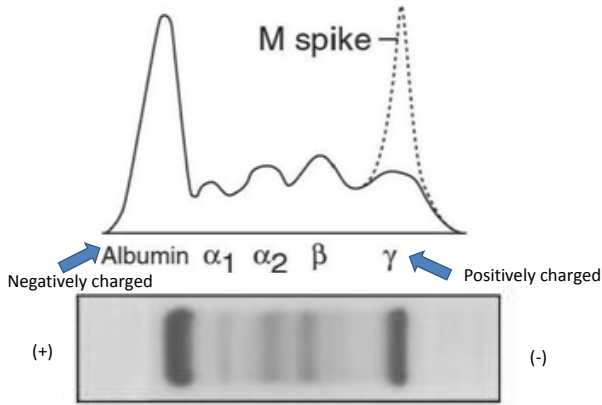
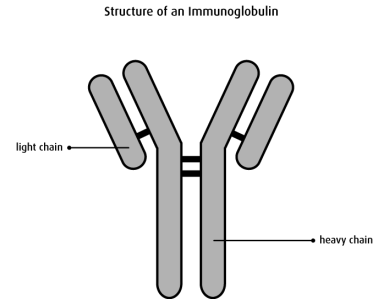


Monoclonal Gammopathies



- Immunoglobulins mostly circulate intact. They are too big to be filtered by kidney.
- Free light chains occasionally break off but are small and therefore are freely filtered by kidney.
- In CKD light chains accumulate in the blood but light chain ratio (kappa/lambda) should be normal
- In monoclonal light chain diseases there are dysfunctional plasma cells that are secreting just free light chains instead of intact immunoglobulins



IgG or IgA

| | IgG or IgA MGUS | Smoldering MM | Myeloma |
|---------------------------|------------------|-----------------|-------------------|
| 1 Clonal BM plasma cell % | < 10% | >10%* | >10% |
| 2 SPEP M protein (g/dL) | < 3 (IgG or IgA) | >3 (IgG or IgA) | Present |
| 3 Clinical Signs | Absent | Absent | Present (C.R.A.B) |

~1%/year ~10%/year

Myeloma defining symptoms are C.R.A.B

- Calcium elevation
- Renal Failure
 - due to light chains precipitating in tubules
 - or due to hypercalcemia
- Anemia (usually normocytic)
- Bone Lesions

Waldenstrom defining symptoms are B.L.A.H

- B-Symptoms
- Lymphadenopathy or Hepatosplenomegaly
- Anemia
- Hyperviscosity symptoms
 - headaches, vision changes, etc.

Amyloid symptoms

(due to light chain amyloid deposits in organs)

- Cardiomyopathy
- Nephrotic Syndrome from amyloid in glomerulus
- Hepatomegaly
- Neuropathy
- Macroglossia
- Many others

IgM

| | IgM MGUS | Smoldering WM | Waldenstrom | IgM Myeloma |
|--------------------------------------|-----------|---------------|-----------------------|-------------------|
| 1 Clonal BM lymphoplasmacytic cell % | < 10% | >10% | >10% | >10% |
| 2 SPEP M protein (g/dL) | < 3 (IgM) | >3 (IgM) | Present (IgM) | Present (IgM) |
| 3 Clinical Signs | Absent | Absent | Present (WM symptoms) | Present (C.R.A.B) |

rarely

Light Chain Diseases

| | Light Chain MGUS | Smoldering Light Chain | Light Chain MM | AL Amyloidosis |
|---------------------------|------------------|------------------------|-------------------|----------------|
| 1 Clonal BM plasma cell % | < 10% | >10%* | >10% | < 10% |
| 2 SPEP M protein (g/dL) | Absent | Absent | Absent | < 3 g/dl |
| 3 Clinical Signs | Absent | Absent | Present (C.R.A.B) | Amyloid sx |
| 4 UPEP M protein | +/- | >500mg/24h | +/- UPEP | +/- UPEP |
| 5 Free Light Chain Ratio | <0.26 or >1.65 | <0.26 or >1.65 | >100 or <0.01* | <0.26 or >1.65 |

- In 16% of myeloma cases the malignant plasma cells are secreting only free light chains (AKA bence-jones proteins) instead of intact immunoglobulins.
 - The Serum Free Light Chain Assay will show an abnormal kappa/lambda ratio
 - UPEP is positive in 2/3 of these cases
 - SPEP is generally negative
- Light Chain Myeloma patients have the highest risk of renal failure (due to free light chains precipitating in renal tubules)

| Type | Frequency |
|-----------------------|-----------|
| IgG | 52% |
| IgA | 21% |
| Free Light Chain Only | 16% |
| Non-Secretory | 3% |
| IgD | 2% |
| Biclonal | 2% |
| IgM | 0.5% |

Source: "Review of 1027 patients with newly diagnosed myeloma" Mayo Clin Proc 2003

*Note: Treatment was traditionally only given when patients develop myeloma (i.e when they develop symptoms). However, now there is a trend to treat patients very likely to be symptomatic soon...

- >60% plasma cells in marrow
- Free Light Chain ratio >100 or <0.01
- Asymptomatic lesions on MRI, not seen on plain films