Hereditary Spherocytosis

Indications for Ordering

Confirms diagnosis of hereditary spherocytosis when hemolytic anemia and spherocytes are present

Test Description

Test methodology
Red blood cell (RBC) surface protein band 3 staining with eosin-5-maleimide (EMA) analyzed by flow cytometry

Clinical validation
Validated against the clinical diagnosis of hereditary spherocytosis supported by osmotic fragility and/or molecular testing

Tests to Consider

Primary test
RBC Band 3 Protein Reduction in Hereditary Spherocytosis
2008460
• Confirms diagnosis

Related test
Osmotic Fragility, Erythrocyte 2002257
• Functional testing of RBC sensitivity to osmotic stress
• Do not use to distinguish between spherocytes in hereditary spherocytosis and acquired autoimmune hemolytic anemia

Disease Overview

Prevalence – 1/2,000 in northern Europeans

Symptoms
• Hemolytic anemia
  o Pallor
  o Fatigue
  o Jaundice
  o Splenomegaly
• Kernicterus
• Pigmented gallstones

Diagnostic issues
Depending on severity of symptoms, diagnosis of hereditary spherocytosis can rule out other causes of hemolytic anemia
• Examination of a peripheral blood smear is a quick and easy initial screen

• Osmotic fragility can confirm compromised integrity to osmotic stress
• RBC band 3 protein testing is a very sensitive and specific test for the diagnosis of hereditary spherocytosis

Physiology
RBC band 3 protein is a major structural protein of RBCs
• Reduction in the amount of band 3 fluorescence after binding with EMA correlates with spherocytosis

Genetics

Genes – ANK1, EPB42, SLC4A1, SPTA1, SPTB

Inheritance
• Autosomal dominant –75%
• Autosomal recessive –25%

Penetrance – variable

Structure/function
• Chromosomal location – 17q21.31
• Provides structure for the red cell cytoskeleton

Test Interpretation

Sensitivity/specificity
• Clinical sensitivity – 93%
• Analytical sensitivity/specificity – unknown

Results
• Normal
  o Normal staining of band 3 protein with EMA does not suggest hereditary spherocytosis
• Abnormal
  o Decreased staining of band 3 protein with EMA provides evidence for hereditary spherocytosis
  o Three rare disorders may be associated with a positive result for this test
    ▪ Congenital dyserythropoietic anemia type 2
    ▪ Southeast Asian ovalocytosis
    ▪ Hereditary pyropoikilocytosis
• Equivocal
  o Unclear whether the level of band 3 protein staining is normal
  o Insufficient evidence to support or negate a diagnosis of hereditary spherocytosis

Limitations
Not typically used as a screening test, but has been proposed as a screening test by many authorities