BENIGN HEMATOLOGY
TESTING TO DIAGNOSE AND MANAGE HEMOGLOBIN AND RED BLOOD CELL ABNORMALITIES
PROVIDING ACCURATE DIAGNOSES AND INTERPRETATIONS WITH AN EMPHASIS ON CLINICAL SIGNIFICANCE

The Mayo Clinic Metabolic Hematology Laboratory is dedicated to providing accurate diagnoses and interpretations with an emphasis on its clinical significance for your patients. Our cases are signed out by board-certified hematopathologists in the context of comprehensive, algorithmic panels, which guide laboratory testing choices to address a specific clinical question.

Because the incidence of distinct red blood cell disorders varies from common to very rare, these reflexive algorithms guide appropriate testing and minimize unnecessary assays. For hematologists requiring only a single test in the process, many components of these evaluations can also be ordered individually, and our laboratory welcomes input regarding differential diagnoses and test utilization.

BENIGN HEMATOLOGY EVALUATIONS

**HEMOLYTIC ANEMIA EVALUATION (MAYO ID: HAEVP)**
Incorporates all testing related to nonimmune hemolytic anemia, including assays for unstable hemoglobin variants, red blood cell enzyme abnormalities, and red blood cell membrane disorders. It assumes a previous negative direct antiglobulin test (DAT) result.

**HEMOGLOBIN ELECTROPHORESIS CASCADE (MAYO ID: HBELC)**
A reflexive evaluation for the identification and confirmation of hemoglobin variants and beta thalassemias. The degree and complexity of testing is determined by the nature of the case, including the rarity of the hemoglobin variants present. More complex thalassemic and/or hemoglobinopathy conditions are usually best evaluated under the thalassemia and hemoglobinopathy evaluation (THEVP).
THALASSEMA AND HEMOGLOBINOPATHY EVALUATION (MAYO ID: THEVP)
Evaluates patients who have unexplained microcytosis, suspected alpha thalassemia, or complex hemoglobinopathy/thalassemia disorders that are undetectable by electrophoresis alone. This evaluation will also detect hemoglobin variants responsible for microcytosis, such as hemoglobins E or Lepore.

ERYTHROCYTE ENZYME EVALUATION (MAYO ID: EEEVP)
A focused evaluation of hemolytic anemias caused by underlying red blood cell (RBC) enzyme defects. This evaluation is useful for cases in which an enzymopathy is suspected.

NEUROLOGIC ENZYME EVALUATION (MAYO ID: NEEVP)
Evaluates relevant RBC enzymes for cases where the clinical history and physical examination suggest an associated neurologic or musculoskeletal defect in addition to hemolytic anemia.

HEREDITARY SPHEROCYTOSIS EVALUATION (MAYO ID: HSEP)
Links the osmotic fragility (FRAG) test with the eosin-5-maleimide (EMA) band-3 binding test by flow cytometry studies. The FRAG test and the EMA binding test are always performed, as abnormal results for both have a very high positive predictive value for hereditary spherocytosis. Also, because RBC membrane disorders can have variable FRAG and EMA binding test results, an evaluation incorporating both studies is important for a more complete interpretation in suspected cases.

METHEMOGLOBINEMIA EVALUATION (MAYO ID: MEVP)
Evaluates patients with unexplained cyanosis or when methemoglobinemia or pesticide exposure is suspected. Acquired and congenital methemoglobinemia can be distinguished using this panel including methemoglobin reductase (METR) deficiency and hemoglobin M variants.

ERYTHROCYTOSIS EVALUATION (MAYO ID: REVP)
Evaluates patients with unexplained erythrocytosis, assuming a previous negative JAK2 V617F result. This comprehensive, but reflexive, evaluation includes an oxygen dissociation curve, which is pivotal in the differential diagnosis of erythrocytosis.

HEREDITARY ERYTHROCYTOSIS MUTATIONS (MAYO ID: HEMP)
Recommended for patients presenting with lifelong erythrocytosis, usually with a positive family history of similar symptoms, in whom a high-oxygen hemoglobin variant has been excluded by a normal p50 result, electrophoresis, and/or alpha and beta globin gene sequencing (see REVP and HBELC). Polycythemia vera should also be excluded prior to testing because it is much more common than hereditary erythrocytosis and can present even in young patients. The HEMP assay is a reflex test for the REVP and should not be ordered if REVP is ordered.

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (MAYO ID: PLINK)
Enables detection of small paroxysmal nocturnal hemoglobinuria (PNH) populations in early PNH as well as in patients with bone marrow failure syndromes (aplastic anemia and myelodysplasia). PNH is a rare but progressive and debilitating hematopoietic stem cell disorder characterized by hemolytic anemia, thrombosis, and underlying bone marrow failure. The underlying defect is absence of glucose phosphate isomerase (GPI)-linked proteins on the cell surface due to a genetic enzymatic defect. The Mayo Clinic Cell Kinetics Laboratory is one of a very few laboratories in the United States that provides a high-sensitivity PNH assay following guidelines by the International PNH Group.
When Virgil Fairbanks, M.D., established the Metabolic Hematology Laboratory at Mayo Clinic in 1965, collaborations with his mentor, Ernest Beutler, M.D., and colleague Max Wintrobe, M.D., Ph.D., laid the foundation for high-quality esoteric testing of hemoglobin and red blood cell disorders.

In this tradition, James Hoyer, M.D., and Jennifer Oliveira, M.D., currently lead a team with unparalleled depth and breadth of expertise in hemoglobin and red cell disorders, from the most common to the rarest. The Mayo Clinic Metabolic Hematology Laboratory has identified more than 400 hemoglobin variants and has also described more than 30.

Importantly, the lab’s diagnostic genetic testing results are evaluated by a dedicated board-certified genetic counselor with extensive expertise in this area. This genetics-trained allied health professional specializes in the translation of genetic information into a clinical context, focusing on the utility and limitations of specific genetic testing methods, familial genetic testing strategy, genetic variant interpretation, and the reproductive risks associated with a test finding.

**CONSULTANTS AND GENETIC COUNSELING STAFF**

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