# Hyperviscosity Syndrome

A clinical diagnosis, not a laboratory one · recognize the triad, look at the fundus, and start plasmapheresis

**Treat the patient**
*not the viscosity*

## THE TRIAD *mucous membranes, eyes, brain. Look for all three*

### MUCOSAL BLEEDING

**Epistaxis, gingival bleeding, GI bleeding.** The paraprotein coats platelets and interferes with clotting factors, so the patient bleeds **despite a normal platelet count**.

### VISUAL CHANGE

Blurring, decreased acuity, sometimes sudden loss. **Do fundoscopy yourself: dilated, tortuous, segmented retinal veins ("sausage-link" or box-car)**, flame hemorrhages, papilledema. **The fundus is the fastest bedside confirmation available.**

### NEUROLOGIC

Headache, dizziness, tinnitus, ataxia, confusion, and at the extreme **seizures, stupor and coma**. Caused by sludging and reduced cerebral perfusion, so it is **reversible if treated promptly**.

## WHO GETS IT *and why the protein type matters more than its quantity*

| Cause | Why it happens |
|---|---|
| **Waldenstrom macroglobulinemia**<br>the classic cause | **IgM is a large pentamer and stays largely intravascular**, so it raises viscosity at far lower concentrations than other immunoglobulins. This is why Waldenstrom causes most cases despite being much rarer than myeloma, and why **plasmapheresis works so well**: the offending molecule is in the compartment you are exchanging |
| **Multiple myeloma** | Uncommon overall, and when it happens it is usually **IgA or IgG3**, which polymerize. **IgG myeloma rarely causes it**, so hyperviscosity in a myeloma patient should prompt you to check which isotype you are dealing with |
| **Hyperleukocytosis**<br>*leukostasis* | **Blast count above roughly 100,000**, most often in AML. A cellular rather than protein hyperviscosity, and the treatment is **cytoreduction**, not plasma exchange |
| **Polycythemia** | Very high hematocrit, in polycythemia vera or severe secondary polycythemia. Treated by **phlebotomy** |

## THE WORKUP *send these together, and warn the laboratory*

| Test | What it adds |
|---|---|
| **SPEP and UPEP with immunofixation, plus serum free light chains** | Identifies and **types the paraprotein**, which is what tells you whether pheresis will help. Quantify the **IgM level** in suspected Waldenstrom |
| **Serum viscosity** | Useful for **tracking** a known patient across pheresis sessions. **Too slow to gate the first treatment decision**, and the symptomatic threshold differs between individuals |
| **CBC with film** | **Rouleaux**, and the white count that identifies leukostasis instead. **Warn the lab**: a high paraprotein can clot analyzers and produce spurious results |
| **Bone marrow biopsy** | Confirms the underlying disease. In Waldenstrom, a **lymphoplasmacytic infiltrate**, and the **MYD88 L265P** mutation is present in the large majority, which supports the diagnosis and informs therapy |
| **Fundoscopy** | Not a laboratory test, but the **fastest confirmatory finding available** and repeatable at the bedside to follow the response |

**Waldenstrom brings a cluster of other paraprotein problems** that are worth asking about in the same consultation: **anti-MAG peripheral neuropathy**, **cold agglutinin disease**, **cryoglobulinemia** and **AL amyloidosis**. Hyperviscosity is only the most acute of them.

## MANAGEMENT *the sequence, and the two things not to do*

| Step | Detail |
|---|---|
| **1. Treat clinically** | **Do not wait for a serum viscosity result to act.** Normal is roughly 1.4 to 1.8 centipoise and symptoms usually appear above about 4, but **the threshold varies widely between patients** and the assay is slow. Symptoms plus the retinal findings are enough |
| **2. Plasmapheresis, urgently** | The definitive immediate treatment for **paraprotein-driven** hyperviscosity. It removes the protein fast and reverses the symptoms, but it does **nothing about the clone producing it** |
| **3. Treat the underlying disease** | Start definitive therapy for the myeloma or Waldenstrom, otherwise the viscosity simply returns. Pheresis is a bridge, not a treatment |
| **⚠ Do NOT transfuse red cells first** | **Transfusing before pheresis raises viscosity further and can precipitate decompensation.** If the patient is anemic and hyperviscous, **pheresis first, transfuse after**. This is the commonest serious error in the syndrome |
| **⚠ Beware rituximab in IgM disease** | Rituximab can cause an **IgM "flare"**, a transient rise that can tip a borderline patient into symptomatic hyperviscosity. **Reduce the IgM by pheresis first** when the level is high |
| **If pheresis is not available locally** | **Arrange urgent transfer** and do not improvise. **Hydrate**, hold anything that raises viscosity, avoid diuretics, and **do not transfuse**. Discuss starting disease-directed therapy with hematology while transfer is arranged, since reducing production helps once the acute exchange is done |
| **Follow the response** | Track **symptoms and the retinal appearance**, supported by the paraprotein level. Symptoms usually improve within hours of a single exchange, and **recurrence means the underlying disease is still untreated**, not that pheresis failed |

## PEARLS & LAB TRAPS

- **A high paraprotein causes pseudohyponatremia.** The measured sodium is low while **measured osmolality is normal**, because the protein displaces plasma water. This is a laboratory artifact of indirect ion-selective electrodes: **do not treat it**, and do not confuse it with true hypotonic hyponatremia.
- **Consider cryoglobulinemia in the differential.** It also complicates paraprotein disorders, but presents with **palpable purpura, arthralgia and neuropathy**, is cold-precipitable, and needs the sample kept warm on the way to the lab or the result is falsely negative.
- **Rouleaux and a very high ESR are the incidental clues** that should prompt protein studies in someone with vague symptoms, alongside a **low or negative anion gap** from a cationic paraprotein.
- **In leukostasis, avoid red cell transfusion for the same reason**, and remember that platelets can be given freely because they do not meaningfully raise viscosity. Treat with hydroxyurea or induction, and give tumor lysis prophylaxis at the same time.

**References:** American Society for Apheresis guidelines on therapeutic apheresis · International Workshop on Waldenstrom Macroglobulinemia consensus · published series on hyperviscosity syndrome and retinopathy.

*Educational aid; verify against current guidance, local formulary and patient factors.*