

How Should Patients with Symptomatic Hyperviscosity Syndrome and Cryoglobulinemia be Managed?

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Hyperviscosity Syndrome (HVS) was described by Jan Waldenström in his original 1944 report of the disease that bears his name. The syndrome commonly consists of mucous membrane bleeding, retinopathy with visual disturbances, and a variety of neurological disorders. By the late 1950s, it was shown that the retinopathy could be reversed by plasmapheresis. IgM in excess of 4 gm/dL causes serum viscosity to rise exponentially. The “symptomatic threshold” tends to be reproducible in the same patient but varies between patients. This is likely due to differences in intrinsic viscosity among IgM paraproteins. Measurement of relative serum viscosity using the Ostwald tube remains a simple and reliable method. Because HVS can be diagnosed from fundoscopic examination and usually is reversible by plasmapheresis, prompt recognition is important for institution of proper therapy.

Cryoglobulins (cryos) are immunoglobulins in plasma or serum which precipitate or gel at $<37^{\circ}$ and dissolve on rewarming. Other components such as complement or viral RNA may be present in the cryoprecipitate. Some patients are asymptomatic but others have cold sensitivity with varied manifestations including purpura, arthralgias, weakness, acrocyanosis, Raynaud’s phenomenon, gangrene and renal functional impairment. Proper collection is essential if a cryoglobulin is suspected. The blood must be allowed to clot at 37° and red cells centrifuged promptly. The quantity of cryoprecipitate will be underestimated or totally lost if the specimen is not collected at 37° . Type I cryos are composed of monoclonal immunoglobulins and are frequently concentration-dependent. Type II or mixed cryos are more common and consist of monoclonal IgM-polyclonal IgG immune complexes with rheumatoid factor positivity. Mixed cryos are associated with Hepatitis C. They have higher thermal amplitude and precipitate at lower concentrations than single component cryos. Either Type I or II cryos can be associated with Waldenström’s Macroglobulinemia. Cryos have a dramatic effect on serum viscosity and make HVS more likely and severe. Mixed cryos may respond to corticosteroids, cyclophosphamide, interferon or other chemotherapy agents. Patients should be advised to stay warm.