



MEDICAL LABORATORY
No. 8673

Chelsea and Westminster Hospital **NHS**
NHS Foundation Trust

The Hillingdon Hospitals **NHS**
NHS Foundation Trust

Imperial College Healthcare **NHS**
NHS Trust

Paraprotein & Myeloma Screening Laboratory Quick Guide

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Presenting clinical features of multiple myeloma

- Hyper**C**alcaemia (>2.75 mmol/L)
- Impaired **R**enal function (Creat >173 mmol/L)
- **A**naemia (Hb <10 g/dL)
- **B**one disease (Lytic Lesions/Fractures)
- Recurrent bacterial infection
- Hyperviscosity

NICE 2016 Guidelines (NG35): Laboratory investigations for suspected myeloma

- Detection of PP/Myeloma/MGUS: Use **serum protein electrophoresis** and **sFLC** assay
- Do not use serum protein electrophoresis, immunofixation, sFLC or urine electrophoresis (BJP) alone to exclude a diagnosis of myeloma
- ~20% of MM is light chain only

MGUS	Asymptomatic	Symptomatic
M Protein < 30 g/L	M Protein ≥ 30 g/L <i>or</i>	M protein present in serum and/or urine (or sFLC Ratio ≤0.01 or ≥100)
Bone marrow clonal plasma cells < 10%; low level of plasma cell infiltration	sFLC Ratio ≤0.01 or ≥100 <i>or</i> Bone marrow clonal cells ≥ 10%	Bone marrow clonal plasma cells or biopsy proven plasmacytoma
<u>No</u> related organ/tissue impairment	<u>No</u> related organ/tissue impairment	Myeloma-related organ/tissue impairment

What to do with high globulin results?

- ↑ Globulins: non-specific marker, can be associated with inflammation/infection/immune disorders as well as paraproteinaemia & MM
- **Globulins ≥ 40 g/L**: Consider *PEP* and *sFLC* if paraproteinaemia is suspected
- **Globulins ≥ 50 g/L**: significant ↑ likelihood of paraproteinaemia. Recommend *PEP* and *sFLC* if not done previously

Laboratory investigations

- Screening Tests: FBC, Renal Function, Bone Profile, Total Protein, Serum Immunoglobulins, Serum PEP, Serum FLC &/or Urine PEP (preferably 2nd Void/24hr)
- Establish Diagnosis: Immunofixation of serum/urine, Bone marrow aspirate + trephine biopsy with plasma cell phenotyping
- Estimation of Tumour Burden/Prognosis: FISH, Quantitation of M protein, albumin, $\beta 2M$, LDH, sFLC

MGUS: Monoclonal Gamopathy of Unknown Significance

- Paraprotein (PP) with no apparent clinical effects (incidental findings in elderly ~7% in 9th decade)
- Use risk MGUS stratification to guide management decisions
- Initially recheck in 3 – 6 months (?transient or persistent)
- Average risk of progression to B Cell Malignancy is 1%/yr

What do serum Free Light Chain results mean?

κ	λ	κ/λ	<u>Interpretation</u>
N	N	N	FLC levels and ratio NORMAL – No monoclonal FLCs detected
↑	↓	↑	FLC ratio HIGH - Monoclonal Kappa FLCs (? Possible Myeloma, MGUS, NHL, AL amyloidosis, CLL)
↓	↑	↓	FLC ratio LOW - Monoclonal Lambda FLCs (? Possible Myeloma, MGUS, NHL, AL amyloidosis, CLL)
↑	↑	N	FLC Ratio NORMAL – No monoclonal FLCs detected (Potential causes of ↑sFLC: Infection, Inflammation, Autoimmune, Renal Impairment)

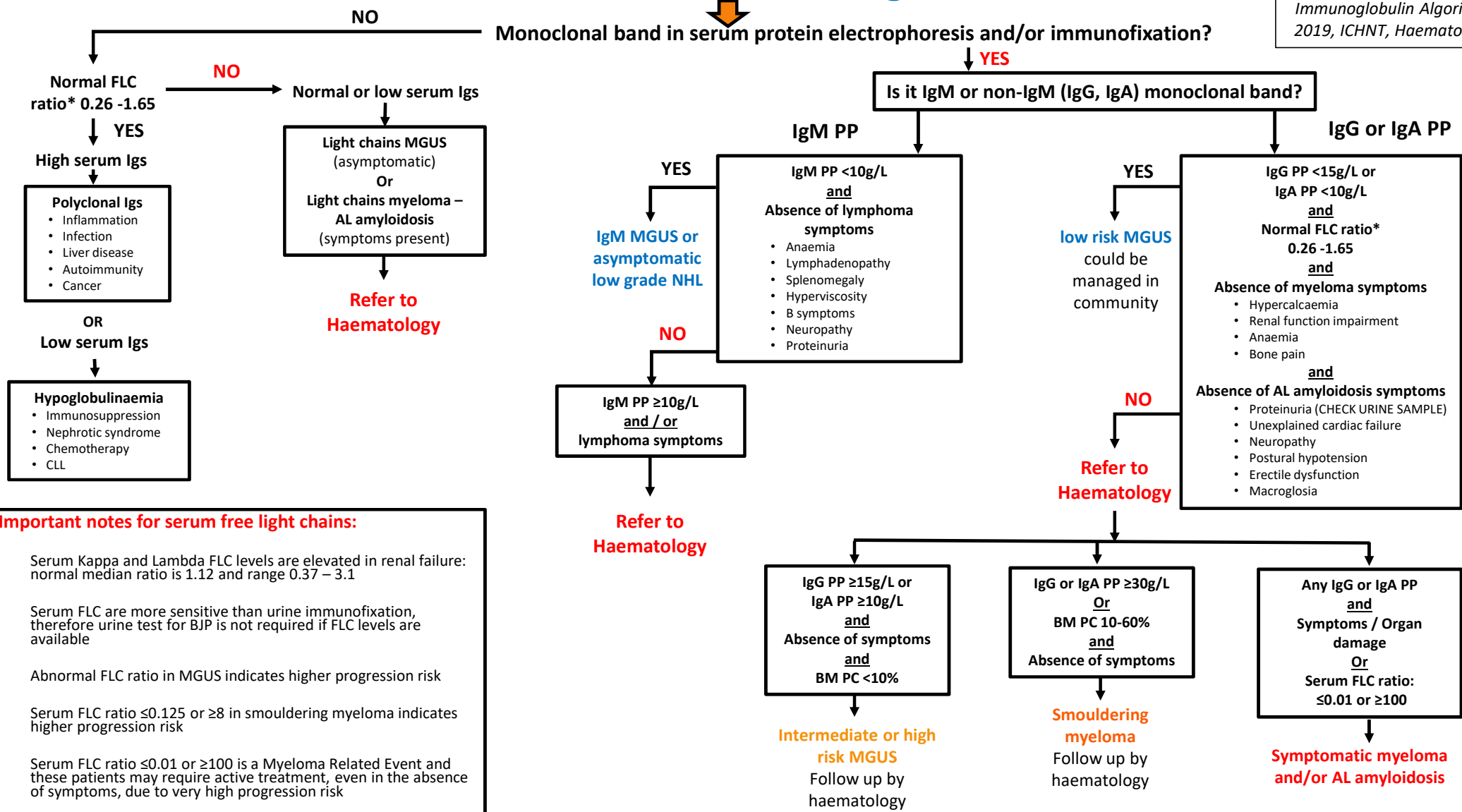
- Serum free light chains (sFLC), serum marker; equivalent to BJP
- sFLC ratio ≤ 0.01 or ≥ 100 : Myeloma related event (MRE), requiring urgent referral
- Abnormal sFLC ratio in MGUS indicates higher progression risk
- sFLC ratio ≤ 0.125 or ≥ 8 in smouldering/asymptomatic myeloma: ↑ progression risk

sFLC Ratio	Action
≥ 100 or ≤ 0.01	Meets criteria for symptomatic myeloma <u>Urgent referral to Haematology</u>
>10 or <0.1	Abnormal serum free light chain ratio. Suggest referral and/or discussion with Haematology
0.1 – 0.2 or 5 – 10	Mildly abnormal serum free light chain ratio. ?Possible Light Chain only MGUS, amyloidosis or other light chain disorder. Suggest discuss with Haematology
0.2 – 0.25 or 1.66 – 5	Likely minor abnormality of sFLC. If normal serum electrophoresis, likely causes may include inflammation or impaired renal function. Suggest repeat analysis in 3 – 6 months and consider 24hr urine Bence Jones protein
For impaired renal function: sFLC Ratio reference range is 0.37 to 3.10	

Note: different sFLC assay results can not be compared

Abnormal Serum Immunoglobulins?

Abnormal Serum Immunoglobulin Algorithm 2019, ICHNT, Haematology



*** Important notes for serum free light chains:**

- Serum Kappa and Lambda FLC levels are elevated in renal failure: normal median ratio is 1.12 and range 0.37 – 3.1
- Serum FLC are more sensitive than urine immunofixation, therefore urine test for BJP is not required if FLC levels are available
- Abnormal FLC ratio in MGUS indicates higher progression risk
- Serum FLC ratio ≤0.125 or ≥8 in smouldering myeloma indicates higher progression risk
- Serum FLC ratio ≤0.01 or ≥100 is a Myeloma Related Event and these patients may require active treatment, even in the absence of symptoms, due to very high progression risk