Factor XIII Deficiency

Indications for Ordering

**Factor XIII Activity**
- Preferred first-line test to diagnose inherited or acquired factor XIII (FXIII) deficiency
- Appropriate for evaluation of individuals with a bleeding disorder presenting with normal prothrombin time (PT), partial thromboplastin time (PTT), and platelet count test results
- Monitor therapy in individuals being treated for FXIII deficiency
- To confirm abnormalities identified in the qualitative FXIII assay (clot solubility test)

**Factor XIII, Qualitative, with Reflex to Factor XIII 1:1 Mix**
- Most useful if severe FXIII deficiency is suspected (<1% of normal activity)
- To distinguish between FXIII deficiency and a FXIII inhibitor

Test Description

**Factor XIII Activity**
- Chromogenic assay
  - Consumption of NADPH is measured spectrophotometrically
    - Decrease in absorbance is directly proportional to FXIII activity
  - Can quantitate factor activity as low as 5% of normal

**Factor XIII, Qualitative, with Reflex to Factor XIII 1:1 Mix**
- Qualitative solubility test
  - If clot lysis occurs in the initial testing, factor XIII 1:1 mix added

Tests to Consider

**Primary tests**
- Factor XIII Activity 2006182
  - First-line test to diagnose FXIII deficiency
  - More specific than qualitative assays for FXII
- Factor XIII, Qualitative, with Reflex to Factor XIII 1:1 Mix 2002819
  - Most useful for acquired or severe FXIII deficiency testing
  - Abnormal results should be confirmed with quantitative testing

Disease Overview

**Incidence** – ~1/1 million

**Inherited** – rare autosomal recessive FXIII deficiency

**Symptoms**
- FXIII deficiency
  - Suspect if coagulation screening tests are normal (eg, PT, PTT, platelet count, and thrombin time)
  - Two forms – inherited, acquired
    - Inherited
      - Delayed postsurgical or traumatic bleeding
      - Umbilical cord bleeding
      - Central nervous system hemorrhage
      - Poor wound healing
      - Recurrent miscarriages
    - Acquired
      - Often presents as severe deficiency
      - Caused by decreased production or increased consumption of FXIII
      - Associated with a number of medical conditions
        - Major surgery
        - Thrombosis
        - Inflammatory bowel disease
        - Liver cirrhosis
        - Sepsis
        - Disseminated intravascular coagulation
      - Associated with autoantibodies that form against FXIII
    - Associated with autoimmune disease
    - Malignancy
    - Drugs
      - Isoniazid
      - Penicillin
      - Phenytoin
      - Idiopathic

**Physiology**
- FXIII is essential for normal hemostasis
- FXIII covalently crosslinks fibrin polymers to form a stable fibrin clot
- FXIII circulates in the plasma as tetramer of 2 catalytic A subunits and 2 carrier B subunits
- Activated by thrombin and calcium into FXIIla
  - Involved in wound repair, cytoskeletal remodeling, phagocytosis, placental attachment, and inflammatory processes
Test Interpretation

Results

• Activity test
  o Reference interval – FXIII activity, 69-143%
  o Severe bleeding usually does not occur until FXIII level <1-3%
  o Mild or moderate deficiencies may be associated with increased bleeding risk in some cases

• Qualitative reflex test
  o No lysis within 24 hours
    ▪ Clot lysis only occurs in samples with <1% of normal activity

Limitations

• Activity test
  o A low FXIII level does not distinguish deficiency from a low value due to FXIII autoantibodies
  o False-negative (artificially increased) results
    ▪ Lipemic plasma
    ▪ Elevated ammonia
    • Potential interference can be minimized by obtaining a parallel plasma blank measurement to correct for endogenous ammonia in the individual sample
  o False-positive (artificially decreased) results
    ▪ Icteric plasma

• Qualitative reflex test
  o Normal results do not exclude deficiency
  o Does not identify
    ▪ Mild or moderate deficiency
    ▪ Heterozygous carriers for FXIII deficiency
    ▪ Treated, yet deficient, individuals
    ▪ Individuals with weak FXIII inhibitors that do not decrease FXIII activity to <1% of normal