



# Screening for Hyperviscosity Syndrome

---

***Choosing the right  
technology***

---

***Benson Viscometers***

## Research Sources & References

1. **Lowe GDO, Somer T.** Baillière's Clinical Haematology. September 1987. Blood Rheology and Hyper viscosity Syndrome Vol1/Number 3.
2. **Harkness, J.** Measurement and Clinical Value of the plasma viscosity. ( read to a joint meeting of the British Microcirculation Society and Royal Microcirculation Society. 3rd Feb,1965)
3. **Ryan C, Olarinde O, Kinghorne G, Paul B.** Plasma Hyperviscosity syndrome secondary to HIV infection: a case report. British HIV Association. April 2006
4. <http://www.patient.co.uk/showdoc/40001867/>
5. **Rampling MW;** Hyperviscosity as a complication in a variety of disorders. Semin Thromb Hemost. 2003 Oct;29(5):459-65. [abstract]
6. **Gertz MA, Fonseca R, Rajkumar SV.** Waldenström's Macroglobulinemia. The Oncologist Vol.5, No 1, 63-67, February 2000.
7. **NICE 2005;** Referral Guidelines for suspected Haematological Cancer.
8. <http://www.arthritis-treatment-and-relief.com/blood-plasma-viscosity-inflammation.html>
9. **Harkness J( 1971)** The viscosity of Human blood plasma; Its measurement in health and disease. Biorheology 8: 171-193
10. **Ng T.** Erythrocyte sedimentation rate, plasma viscosity and C-reactive protein in clinical practice. Br J Hosp Med 1997;58:521-3
11. **Brittain GPH, Mcilwaine GG, Bell JA, Gibson JM,** Plasma viscosity or erythrocyte sedimentation rare in the diagnosis of giant cell arteritis. Br J Ophthalmol 1991; 75:656-9
12. **Gudmundsson M, Nordborg E, Bengtsson B-A, Bjelle A.** Plasma Viscosity in giant cell Arteritis as a predictor of disease activity. Ann Rheum Dis 1993; 532: 104-9

# Table of Contents

Introduction.....	4
Key points of discussion .....	4
Background.....	4
Associated Diseases.....	5
Common Conditions: .....	5
Complications .....	7
Investigations for Hyperviscosity Syndrome.....	7
Treatment Strategies.....	8
Patient Management.....	8
Final Comments .....	12

## Introduction

This discussion document is primarily aimed at plasma hyperviscosity especially concerning the detection and the importance of regular monitoring of the patient condition. The clinical summaries below are derived from the wealth of literature available in print and on the web, consequently further reading is recommended for a fully comprehensive view of clinical opinion.

Key points of discussion

- ❖ Clinical Implications of hyperviscosity and hyperviscosity syndrome
- ❖ Patient management
- ❖ Correct monitoring technology

## Background

Plasma hyperviscosity is a secondary condition which may be present in a large number of clinical states. The increase in the viscosity of plasma usually results from increased circulating monoclonal (paraproteinaemic) and polyclonal immunoglobulin disorders. The excessive intravascular paraproteins result in rheologically impaired microcirculation, together with hypervolaemia. This forms the basis of HVS<sup>1</sup>

Increases in fibrinogen,  $\alpha_2$ macroglobulin and immunoglobulins increase both plasma viscosity and red cell aggregation which correlate well with non-specific measurements made by Plasma Viscosity and ESR systems. However in extreme cases of plasma hyperviscosity, the suspending plasma may decrease cell aggregation. In this situation, ESR falls to low or zero levels as well as the increased plasma density decreasing the sedimentation of aggregates. This has consequences for monitoring patients with these complex conditions.

*Hypoviscosity, normally the result of low immunoglobulin or fibrinogen as seen in hypoproteinaemia is not discussed in this article.*

## Associated Diseases

Hyperviscosity in adults is most commonly seen in association with<sup>2,3,4</sup>

- Acute and chronic Infections such as pneumonia, tuberculosis and HIV
- Myocardial Infarction
- Plasma cell neoplasia
- Myeloma
- Connective tissue diseases
- Chronic hypoxia
- Paraneoplastic syndromes; when it results from the high concentrations of circulating immunoglobulins, cryoglobulins and paraproteins,

## Common Conditions:

Common conditions in which hyperviscosity occurs are as a result of a raised Haematocrit, or due to increased levels of circulating plasma components. Many conditions may produce this state including<sup>5,6,7</sup>.

- Waldenströms Macroglobulinaemia (most common cause)
- Multiple Myeloma
- Connective tissue disorders e.g. rheumatoid arthritis
- Any Inflammatory Conditions

## Plasma Hyperviscosity Syndrome

Table 1 shows a summary of the pathological impact of relevant paraproteins in relation to Hyperviscosity Syndrome.<sup>2</sup>

<b>Disease</b>	<b>Basic Mechanisms of HVS</b>	<b>PV Range (mPa)■</b>
<b>Macroglobulinaemia of Waldström</b>	<b>IgM-paraproteins</b> <b>High Concentrations and polymers</b>	<b>&gt;3.00</b>
<b>Multiple Myeloma</b>	<b>IgG-paraproteins-</b> <b>Extremely high concentrations</b> <b>Unstable or stable aggregates</b> <b>High concentration of asymmetric paraproteins</b> <b>IgA-paraproteins</b> <b>Polymer formation</b> <b>IgE-paraproteins</b>	<b>2.01-3.00</b>
<b>Autoimmune and rheumatic diseases</b>	<b>Aggregates of rheumatoid factors and intermediate complexes</b> <b>Polyclonal IgG-polymers</b>	<b>1.75-2.00</b>
	<b>Normal Range</b>	<b>1.5-1.72</b>

Table 1 Causes and basic mechanisms of Plasma Hyperviscosity syndrome

■ Data from Benson Viscometers Ltd

### Complications

Increased Viscosity and reduced blood flow are included in the complications associated with this syndrome which include

- Bleeding from the mucous membranes caused by Paraproteins interfering with platelet function
- Cardiopulmonary symptoms such as shortness of breath, hypoxaemia, acute respiratory failure and hypotension
- Confusion and mental status changes as a result of the increased viscosity and decreased cerebral blood flow together with CNS manifestations such as lethargy, headache, Nystagmus, deafness, convulsions and loss of vision
- Dilation of the retinal veins and retinal haemorrhages
- Renal Failure

**Rapid relief from Hyperviscosity is critical to ensure immediate reduction of the risk from these associated complications.**

### Investigations for Hyperviscosity Syndrome

- Plasma viscosity – Definitive test
- Blood film may show rouleaux formation- suggestive of increased viscosity
- FBC and differential cell count
- Platelet count
- Clotting screen

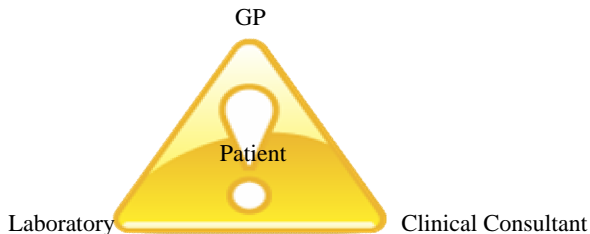
Other investigations to determine the underlying cause e.g. bone marrow aspiration, urine and serum electrophoresis, auto-antibody levels and testing for Bence Jones Proteins.

## Treatment Strategies

Management of patients with Hyperviscosity Syndrome will depend on the underlying conditions. Strategies may include plasmapheresis or plasma exchange as the most efficient or rapid means by which harmful paraproteins can be removed from the circulation. Concomitant Treatment of the underlying cause of the hyperviscosity with specific cytotoxic drugs or chemotherapy may be required.

## Patient Management

Post the acute stage of patient diagnosis, regular review and blood testing is required in order to ensure that there is no deterioration of the patient's condition. Use of the correct monitoring tests is essential in order to ensure appropriate management by Healthcare Professionals



Referral guidelines for treatment of many of the underlying conditions and associated conditions may refer equally to Erythrocyte Sedimentation Rates, Plasma Viscosity or C reactive protein as one of the screening tests<sup>7</sup>.



### C - Reactive Protein

Given that C-Reactive Protein levels may be a better indicator of the acute phase response during the first 24 hours of an inflammatory process<sup>8</sup>, and considering that they are more expensive and more time consuming to perform, then ESR and Plasma Viscosity tests are more appropriately performed as part of the patient review process.

### Erythrocyte Sedimentation

Scientific study and several publications have demonstrated that the use of ESR for monitoring hyperviscous states is inaccurate and misleading.

G.D.O Lowe in Baillière's Clinical Haematology argues quite clearly that 'while ESR has a time honoured place as a non-specific screening test for organic disease and monitoring disease activity, it may give misleading results since it is also affected by variations in Haematocrit'

Haematocrit affects the degrees of red cell interaction before settling and so ESR increases as the Haematocrit falls and is therefore a poor measure of the effect of plasma or red cell abnormalities on blood flow. ESR is unreliable as a quantitative measure unless corrected for the effect of Haematocrit.

Additional issues, such as difficulties in appropriate quality control testing and adjustments for age and sex of the patient questions the reliable use of ESR for Hyperviscosity screening. Table 2 provides more detail of potential issues.

**Erythrocyte Sedimentation is not directly linked to plasma viscosity and so can give misleading results.**

Plasma Viscosity

Since Harkness<sup>9</sup> in 1971 early investigations into the potential of measurement of Plasma Viscosity, there have been a number of research publications that have compared the advantages of plasma Viscosity over ESR measurements.

Patient	Screening/ Treatment	Plasma Viscosity	ESR
Chronic Arthritis	Prediction in patients with early rheumatic disorders	YES  (combined with Serum Viscosity)	NO
Plasma Hyperviscosity	Diagnosis without false negatives	YES	NO
Poikilocytosis Rheumatology  Chronic Malignancy	Associated with Anaemia	PV correlates well with disease progression <sup>10</sup>	ESR rate increase will be difficult to interpret  Use of ESR to monitor therapy becomes subjective
Polycythaemia	>50%	PV measurements unaffected	Normal ESR results found irrespective of underlying disease

Patient	Screening/ Treatment	Plasma Viscosity	ESR
Anti-inflammatory Treatments	Steroids	PV results improve only with arrest of the inflammatory process	ESR readings will give normal results even with elevated Plasma viscosity levels <sup>11</sup>
	Salicylate Therapy	PV results NOT affected directly by the drug	Drug effect lowers ESR reading
	Glucocorticoids	PV Monitoring prediction of Flare ups <sup>12</sup>	NO
Variation of reference ranges with age, sex, smoking and pregnancy		Normal range the same for both sexes  Less variation for other factors	Normal ranges for men and women different.  More variation for other factors
Patient Management	Inter system effect	One standard for universally comparable results	System variations and methods will not allow comparisons

Table 2

## Final Comments

Use of ESR has become the routine requirement for screening and monitoring patients with inflammatory conditions. Considering that ESR is not directly linked to plasma viscosity and has un-correctable dependence on Haematocrit limits, its use to monitor plasma protein changes can sometimes give misleading results.

ESR shows poor sensitivity in the range of screening for organic disease or diagnosis – the very reasons for which most physicians request an ESR test.

Rapid relief from Hyperviscosity is critical to ensure immediate reduction of the risk from associated acute complications.

Technological advances in monitoring technology now mean that plasma viscosity can be determined simply and rapidly to give indications of the underlying patient condition without the disadvantages seen with ESR

Benson Viscometers Ltd  
Croft Quarry  
West Williamston  
Pembrokeshire SA68 0TN  
Phone: +44 (0) 1646 650065  
Fax: +44 (0) 1646 650066  
Email: [sales@bensonviscometers.com](mailto:sales@bensonviscometers.com)  
[www.bensonviscometers.com](http://www.bensonviscometers.com)

Issue: 11/07