Hemolytic Anemias Testing

**INDICATIONS FOR TESTING**
Patient with anemia and evidence of hemolysis

**ORDER**
- CBC with Platelet Count and Automated Differential
- Reticulocytes
- Lactate Dehydrogenase (LDH)
- Haptoglobin
- Bilirubin

**Presence of the following may provide clues to the etiology of the anemia**
- Increased reticulocyte count, LDH, bilirubin
- Decreased haptoglobin
- Abnormal peripheral smear
  - Polychromasia, spherocytes, schistocytes, sickle cells, stomatocytes, Heinz bodies, basophilic stippling, unusual red cell inclusions, and agglutination

**Note:** Lack of any of the above does not rule out hemolytic anemia

**DIC**
- Increased
- Normal Clinical presentation consistent with TMA

**ORDER**
- D-Dimer

**Pregnant**
- Consider HELLP

**ADAMTS13 Reflex Panel or ADAMTS13 Activity**
- If infection suspected, consider malaria, bartonella (oroya fever), babesia

**TTP**
- Atypical HUS
- Classical HUS

**ORDER**
- RBC Band 3 Protein Reduction in Hereditary Spherocytosis
  - Consider molecular testing
  - Acquired

**RBC Membrane Disorder**
- Direct Coombs (Anti-Human Globulin)
  - IgG+
    - Yes
      - +C3
        - Cold agglutinins disease, paroxysmal cold hemoglobinuria (PCH)
          - Confirm PCH with Donath Landsteiner testing
    - No
      - Recluse spider venom, clostridium sepsis
        - Autoimmune hemolytic anemia (consider drug induced, hemolytic disease of the newborn, autoimmune disease)

**Spherocytes, pyroplastocytes, elliptocytes or acanthocytes**
- Consider cold agglutinins disease
- ORDER Direct Coombs (Anti-Human Globulin)
  - Positive for complement
    - Yes
      - Cold agglutinins testing
        - Cold agglutinins disease
    - No
      - Warm autoimmune hemolytic anemia

**ORDER**
- Microangiopathic RBC destruction
  - Schistocytes, thrombocytopenia
    - Sickle cells
      - Consider Sickle cell disease – diverse genotypes: SS, SC, SE, Sβ thalassemia, S Lepore
        - High-performance liquid chromatography (HPLC)
    - Polychromasia only with or without platelet decrease
      - Acquired
        - Basophilic stippling
          - Yes
            - Consider lead poisoning
          - No
            - Consider 5’ nucleotidase testing
        - Unusual red cell inclusions
          - Consider PNH
            - PNH, High Sensitivity, RBC and WBC testing
    - Polychromasia without other reproducible morphologic abnormality
      - Consider cold agglutinins disease
      - ORDER Direct Coombs (Anti-Human Globulin)
        - Positive for complement
          - No
            - Consider one or more of the following tests
              - Pyruvate kinase deficiency
              - Hexokinase deficiency
              - Other enzyme defects
          - Yes
            - Cold agglutinins testing
              - For hemoglobin disorders, consider HPLC, genetic testing
      - Agglutination
      - Consider cold agglutinins disease

**Microangiopathic Hemolytic Anemia (TMA)**
- Consider DIC
  - TTP
  - HELLP
  - HUS
  - aHUS
  - Mechanical cardiac valve
  - Vasculitis
  - Malignant hypertension
  - Decreased protein C, S, anti-Xa, factor 3 activity

**Increased**
- Reduced in RBC Band

**INDICATIONS FOR TESTING**
- Due to recent changes in the algorithm
- Genetic testing
- Consider drug induced
- Drug reactions
- Drug-induced hemolytic anemia
- Consider hereditary spherocytosis
- Consider previously diagnosed autoantibodies
  - Warm autoimmune hemolytic anemia
  - Cold autoimmune hemolytic anemia
  - Autoimmune disease
  - Consider drug induced
  - Drug reactions
  - Drug-induced hemolytic anemia
- Consider hereditary spherocytosis
- Consider previously diagnosed autoantibodies
  - Warm autoimmune hemolytic anemia
  - Cold autoimmune hemolytic anemia
  - Autoimmune disease

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