ARUP Consult

Hemolytic Anemias Testing

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Abbreviations

aHUS	Atypical hemolytic uremic syndrome
DIC	Disseminated intravascular coagulation
EIA	Enzyme immunoassay
G6PD	Glucose-6-phosphate dehydrogenase
HELLP	Hemolysis, elevated liver enzymes, low platelet count
HHA	Hereditary hemolytic anemia
HUS	Hemolytic uremic syndrome
IgG	Immunoglobulin G
PCH	Paroxysmal cold hemoglobinuria
PNH	Paroxysmal nocturnal hemoglobinuria
RBC	Red blood cell
TMA	Thrombotic microangiopathy
TTP	Thrombotic thrombocytopenic purpura
WBC	White blood cell

INDICATIONS FOR TESTING

Signs of anemia hemolysis:
- Elevated reticulocyte count, lactate dehydrogenase, and bilirubin
- Low haptoglobin

ORDER Direct Coombs (Anti-Human Globulin)

- C3 positive → Cold agglutinin disease or PCH → Confirm PCH with Donath Landsteiner testing
- Negative → **PERFORM** Peripheral smear
- IgG positive → Yes → Autoimmune hemolytic anemia (consider drug induced, hemolytic disease of the newborn, autoimmune disease)
- IgG positive → No → Recluse spider venom, clostridium sepsis

Consider Hereditary Hemolytic Anemia Cascade if HHA is suspected based on family history and/or peripheral smear

PERFORM Peripheral smear

- Agglutination → **CONSIDER** Cold agglutinins disease
- Schistocytes, thrombocytopenia → Microangiopathic RBC destruction **CONSIDER** DIC, TTP, HELLP, HUS, aHUS, mechanical cardiac valve, vasculitis, malignant hypertension → **ORDER** D-Dimer
  - Normal AND Clinical presentation consistent with TMA → **ORDER** ADAMTS13 Reflex Panel or ADAMTS13 Activity **OR** *E. coli* Shiga-like Toxin by EIA (depending on presentation)
    - ADAMTS13 activity <10% → TTP
    - Normal → aHUS
    - Positive Shiga toxin and history of diarrheal illness → Classical HUS
  - Pregnant → **CONSIDER** HELLP
  - Increased → DIC
- Sickle cells → Consider sickle cell disease (diverse genotypes): SS, SC, SE, Sβ thalassemia, S Lepore → Hemoglobin evaluation
- Basophilic stippling → Acquired
  - No → Congenital 5'nucleotidase deficiency → Consider 5'Nucleotidase testing
  - Yes → Consider lead poisoning → Consider Lead, Blood (Venous)
- Polychromasia only with or without platelet decrease → **CONSIDER** PNH → **ORDER** PNH, High Sensitivity, RBC and WBC
- Polychromasia or no significant morphologic abnormality → **CONSIDER** RBC enzyme testing (eg, G6PD, pyruvate kinase, etc.) AND Hemoglobinopathies and thalassemias
  - Negative → Suspect congenital dyserythropoietic anemia
- Spherocytes, pyropoikilocytes, or acanthocytes → **CONSIDER** RBC membrane disorder (hereditary spherocytosis, hereditary elliptocytosis, autoimmune hemolysis)
  - **CONSIDER** RBC Band 3 Protein Reduction AND Osmotic Fragility, Erythrocyte
    - Positive → May consider molecular testing (Hereditary Hemolytic Anemia Panel Sequencing)

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