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
  - 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%

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
  - 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