**Paroxysmal Cold Hemoglobinuria (PCH)**

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I. Clinical Features
   A. Incidence and associations
      • Self limiting, acquired hemolytic anemia, typically affects children following viral or bacterial infection
      • Historically PCH was a chronic disease, most commonly found in adults with syphilis
   B. Pathogenesis and presentation
      • Caused by an IgG autoanti-P antibody (Donath-Landsteiner antibody), which binds to RBCs at cold temperatures, and fixes complement on the RBC membrane. However RBCs are only lysed upon warming to 37\textdegree C when complement cascade proceeds to completion.
      • Although usually titer is < 64, autoantibody is potent, can cause sudden onset of severe anemia and fulminant intravascular hemolysis, may be accompanied by high fever, chills, back and leg pain, dark urine.
      • Lab tests consistent with intravascular hemolysis: hemoglobinemia, hemoglobinuria, high LDH, unconjugated bilirubin, decreased haptoglobin
      • Peripheral smear may show anisopoikilocytosis, spherocytes, polychromasia, RBC agglutination, and erythrophagocytosis, the latter is rarely observed in other types of AIHA and should prompt consideration of PCH
   C. Clinical course and treatment
      • Usually resolves spontaneously following resolution of underlying infection in a few weeks and does not recur.
      • Treatment: supportive, steroids and splenectomy are not effective. Maintain adequate hydration to protect kidney function. RBC transfusion may be needed.

II. Serological findings:
   A. Detection of biphasic autoanti-P
      • The anti-P autoantibody rarely causes RBC agglutination above 4\textdegree C, and thus does not interfere with routine pretransfusion tests
      • DAT is usually positive for c3, negative for IgG.
      • Eluate is negative.
      • Antibody not detected by routine antibody screen/ID techniques.
      .Donath-Landsteiner assay is the specific test. Clinical suspicion is required,
   B. Donath-Landsteiner test
      • Specimen must be kept at 37\textdegree C after collection, promptly transported to the blood bank.
      • Serum is mixed with P-antigen positive, ABO compatible reagent cells, with or without the additional normal serum a source of complement.
      • Specimen is divided into 3 sets
         - One is kept at 0\textdegree C
- One is kept at 37°C
- And one is first incubated at 0°C then 37°C.
  - A positive test is when there is visible hemolysis in the last tube but no hemolysis in the other two tubes
  - The autoantibody is transient and disappears quickly during the recovery from the acute illness, rendering false negative Donath-Landsteiner test.

III. Selection of Blood for Transfusion

- P negative units are rare (1:200,000), so usually not used for patients with PCH
- Most patients can still achieve favorable response to P-positive RBCs
- Plasmapheresis before transfusion has been used in rare, life-threatening cases.
- Use of blood warmer is prudent, although not supported by data
- Management of underlying infection aids in resolution of the hemolysis