INDICATIONS FOR TESTING
Suspected hemoglobinopathy

ORDER
Microcytosis (MCV <80 fL)

ORDER
CBC with platelet count and automated differential Blood smear with interpretation

ORDER
Ferritin testing

Low

Abnormal results on peripheral smear

Indeterminate

Target cells
Sickle cells
Heinz bodies

RULE OUT
Splenectomy, splenic atrophy

CONSIDER
HbH disease likely (HbSS, HbSC, HbSE, HbS/β thalassemia, HbS/Hb Lepore)
Consider G6PD deficiency, unstable hemoglobinopathies, HbH disease

CONSIDER
• Genetic testing
• Isopropanol heat stability testing
• G6PD enzyme testing
• Evaluation for α thalassemia

ORDER
Hb evaluation

CONSIDER
• Hb evaluation
• Sickle cell solubility testing
• Beta globin (HBB) gene sequencing

Pathogenic variant detected

β thalassemia confirmed

Non-HbS/C/E

HbA2 elevated

β thalassemia likely

ORDER
Beta globin (HBB) gene sequencing

Pathogenic variant detected

β thalassemia confirmed

HbS/C/E

Other variant Hb

ORDER
Beta globin (HBB) gene sequencing

Pathogenic variant detected

Performed

HbS, HbC, or HbE

Sickle cell disease likely

ORDER
Sickle cell solubility testing

Positive results

Pathogenic variant detected

α thalassemia

PERFORM
Sequence analysis

Pathogenic variant detected

α thalassemia

β thalassemia confirmed

PERFORM
Deletion/duplication analysis

Pathogenic variant detected, but suspicion persists

α thalassemia

No variant detected, but suspicion persists

α thalassemia

Abbreviations
G6PD Glucose-6-phosphate dehydrogenase
Hb Hemoglobin
MCV Mean corpuscular volume

*See the Hemolytic Anemias Testing Algorithm for additional possible abnormal findings.
*Test reflex pattern follows algorithm until a diagnosis is reached.
*Common deletions are -α3.7, -α4.2, -α20.5, -SEA, -MED-I, -FIL, and -THAI.