



Dr Emma-Jane McDonald

Clinical Haematologist
Christchurch

Friday, August 12, 2016

(Room 10)

14:00 - 14:55 WS #26: Managing Common Haematologic Problems in General Practice

15:05 - 16:00 WS #36: Managing Common Haematologic Problems in General Practice (Repeated)

Managing Common Haematologic Problems in General Practice

Dr Emma-Jane McDonald
Haematologist, Christchurch Hospital

Question 1

A 67 year old well man with a recent diagnosis of IgG MGUS has a paraprotein of 8.6, 6 months later it is 10.1.

Which is the most appropriate follow-up?

- a) Continue checking immunoglobulins 3 monthly
- b) Repeat immunoglobulins and serum protein electrophoresis in 3 months
- c) Repeat blood tests in 6 months
- d) Refer to haematology to exclude progression to myeloma
- e) Further blood tests are not needed

Question 2

A 78 year old with IgG MGUS has had a stable paraprotein around 9, at his annual review he is well, his IgG level is 17.

Which is the most appropriate follow-up?

- a) Repeat bloods in 1 year
- b) Repeat bloods in 6 months
- c) Repeat bloods in 3 months
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Question 3

A 58 year old lady with IgG MGUS presents with back pain. She has recently joined the gym. Her IgG level 1 year ago was 14, 3 months ago it was 24.

How do you manage her?

- a) Prescribe NSAIDs for her musculoskeletal back pain and arrange to review her in 3 months
- b) Prescribe NSAIDs and arrange for a back x-ray
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- d) Prescribe analgesia and repeat her bloods
- e) Urgent referral to haematology

Question 4

A 75 year old lady has a persistent lymphocytosis over 6 months, the lymphocyte count is around 7, she is well.

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- a) Referral to haematology for assessment
- b) Send blood for immunophenotyping to clarify whether she has an underlying lymphoproliferative disorder
- c) Repeat CBC in 3 months
- d) Request a CT scan to look for lymphadenopathy
- e) Inform the patient they have chronic leukaemia which does not require any treatment

Question 5

A 72 year old lady has had a persistent lymphocytosis for over a year. Immunophenotyping confirmed the presence of a clonal population of lymphocytes however the absolute number was less than 5. She was labelled with monoclonal B lymphocytosis. Her lymphocyte count is now 15, she is well. How do you manage her?

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Question 6

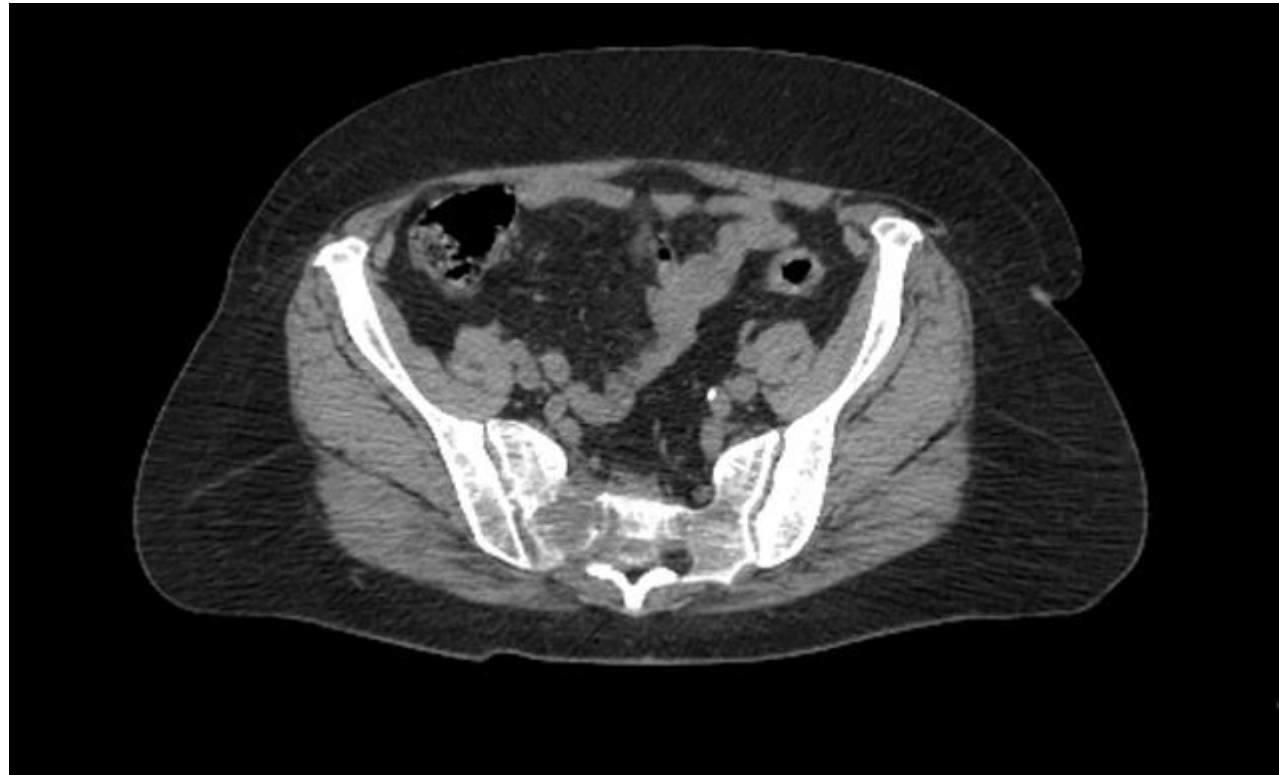
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- a) This is likely to be viral, suggest analgesia, rest etc
- b) Perform an FNA of the lymph node to exclude an underlying lymphoma before sending a referral in for assessment
- c) Send an urgent referral to haematology for assessment
- d) Send a referral to ENT for a lymph node biopsy

Case 1

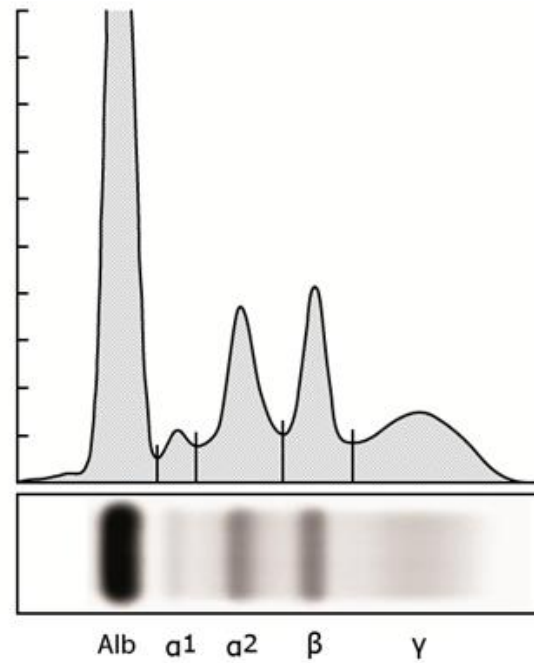
- 71 year old lady
- 19 year history of IgG MGUS
- T4 vertebral # 2014
- February 2015, referral to haematology
 - 1-2 months Rt tibial tuberosity pain
 - Limping
 - Aches at night
 - Tired



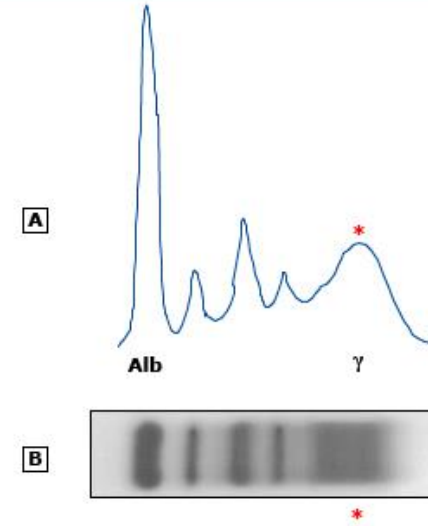
- Hb 95 Neut 1.4 Plt 123
- Creat 97
- Total protein 116 Albumin 33
- Calcium 2.4

- Diagnosed with myeloma
- Commenced chemotherapy
 - 13 weeks treatment, stopped due to side effects
 - VGPR
- 2nd line chemo 1yr later
 - Poorly tolerated
 - Stable disease
- Due to commence 3rd line treatment

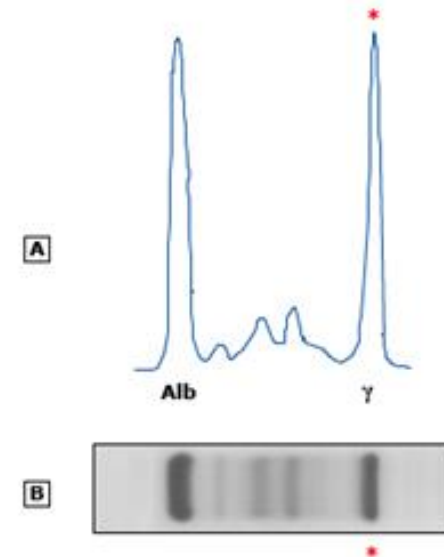
Normal pattern on serum protein electrophoresis



Polyclonal gammopathy



Monoclonal pattern on serum protein electrophoresis (SPEP)



MGUS

- Asymptomatic
- Very common
 - 1% patients >25yrs
 - 3% >70yrs
 - 10% >80yrs
- Absence of
 - ↓Hb, ↑creatinine, ↑calcium, bone lesions

Leukemia

Leukemia (2010) **24**, 1121–1127;

Monoclonal gammopathy of undetermined significance (MGUS) and smoldering (asymptomatic) multiple myeloma: IMWG consensus perspectives risk factors for progression and guidelines for monitoring and management

R A Kyle¹, B G M Durie², S V Rajkumar¹,
on behalf of the International Myeloma
Working Group

<i>Risk group</i>	<i>No. of patients</i>	<i>Relative risk</i>	<i>Absolute risk of progression at 20 years (%)</i>	<i>Absolute risk of progression at 20 years accounting for death as a competing risk (%)</i>
Low-risk (serum M protein <1.5gm/dl, IgG subtype, normal FLC ratio (0.26–1.65))	449	1	5	2
Low-intermediate-risk (any 1 factor abnormal)	420	5.4	21	10
High-intermediate-risk (any two factors abnormal)	226	10.1	37	18
High-risk (all three factors abnormal)	53	20.8	58	27

Assessment

- 6-12 monthly check
 - History
 - Weight loss, bone pain, sweats
 - Examination
 - Lymphadenopathy, hepatosplenomegaly
 - Bloods
 - CBC, electrolytes, calcium, immunoglobulins
- Immediate reassessment if symptoms

Referral criteria

At review, request [haematology assessment](#) if:

- lymphadenopathy.
- significant rise in the level of monoclonal protein over a few months i.e., > 25% provided the absolute minimum rise is > 5 g per L.
- significant cytopenias.
- progressive renal impairment or development of bone pain.

- If multiple myeloma and associated spinal cord compression, hypercalcaemia, or renal failure, request [acute haematology assessment](#).
- Request [haematology assessment](#) for:
 - multiple myeloma.
 - MGUS:
 - If high risk of progression.
 - If [+ concerns](#) at review.

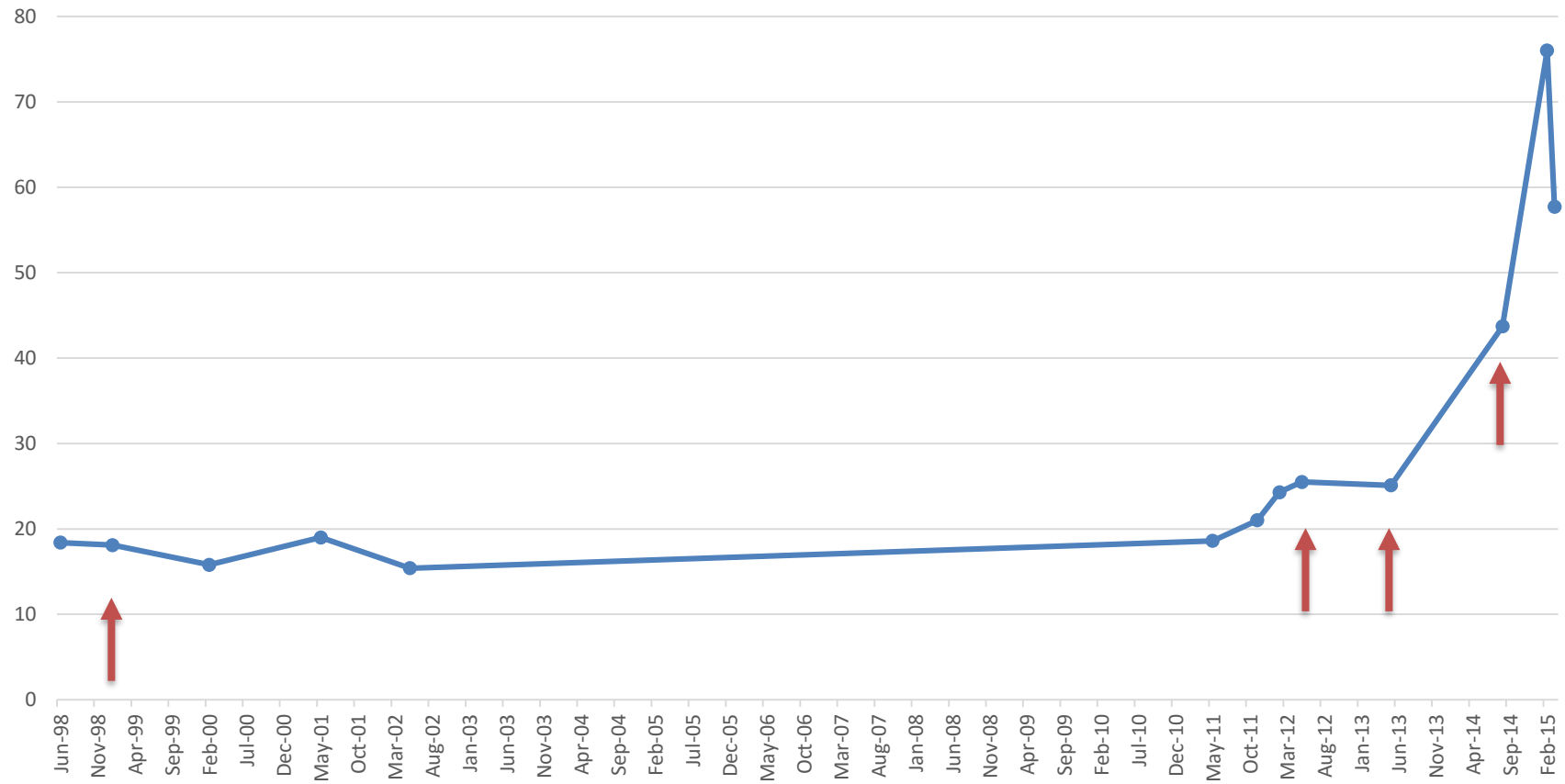
Clinical suspicion of myeloma criteria

Ministry of Health criteria for determining or confirming the 'high suspicion of cancer' flag.

M-protein in serum and/or urine **and** ≥ 1 of the following:

- otherwise unexplained hypercalcaemia (> 2.75 mmol/L)
- otherwise unexplained renal impairment – creatinine clearance < 40 mL/min
- otherwise unexplained anaemia – Hb < 100 g/L
- bony lytic lesions on radiologic imaging.
- serum monoclonal protein (IgG or IgA > 30 g/L or involved:uninvolved [+ serum free light chain ratio](#) > 100.

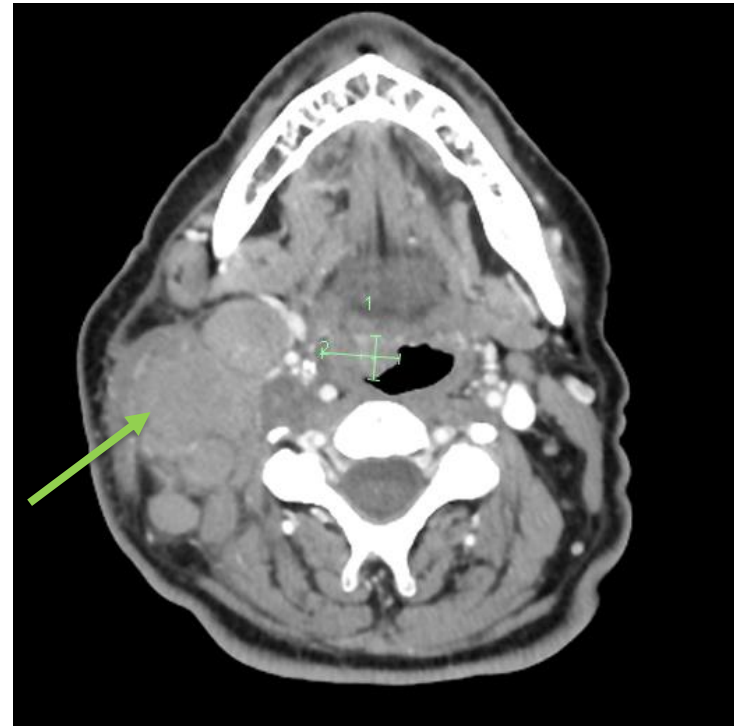
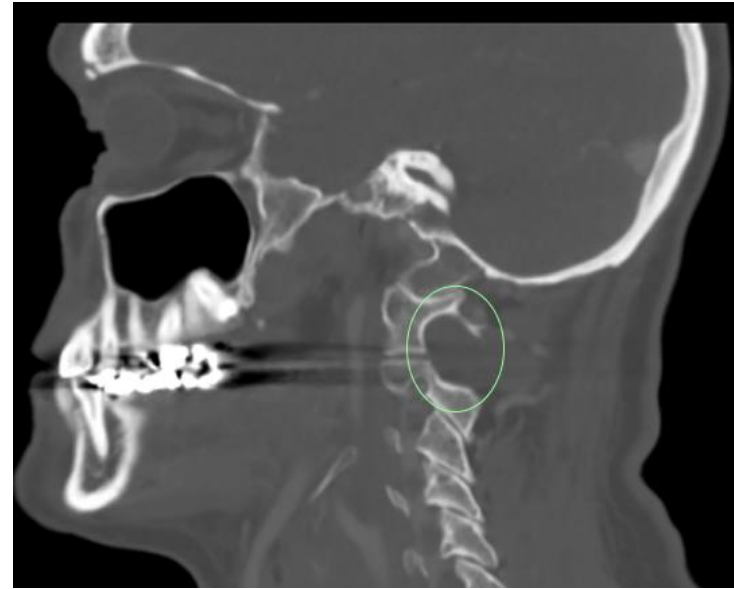
IgG levels



Lymphadenopathy

- 62 year old female
- Presented to GP with 2/52 Hx painless neck lump, some dysphagia
- Discussed with registrar
 - Send referral
 - FNA in community – non-diagnostic

- Approx 3/52 later
 - Clinic appt
 - Rapid increase in size of node
 - Repeat FNA
 - Urgent CT – done next day
- 1/52 later
 - FNA shows High grade B cell NHL



- 3/52 later
 - Urgent referral to haematology
- 5/7 later
 - New patient appointment with haematology
 - Commenced chemotherapy 2/7 after
- Currently
 - Completed 5 cycles chemo
 - Mass no longer palpable

Faster Cancer Treatment

Faster cancer treatment - improving quality of care across the patient cancer pathway



Lymphadenopathy pathway

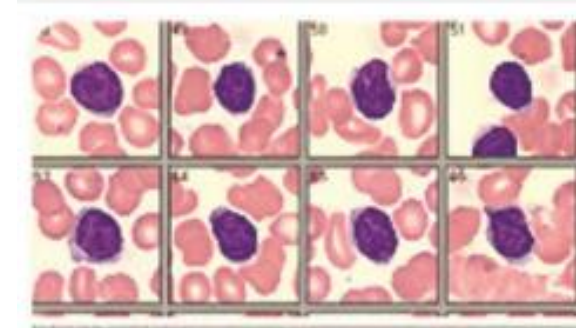
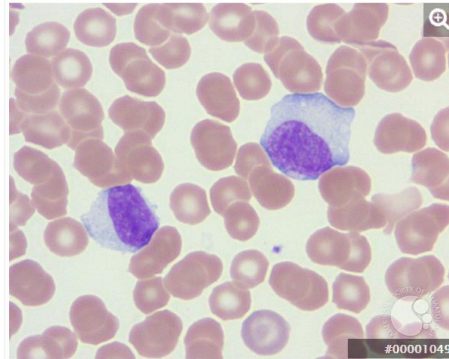
- No clear guidance
 - Coming soon to HealthPathways
- My personal view

- History
 - Duration of lump
 - B symptoms
 - Infective symptoms
 - Clear other cause
 - Lymphadenopathy causing symptoms
- Examination

- Referral for lymph node biopsy
 - ORL
 - General surgery
- Referral to Haematology or Oncology
- Bloods

- Don't forget the patient

Peripheral blood lymphocytosis



Transient	Persistent
Viral infection Pertussis	Smoking Autoimmune conditions Post splenectomy Clonal proliferations

Assessment

Look for:

- Clinical signs of infection or inflammation.
- Lymphadenopathy or hepatosplenomegaly.

Management

1. If well or mild symptoms, recheck white count in 1 to 2 months. Reactive lymphocytosis generally resolves within 2 months.
 - A stable increased lymphocyte count in an otherwise well person is unlikely to require treatment and does not always need further assessment.
 - Asymptomatic [B-CLL](#) does not benefit from earlier treatment.

Monoclonal B lymphocytosis

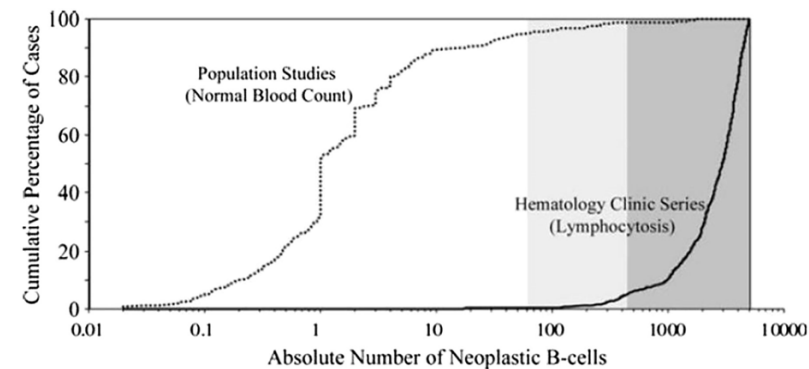


Monoclonal B-cell lymphocytosis and early-stage chronic lymphocytic leukemia: diagnosis, natural history, and risk stratification

Paolo Strati, Tait D. Shanafelt

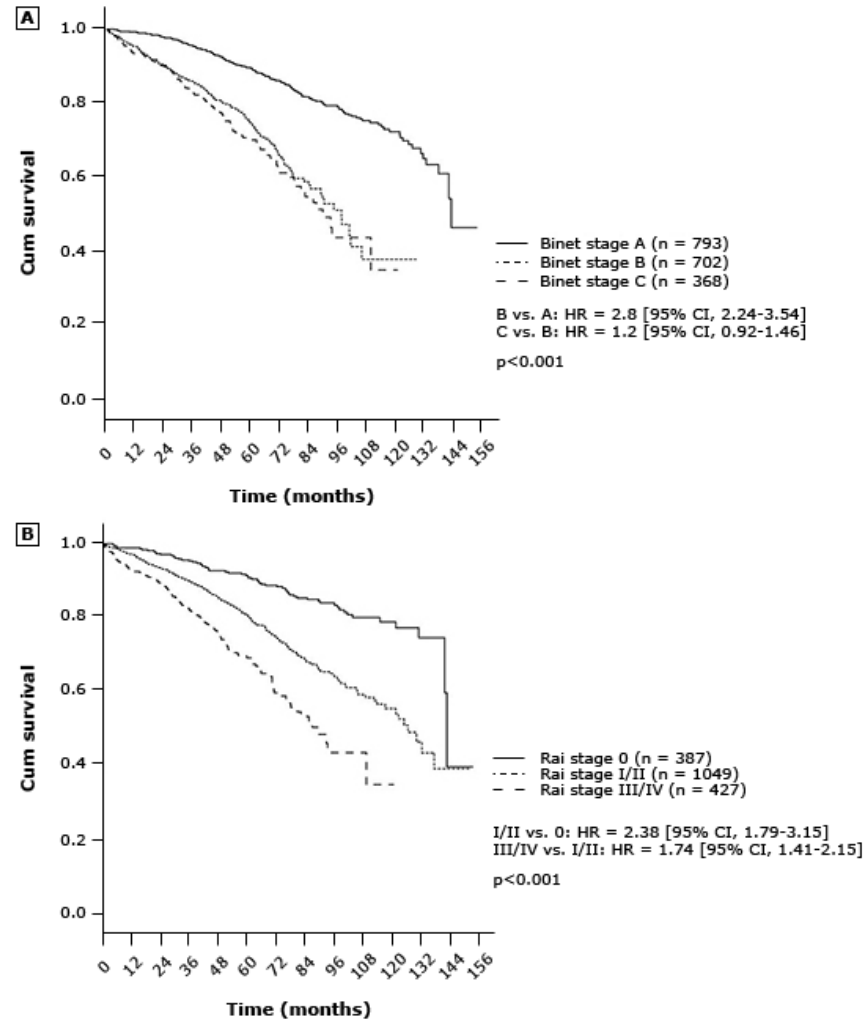
Blood 2015 126:454-462; doi:10.1182/blood-2015-02-585059

- Clonal B cells $<5 \times 10^9/L$
- No other signs of lymphoproliferative disorder
- Low / high count



Paolo Strati, and Tait D. Shanafelt Blood 2015;126:454-462

Survival curves of chronic lymphocytic leukemia (CLL) by Rai and Binet stage



Overall survival by Binet (A) and Rai (B) stage of 1863 patients with previously untreated chronic lymphocytic leukemia.

This research was originally published in *Blood*. Pflug N, Bahlo J, Shanafelt TD, et al. Development of a comprehensive prognostic index for patients with chronic lymphocytic leukemia. *Blood* 2014; 124:49-62. Copyright © 2014 American Society of Hematology.

Managing lymphocytosis

Follow up and Monitoring

Assess 6 monthly for the first year, then yearly if stable or slow, asymptomatic progression.

1. Arrange blood tests with a CBC:
 - The [+ rise of white blood cells \(WBC\)](#) is less important than the development of any cytopenias, night sweats, or weight loss.
 - The surface markers do not need to be repeated when the lymphocyte count increases.
2. Ask about a history of infections, weight loss, fatigue, night sweats, enlarged lymph nodes.
3. Check weight and examine for lymphadenopathy and hepatosplenomegaly.
4. Screen for [+ other malignancies](#).
5. Offer and recall for annual flu vaccination.
6. Educate about presenting early if there is any infection or shingles.

Haemochromatosis

- Haematology
 - Abnormal Bleeding or Bruising
 - Anaemia in Adults
 - Anticoagulation
 - B12 Deficiency
 - B-Cell Chronic Lymphocytic Leukaemia (B-CLL)
 - Haemochromatosis and Raised Ferritin**



- Request assessment for all homozygous HH with iron related tissue damage to the appropriate service,
 - Gastroenterology Department if liver dysfunction
 - Cardiology Department if cardiac dysfunction
 - Rheumatology Department if arthritis

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Take home points

- MGUS is very common
- Myeloma is rare but is associated with significant morbidity and mortality
- FNA – is this really required?
- Refer lymph nodes to surgeons and haematology/oncology
- MBL is the MGUS of CLL
- MBL and Stage A CLL do not require treatment
- Refer haemochromatosis patients to NZBS or relevant specialty