

Understanding Blood and Bone Marrow Tests

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The CBC

- **CBC= complete blood count**
- **What do I pay attention to:**
 - **WBC**
 - **HgB**
 - **MCV**
 - **Platelets**

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WBC

- **WBC= white blood cells count**
- **There are many different white cells, so you need to look at the differential.**
- **Neutrophils and lymphocytes are the ones I look at first.**
- **Elevated white cells can be caused by many things: infection, steroids, cancer.**
- **Low white cell count can be related to infection (viral), chemotherapy, and cancer (pre leukemia conditions)**

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Neutrophil count

- **Neutrophils are the first line of defense against bacteria.**
- **Low count most likely related to chemotherapy. We worried about them if they are below 500 or 0.5 depends on the unit**
- **High count is either related to infection or recent steroids use like dexamethasone.**

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Lymphocyte Count

- They are the special force, highly trained and are good against viruses.
- Low count mostly related to chemotherapy and steroids. Generally, they are lower in African American.
- There is no magic cutoff but less than 200 or 0.2 may lead to serious infections.
- High level can be related to leukemia like picture

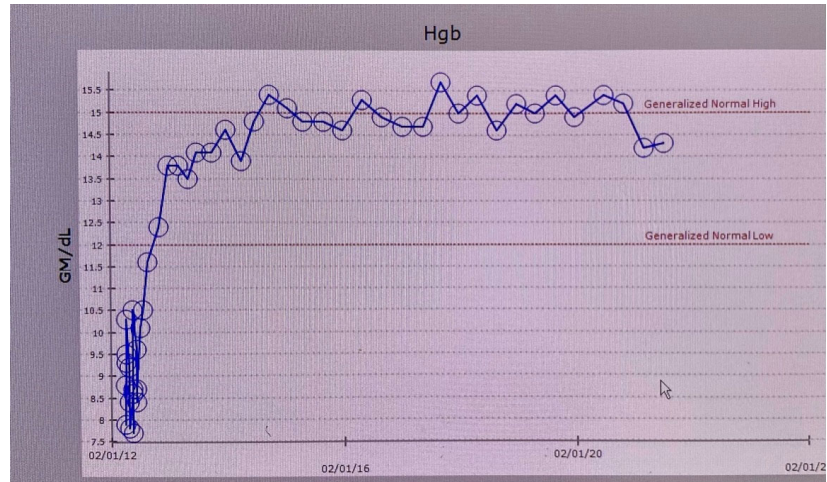
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Hemoglobin

- Carries oxygen to our organs.
- Low level is labeled anemia.
- Low level can be cause by plasma expansion too much water in the vein because of high IgM stay tune we will discuss later.
- Anemia can be caused by Waldenstrom cells infiltrating the bone marrow, or related to iron deficiency, B12 or folate deficiency, low thyroid or testosterone levels

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Follow the Hgb

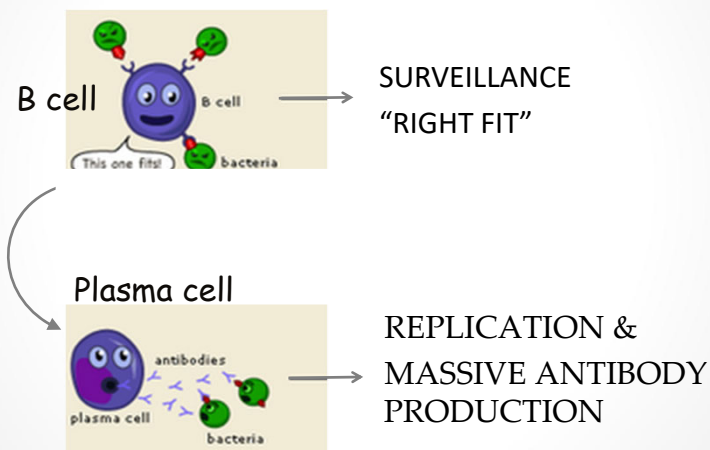


Platelets

- They stop bleeding
- Too low counts leads to bleeding and too high leads to clotting.
- Bleeding can be related to clotting factor low level.
- In general, most people they will not have spontaneous bleeding until level is below 10k.

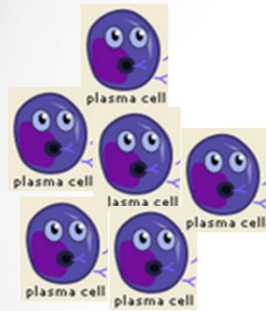
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Plasma cells make antibodies (immunoglobulin)
to block bacteria and viruses



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Waldenstrom is a cancer of plasmalymphocytes

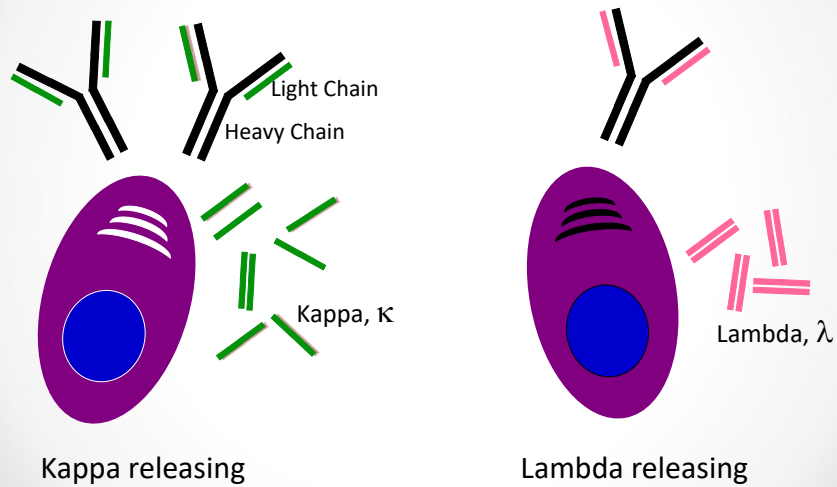


- WM = too many plasmalymphocytes and plasma cells

- Each WM cell (clone) makes and releases one type of IgM antibody (gamma globulin) into the circulation (monoclonal gammopathy)

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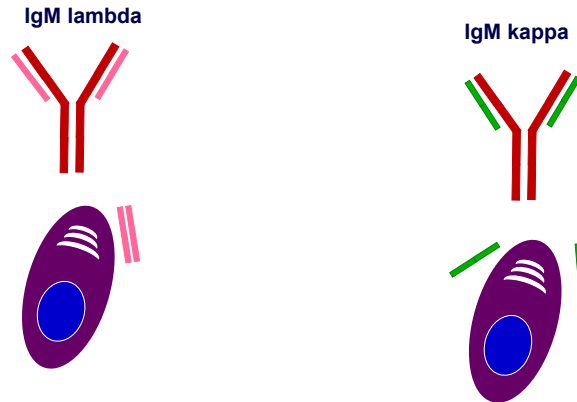
Plasma cells secrete intact antibody and free light chains



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Each patient with WM usually has one cancerous plasma cell clone that secretes a lot of one type of antibody

Antibody = Immunoglobulin = Ig

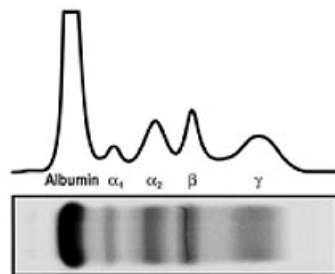


70% of the cases are IgM kappa

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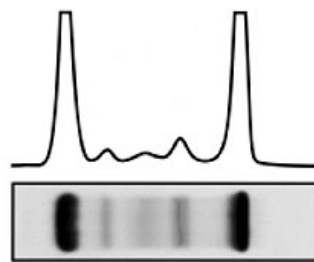
Serum Protein electrophoresis (sPEP)
Immune fixation (IF)

Normal profile



MAYO CLIN PROC. 2001;76:476-487
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AND RESEARCH

Monoclonal protein = M-spike



You may need it once to document monoclonality

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Immunoglobulin levels

- There are three that are reported IgG, IgA and IgM.
- I pay attention to the IgM and IgG.
- IgA is a good antibody that help protect our sinuses, throat and lungs. The good news is that we do not need too much of it and no one knows what to do with very low level like 10 mg/dl.

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IgG

- Most common antibodies and it is what helps us survive all these years.
- Infection or vaccination leads to the generation of IgG to protect us.
- Immunity can last for long time or short time, so revaccination is needed sometimes.
- Low IgG level due to therapy is common.
- Level below 200 mg/dl can increase risk of infection so we may supplement you.

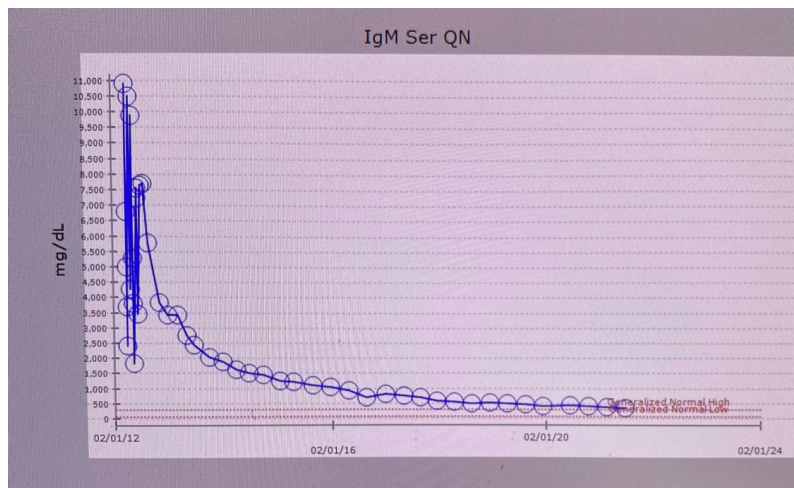
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IgM

- The first antibody we make after vaccination or infection.
- Very heavy molecule. Too much of it makes the blood thick (hyperviscosity)
- Following IgM level is reliable test of the status of your disease.
- There is no magic number when to have symptoms but usually above 5000 mg/dl.

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The right curve



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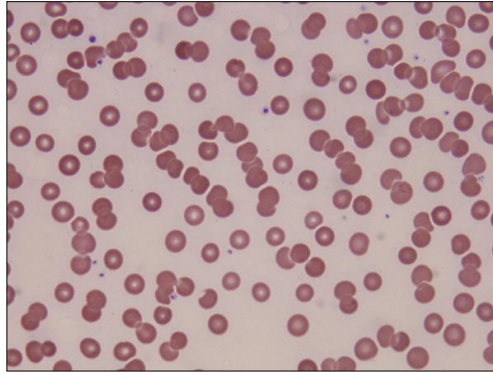
Viscosity

- It is a good test and should be ordered on those with symptoms or IgM > 4 gm/dl.
- The relationship between IgM and viscosity is not linear an increase of 1.5 gm/dl is more significant to someone with IgM above 5 compared to someone with IgM 1 2/3 gm/range

CMP (chemistry)

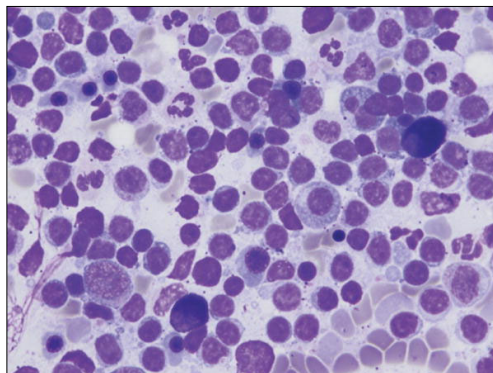
- Electrolytes (Na, K Phos, Mg, Chloride)
- Kidney function: creatinine, BUN
- Liver function (AST, ALT, Alk phos, bilirubin)
- LDH: very important high level may indicate aggressive transformation of the disease.

Blood Smear



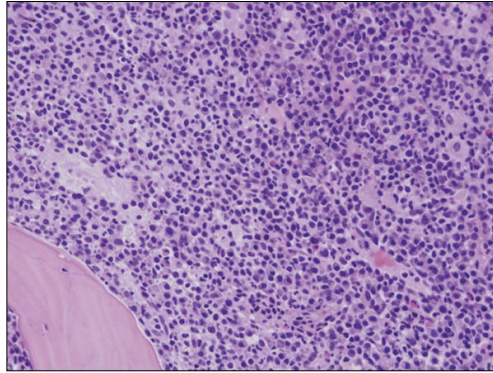
Peripheral blood smear showing rouleaux in a patient with Waldenström macroglobulinemia (Wright-Giemsa, x1000).

Bone marrow aspirate



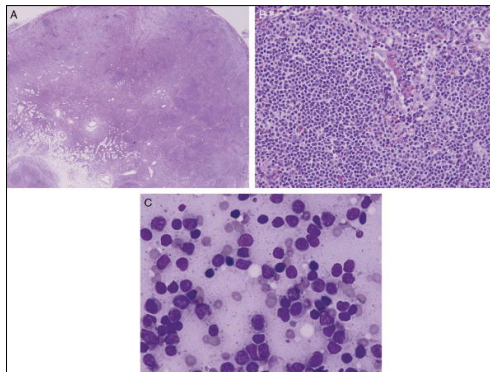
Bone marrow aspirate smear in a patient with Waldenström macroglobulinemia. The smear shows a range of small lymphocytes, plasmalymphocytes, and plasma cells consistent with lymphoplasmacytic variant. Mast cells are also present in the field (Wright-Giemsa, x1000).

Bone marrow biopsy



Bone marrow biopsy specimen involved by Waldenstrom macroglobulinemia in a diffuse pattern (hematoxylin-eosin, x200).

Lymph Node Biopsy



Lymph node biopsy specimen involved by Waldenstrom macroglobulinemia. A, The neoplasm has a paracortical and medullary pattern of involvement (hematoxylin-eosin, x20). B, The neoplasm is composed mostly of small lymphocytes with occasional plasma cells consistent with lymphoplasmacytoid variant. A sinus is patent in this field (hematoxylin-eosin, x400). C, A touch imprint showing small lymphocytes and a few plasmacytoid lymphocytes (Wright-Giemsa, x1000).

MYD 88 mutations

- MYD 88 control lymphocytes survival
- Point mutation is the most common genetic abnormalities
- Together with Bruton Tyrosine Kinase promote survival of tumor cells.

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CXCR4 mutations

- Patients with CXCR4 mutations have higher bone marrow involvement, higher IgM levels, symptomatic hyperviscosity, and a more aggressive disease at diagnosis with reduced sensitivity toward the BTK—inhibitor ibrutinib.
- Presence of these mutations was associated with a shorter treatment-free survival compared to patients without CXCR4 mutation.

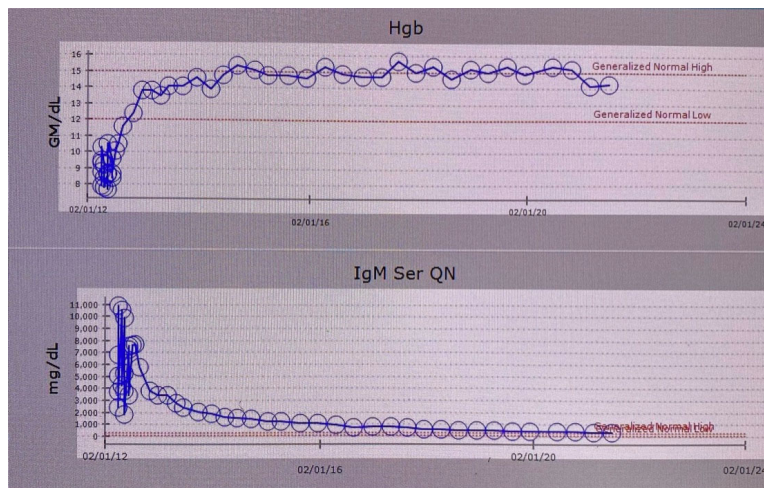
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MYD 88 and CXCR4

MYD 88 mutated	CXCR4 wild type	Common and respond well to BTK inhibitor
MYD 88 mutated	CXCR4 mutated	Aggressive disease
MYD wild type		Aggressive disease and less responsive to BTK inhibitors.

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Putting it together, the graph I love



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