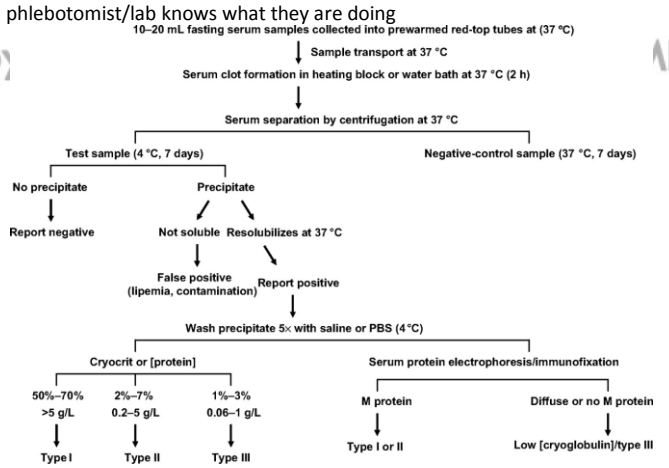
Cryoglobulinemia

- Cryoglobulins (CGs) are immunoglobulins that precipitate when <37°C causing either hyperviscous/thrombotic symptoms and/or inflammatory/vasculitic symptoms
- Epidemiology: 3F:M, ~50yo, 1/100,000 people have symptomatic CG but most healthy people have CGs but they are asymptomatic
- 70% Essential vs 30% Secondary
- NB cold agglutinins (IgM against RBCs seen in Measles, Mumps, Mono, Mycoplasma) vs cryo
- Minute levels of CGs are detectable in healthy people suggesting that symptomatic CG occurs when:
    - chronic immune stimulation (autoimmune/infection)
    - lymphoproliferative state (cancer)
    - defective clearance (essential)
- Brouet Classification (NB Type II and III are collectively called mixed CGs)
    - Type I
        - CG: Monoclonal IgM
        - Etiology: 1º Lymphoproliferative State (**Plasma Cell Dyscrasias**, CLL, Lymphomas) 2º Essential
        - Symptoms: b/c most are IgM and since IgMs circulate as five IgMs together, symptoms are typically hyperviscous/thrombotic symptoms when IgM precipitates and cause ischemia and eventual infarction of all/any organs
    - Type II
        - CG: Polyclonal Ig + Monoclonal IgM with RF activity
        - Etiology: 1º Essential 2º Infection (Viral (**HCV**, many other viruses), Bacteria (endocarditis, post-Strep, Syphilis, Lyme, Rickettsia, Brucella), Parasite (many), Fungal (Coccidio))
        - Symptoms: b/c Igs are polyclonal many different types of ICs can form thus symptoms are typically inflammatory/vasculitic symptoms when Ig precipitate out and attract complement
    - Type III
        - CG: Polyclonal Ig
        - Etiology: 1º Essential 2º Autoimmune Disorder (**SLE, RA**, PM, Sjogrens, Scleroderma, Vaculitis, IBD)
        - Symptoms: (similar to Type II)
- S/S
    - Skin: petechia to palapable purpura to infarction/ulcer of lower extremities, Raynaud's, Livedo Reticularis, Acrocyanosis
    - MS: Arthralgias/Arthritis to Myalgia/Myositis
    - CNS: Peripheral Neuropathy
    - Pulm: Small Airway Disease with cough/dyspnea
    - Kidney: MPGN
    - GI: Ab Pain
    - BM: Failure w/ Pancytopenia
    - NB **Meltzer's Triad** (palpable purpura, arthralgia, myalgia)
- Dx
    - Cryocrit
        - Normal Pts <80mcg/dL vs CG Pts >1-10mg/dL (Type II/III >1mg/dL and Type I >10mg/dL)
        - NB there is a special process in how blood is drawn, prepared, and evaluated, so make sure the phlebotomist/lab knows what they are doing



    - CBC
        - pseudoleukocytosis and psuedothrombocytosis b/c the CGs precipitate in the smear and are falsely interpreted as WBC and Plt by automated cell counters
    - Complement
        - Type I: normal complement b/c the IgM alone precipitating
        - Type II/III: low C3/4 reflecting consumption of complement as they form IC and precipitate
    - APR
        - Elevated ESR/CRP

    - Auto-Antibodies
        - ALWAYS check for ANA/RF
    - Infectious Serology
        - ALWAYS check for HCV
    - Biopsy (cutaneous necrotizing vasculitis characterized by destruction of dermal blood vessels in conjunction w/ infiltration of neutrophils in and around vessel wall)
- Tx
    - CG does not confer a significant M/M risk over and above the underlying conditions thus the main treatment is managing the underlying condition
    - Mild: NSAIDs, avoid the cold
    - Moderate: Steroids + Immunosuppressants
    - Severe: Plasmapharesis