rate of folate deficiency of 0.3%. A similar study found just 0.4% of patients with low serum folate levels. In a Canadian study after implementation of folate fortification showed low serum folate (<6.8 nmol/L) and RBC folate (<417 nmol/L) levels in 0.5% and 0.7% of patients, respectively.

When examining only patients with macrocytic anemia, the rates of folate deficiency are only slightly higher than the general population. In 2 studies, each of the 2 studies of inpatients uncovered just 1 patient with macrocytic anemia and concomitant low serum or RBC folate levels. Other studies reveal rates of serum folate deficiency in patients with macrocytic anemia and macrocytosis of 2.8% and 1%, respectively, and RBC folate deficiency rates in patients with macrocytosis of 1.8%.

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