INDICATIONS FOR TESTING
Patient with anemia and evidence of hemolysis

ORDER
- CBC with Platelet Count and Automated Differential
- Reticulocytes, Percent & Number
- Lactate Dehydrogenase, Serum or Plasma
- Haptoglobin
- Bilirubin, Total, Serum or Plasma

Presence of the following may provide clues to the etiology of the anemia
- Increased reticulocyte count
- Abnormal peripheral smear
  - Polychromasia, spherocytes, schistocytes, sickle cells, stomatocytes, Heinz bodies, basophilic stippling, unusual red cell inclusions, and agglutination
Note: lack of any of the above does not rule out hemolytic anemia

Proceed based on above findings

Consider environmental factors, mechanical cardiac valve, vasculitis, malignant hypertension — no

increased D Dimer decreased fibrinogen → DIC

Consider
- DIC
- TTP
- HELLP
- HUS

yes

ADAMTS13 activity → TTP

decreased platelets ← Suggests microangiopathic RBC destruction ← Schistocytes

Sickle cells → Consider Sickle cell disease – diverse genotypes: SS, SC, SE, Sβ thalassemia, S Lepore → HPLC

Consider malaria, bartonella (oroya fever), babesia ← Unusual red cell inclusions

Basophilic stippling — acquired — no → Congenital 5' nucleotidase deficiency → 5' nucleotidase testing

acquired — yes → Consider lead poisoning → Serum lead level

Consider molecular testing ← no

Direct Coombs (Anti-Human Globulin) ← yes

acquired ← Osmotic Fragility, Erythrocyte (usually positive) ← Consider RBC membrane disorder (hereditary spherocytosis, hereditary elliptocytosis, autoimmune hemolysis) ← Spherocytes, pyropoikilocytes, elliptocytes or acanthocytes

Polychromasia only with or without platelet decrease → Consider PNH → Paroxysmal Nocturnal Hemoglobinuria Panel, RBC and WBC

IgG+ — no → Recluse spider venom, clostridium sepsis

IgG+ — yes → Autoimmune hemolytic anemia (consider drug induced, hemolytic disease of the newborn, autoimmune disease)

+C3 → Cold agglutinins disease, paroxysmal cold hemoglobinuria (PCH) → Confirm PCH with Donath Landsteiner testing

Polychromasia without other reproducible morphologic abnormality → Consider
- Pyruvate kinase deficiency
- Hexokinase deficiency
- Other enzyme defects
→ Consider one or more of the following tests
- Pyruvate kinase
- Hexokinase
- Glucose phosphate isomerase

Cold agglutinins disease ← Cold agglutinins testing ← + for complement ← Direct Coombs (Anti-Human Globulin) ← Consider cold agglutinins disease ← Agglutination

Heinz bodies → Consider
- Glucose-6-Phosphate dehydrogenase deficiency
- Unstable hemoglobin defects
- Glutathione metabolism defects
- Hemoglobin H disease
→ Consider one or more of the following tests
- Isopropanol heat stability testing
- Glucose-6-Phosphate Dehydrogenase (G6PD) 2 Mutations
- Enzymes of glutathione cycle
→ For hemoglobin disorders, consider HPLC, genetic testing