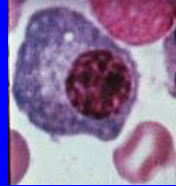


**IgM Myeloma and Waldenstrom's
Macroglobulinaemia (WM/LPL): *Introduction
of new Myeloma/Waldenstrom's FISH
panels which help to distinguish these two
entities.***

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IgM Myeloma



- IgM monoclonal gammopathy,
- plasma cell proliferation on bone marrow biopsy,
- clinical findings -hypocalcaemia, renal impairment, anaemia, and lytic bone lesions,
- CD138+, CD20-

WM/LPL

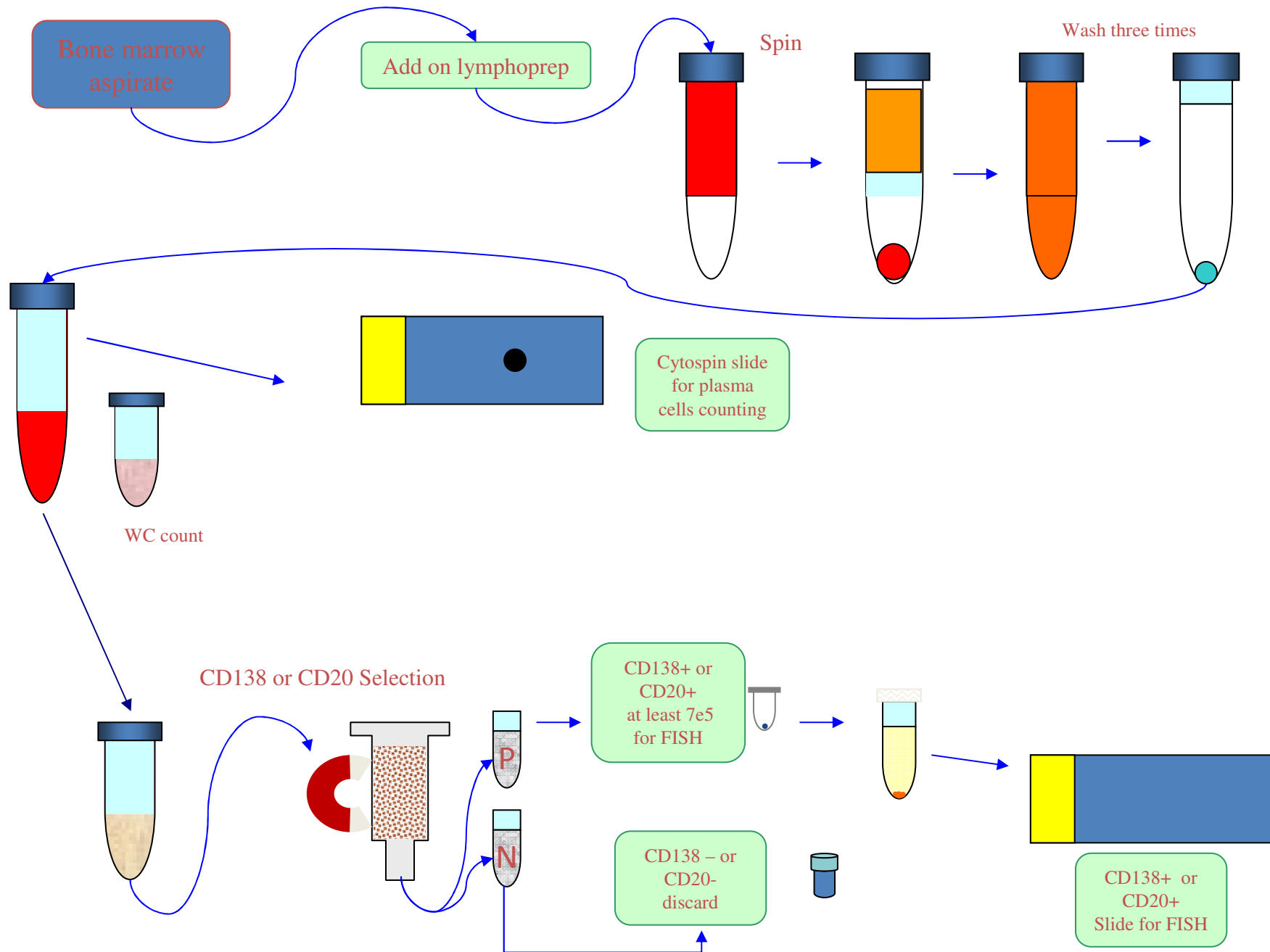
- IgM monoclonal gammopathy
- >10% of lymphoplasmacytoid cells'
- Anaemia, hepatosplenomegaly, mucocutaneous bleeding
- CD20+, CD19+, CD138-

A recent study demonstrated the presence of t(11;14), leading to cyclin D1 dysregulation, in 7 of 8 patients with IgM MM.

The association of 6q deletion with WM, and proposed it to be able to distinguish WM from IgM monoclonal gammopathy of undetermined significance (MGUS) or MM.

FISH- IgM Myeloma and WM

- FISH testing on enriched BMA samples - CD138+ve and/or CD20+ve separated cells only
- Referrals for WM – evaluation of presence of plasma cells, when present CD138 and CD20 cell separation is performed.
- FISH probes used on CD20+ve cells:
 - » Del(6)(q23) – MYB
 - » PAX5 break apart
 - » CEP3
 - » CEP12
- FISH Probes used on CD138+ve cells:
 - » IGH (14q32) break apart
 - » IGH/CCND1 dual fusion (t(11;14)(q13;q32))
 - » TP53 deletion
 - » 1q21/1p32.2
 - » 5/9/15 CEP (LSI D5S23/D5S721, CEP 9, CEP 15)



Materials and Methods

- 25 BM samples from patients referred for WM and IgM Myeloma
- Cell separation using microbeads and AutoMacsPro (Miltenyi Biotech Ltd.) :
 - CD20+ve and CD138+ve separation in 9 samples
 - CD138+ve only in 3 samples
 - CD20+ve in 8 samples
 - 5 samples failed (insufficient number of cells after separation)
- FISH on CD20+ve cells: del MYB (6q23), PAX5 (9p13), CEP3 and CEP12.
- FISH on CD138+ve cells: del TP53, CKS1B/CDKN2C (1q21/1p32.3), IGH break apart, IGH/CCND1 dual colour dual fusion, 5/9/15 CEP (LSI D5S23/D5S721, CEP 9, CEP 15)

Results

- Out of 25 samples received 5 samples failed (20%) due to insufficient number of cells after separation.
 - Out of 20 samples 16 had a final diagnose as WM,
 - Out of 16 WM samples 38% (6/16) were abnormal:
 - 19% were carried MYB (6q23)deletion (3/16),
 - 6% trisomy 3 only (1/16),
 - 6% trisomy 12 only (1/16),
 - 6% trisomy 3 and PAX5 rearrangement (1/16)
- Remaining four samples were diagnosed as IgM Myeloma-
in all samples IGH/CCND1 fusion was detected (100%),

Results cd

- In one case when FISH was used on CD13+ve and CD20+ve cells the patient have been diagnosed with CD20+ve IgM Myeloma,
- In the remaining CD20+ve and CD138+ve samples FISH panel results for IgM myeloma panel were normal.

Summary

- IgM MM is a discrete clinical entity that should be distinguished from WM.
- The bone lytic lesions should not be used as the only feature helping to distinguish IgM MM from WM, as a case report found in the literature showed a patient diagnosed with WM and bone lytic lesions.
- Results presented showed the usefulness of the cell separation method for BM enrichment with the use of CD20 and CD138 microbeads and AutoMacPro separator (Miltenyi Biotech Ltd) in WM and IgM myeloma.
- All FISH results concurred with the suspected diagnosis (3 IgM Myeloma and 16 WM) except one where CD20+ve IgM myeloma was detected.
- FISH panels covered detection of the most important abnormalities in WM and IgM myeloma.
- In our study FISH panels helped to differentiate the diagnosis of IgM myeloma and WM in all 10 cases where abnormal results were detected.