Hereditary Spherocytosis

Indications for Ordering

Use to confirm 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

- Use to confirm diagnosis of hereditary spherocytosis when hemolytic anemia and spherocytes are present

Related Test

Osmotic Fragility, Erythrocyte 2002257

- Functional testing of RBC sensitivity to osmotic stress

Disease Overview

Prevalence: 1/2,000 in northern Europeans

Symptoms

- Hemolytic anemia
  - Pallor
  - Fatigue
  - Jaundice
  - 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%

Penetration: 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
  - Normal staining of band 3 protein with EMA does not suggest hereditary spherocytosis
- Abnormal
  - Decreased staining of band 3 protein with EMA provides evidence for hereditary spherocytosis
  - Three rare disorders may be associated with a positive result for this test
    - Congenital dyserythropoietic anemia type 2
    - Southeast Asian ovalocytosis
    - Hereditary pyropoikilocytosis
- Equivocal
  - Unclear whether the level of band 3 protein staining is normal
  - 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