# Some Common Haematological Problems in General Practice

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# Some Common Haematological Problems in General Practice

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# Learning Objectives – an overview of:-

- Leucocytosis & Lymphocytosis
- Neutropenia
- Anaemia
- Thrombocytopenia
- Paraprotein

# Leucocytosis

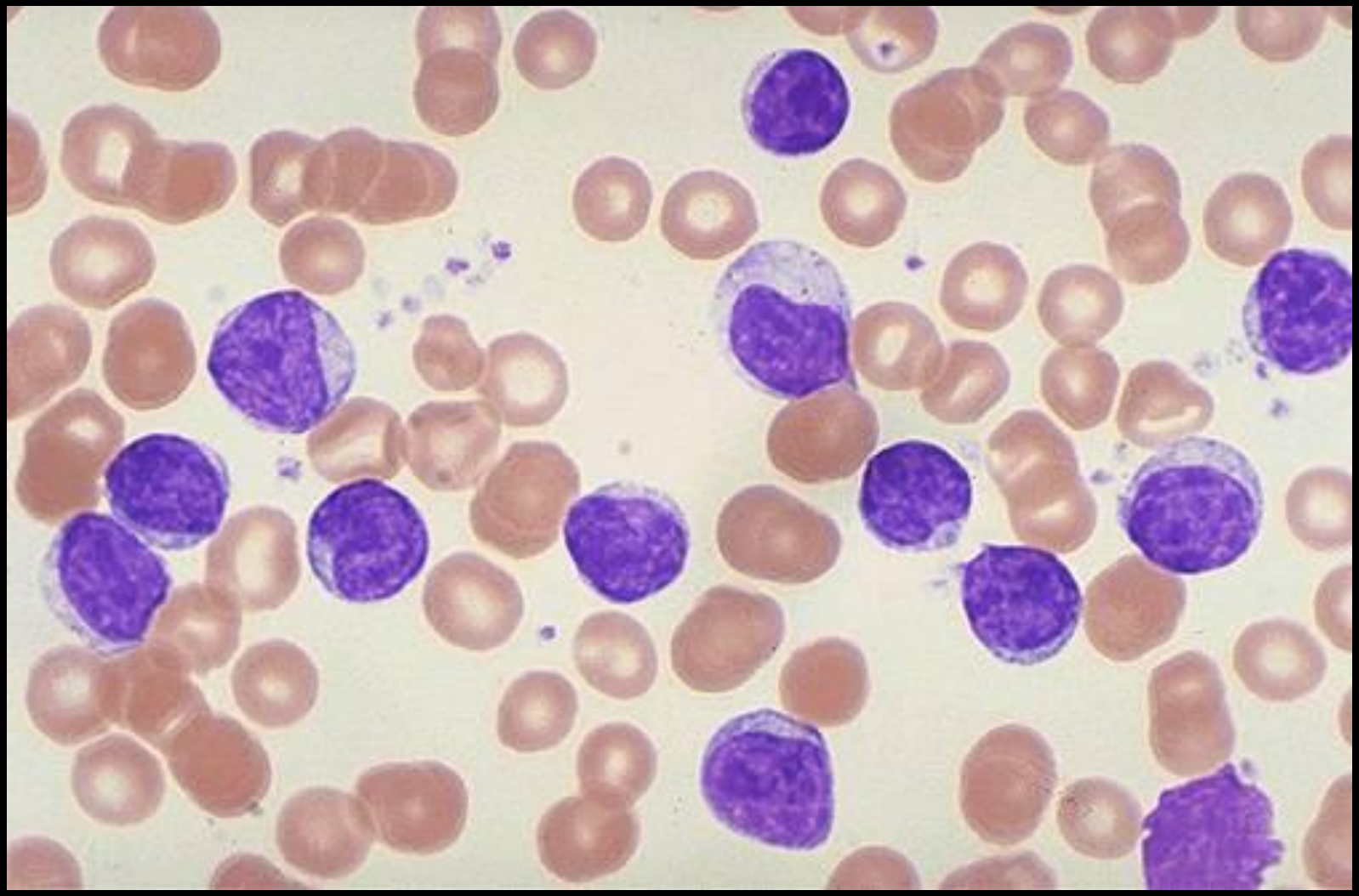
- Most patients with a leucocytosis do not have a haematological malignancy
- Careful history taking is important - fevers, diarrhoea, drugs (e.g. lithium), smoking
- Examine skin, liver, spleen, lymph nodes
- Ask for a blood film - what is the white cell differential, what do the white cells look like, and is the rest of the FBC normal?
- Consider repeating the blood count 2- 4 weeks later before referring to haematology. The white cell count may have settled in this time.

# Case - lymphocytosis

- Mr B  68 yr old
- Feels tired
- FBC - lymphocytosis 5 x $10^9$/L

- What do you do?
  - Consider infection
  - ? Palpable lymph nodes ? Palpable spleen
  - Check if the rest of the FBC is normal.
  - Repeat FBC in 3 - 6 months and request a blood film

# Asymptomatic Lymphocytosis



# Asymptomatic Lymphocytosis

| Lymphocyte count | Investigations |
|---|---|
| >10 x $10^9$/L | Refer to haematology for investigation |
| >3.5 and <10 x $10^9$/L<br>Rest of blood count normal.<br>No lymphadenopathy or splenomegaly | Repeat FBC and Blood film in 3 - 6 months:<br><br>**If lymphocytes are lower or the same level:** no further investigation or monitoring required but repeat blood count in 1 year<br><br>**If lymphocytes are > 10 x$10^9$/L:** refer to haematology for investigation |
| >3.5 and <10 x $10^9$/L<br>**and**<br>anaemia or thrombocytopenia or lymphadenopathy or splenomegaly | Refer to haematology for investigation |



See CLL advice sheet

# Asymptomatic lymphocytosis

- Early CLL - Stage A

  Normal Hb, neutrophils, platelets

  - Does not require treatment (usually)

  - Immunosuppressed
    - Treat shingles with anti-viral drugs
    - May increase risk of bacterial infection
    - Annual ‘flu vaccination and consider for Pneumovax

  - May be associated with increased risk of other malignancies

  - Should be monitored with blood count and clinical assessment every few months initially

# Case - neutropenia

- Mr B  60 year old African
  - Incidental finding of neutrophils 1.0 x $10^9$/L

# Isolated neutropenia

- The severity of neutropenia is categorised as:
  - Mild: neutrophils 1.0 - 1.5 $x10^9/L$
  - Moderate: neutrophils 0.5 – 1.0 $x\ 10^9/L$
  - Severe: neutrophils <0.5 $x\ 10^9/L$

# Causes of Neutropenia

- Transient
- Persistent

# Transient Neutropenia

- Viral infections - neutropenia usually only lasts ≤ 2 weeks and there are seldom any clinical problems.

- Occasionally, the neutropenia may persist for months.

# Persistent Neutropenia

- Benign ethnic neutropenia.
  - Neutrophil counts down to 1 x $10^9$/L are a relatively common finding in individuals of African-Caribbean or Middle Eastern descent.
- Viral infections
  - EBV, HIV, hepatitis viruses
- Autoimmuine disorders
  - SLE, Rheumatoid Arthritis
- Drugs
  - A long list!
- Splenomegaly (including due to liver disease)
- Haematological diseases
  - Myelodysplasia, leukaemia, lymphoma, myeloma, B12/folate deficiency etc.)

# Evaluation of a patient with neutropenia

- History:
  - ✓ Symptoms of recurrent infection?
  - ✓ History of recurrent infections
  - ✓ Drug history
  - ✓ Family history of infections
  - ✓ Records of past FBCs to establish the chronicity of the neutropenia
  - ✓ Risk factors for HIV, TB
- Examination: look for
  - Signs of infection: oral mucosa, skin rashes, abscesses, lung infections, perianal/genital area
  - Splenomegaly
  - Other signs of causative medical problems (SLE, malignancy)

# Evaluation of a patient with neutropenia

- Investigations:
  - *Repeat FBC with differential (what is the rest of the count like?)*
  - *Blood film (do the cells look normal?)*
  - Paul Bunnell (IMST)
  - B12, folate
  - Autoantibody screen & rheumatoid factor
  - HIV testing if clinical risk factors are present
  - Blood cultures if the patient is pyrexial (in which case send to hospital)

# Neutropenia
## When should I seek further advice or refer to haematology?

First check:

- How severe is the neutropenia?
- Are there any other abnormalities of the blood count?
- Does the patient have any symptoms relating to the neutropenia?
- How long has the neutropenia persisted for?

Consider referral if:

- Persistent neutropenia <1.3 x $10^9$/L over 6-8 weeks in Caucasian patients with no obvious cause as outlined above
- Neutropenia associated with severe and/or recurrent infection
- Neutropenia associated with other full blood count abnormalities
- Neutropenia associated with splenomegaly (NOT due to liver disease – fulfils 2 week wait criteria)
- Suspected underlying haematological disease: i.e. clinical symptoms or on blood film

# Pragmatic Classification of Anaemias based on the MCV

Microcytic Anaemia

MCV < 80 fl

Iron deficiency

Thalassaemia (α, β)

Chronic disease (e.g. R.A.)

Macrocytic Anaemia

MCV > 100 fl

B12 or folate deficiency

Hydroxycarbamide Rx

Myelodysplastic syndromes

Excess alcohol

Liver disease

Normocytic Anaemia

MCV 80 – 100 fl

- Myelodysplasia
- Recent bleed
- Chronic diseases

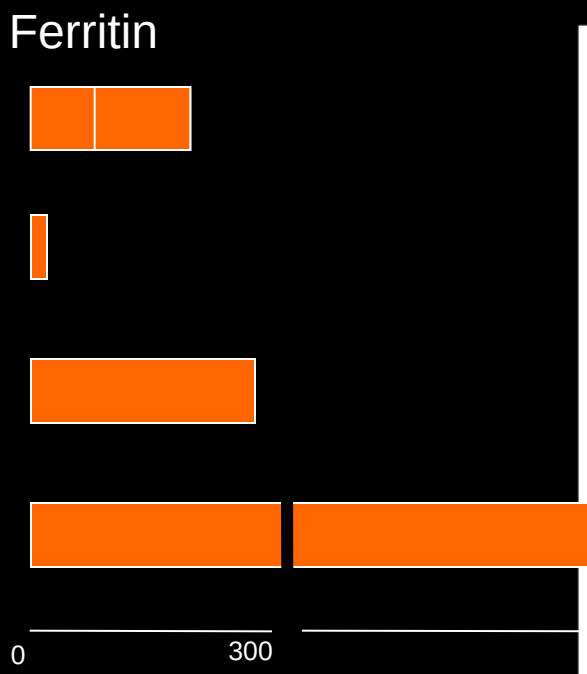
# Case - Anaemia (1)

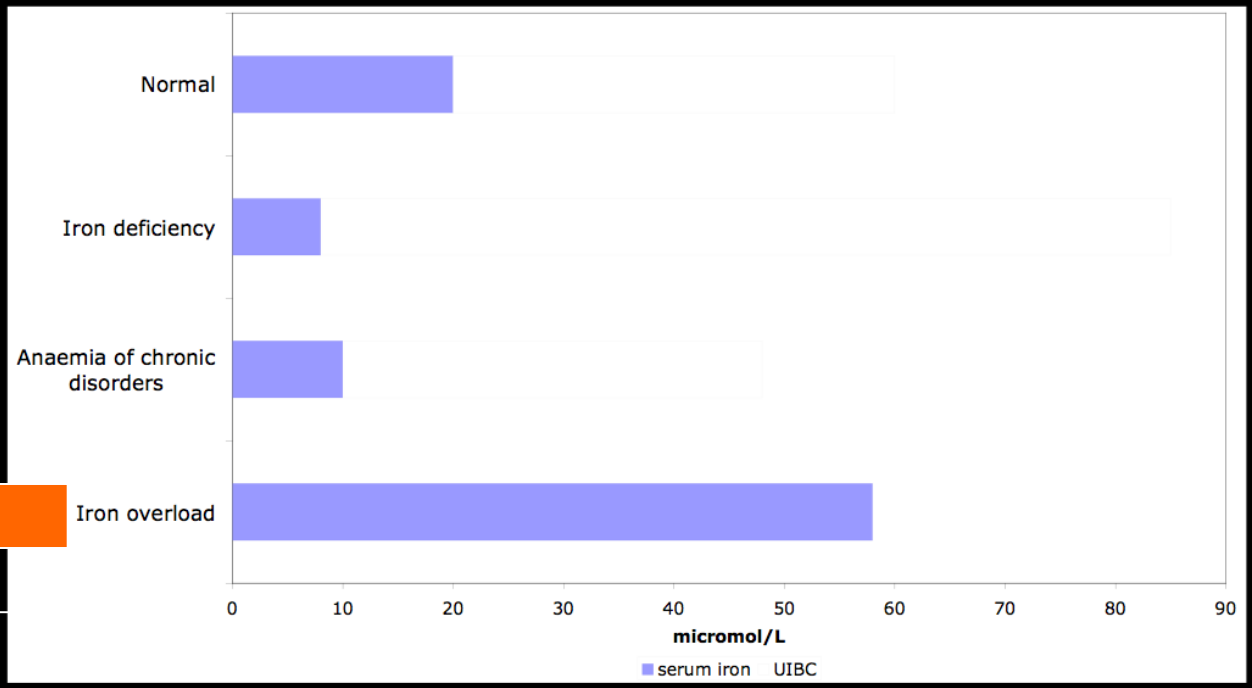
- 54 year old woman - tired all the time
- Known to have rheumatoid arthritis
- Hb 108 g/L, MCV 77 fL, ESR 48 mm/hr
- Serum Fe 5 µmol/l (low)
- Commenced on oral iron
- After 6 weeks - no improvement in symptoms or Hb
- Question - is this iron deficiency?

# Case - Anaemia (2)

- 67 year old man
- Pale and breathless on exertion
- Losing weight
- Liver edge palpable
- Hb 66 g/L, MCV 72 fL, MCH 23 pg
- Serum Fe 5 µmol/l, TIBC 80 µmol/l
- Ferritin 10 µg/l
- ? Refer to Haematology ? **(No!)**

# Ferritin, serum iron and TIBC




U=unsaturated

## *Causes of Iron-deficiency Anaemia*

| | |
|---|---|
| Menstrual bleeding | Most frequent cause in young women |
| Pregnancy | Diversion of iron to the fetus and placenta |
| Children | Increased demand for Fe during growth |
| Upper GI Bleeding | Cancer, varices, hiatus hernia, gastritis, HHT |
| Lower GI Bleeding | Colon Cancer, angiodysplasia |
| Intestinal malabsorption | Crohn's, coeliac sprue, intestinal surgery, hookworm |
| Urogenital | Bladder cancer, prostate pathology, schistosomiasis |
| Factitious bleeding | |

# Iron deficiency anaemia

- Iron deficiency anaemia is almost never due to a primary haematological pathology.
- In adults consider occult bleeding as the first differential diagnosis if menstrual bleeding +/- multiple pregnancies are not the obvious causes.
- Refer to gastroenterology / gynaecology
- Cut out the middle-man - the haematologist (who will just refer to gastro or gynae)!

# Thrombocytopenia

| Normal Plt count (x 10^9/) | Mild | Moderate | Severe |
|---|---|---|---|
| 150-400 | 100-150 | 30-100 | <30 |

- Consider
  - Is the low plt count acute or chronic?
  - Is it associated with other abnormalities of the blood count?
  - Has the FBC been repeated?
- Does the patient have a history suggestive of infection, autoimmune disease, or malignancy?

# Thrombocytopenia

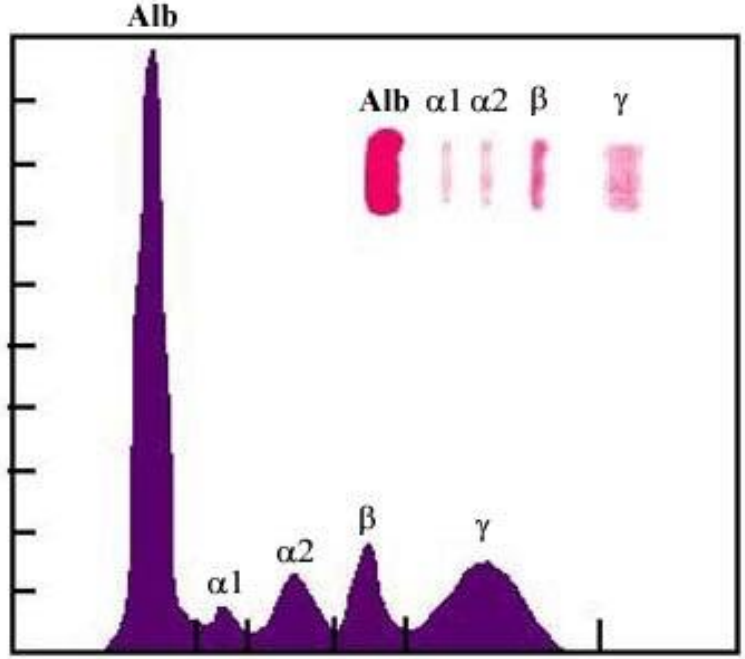
- What drugs is the patient taking (the list is endless!)?
- Examine for spleen, lymph nodes, skin rashes, musculoskeletal abnormalities.
- Ask for a blood film:
  - Platelet clumping
  - May-Hegglin
  - Hypersegmented neutrophils & macrocytosis (B12 / folate deficiency)
  - Lymphocytosis etc. - ? CLL
  - Macrocytosis and Pelgeroid neutrophils - MDS

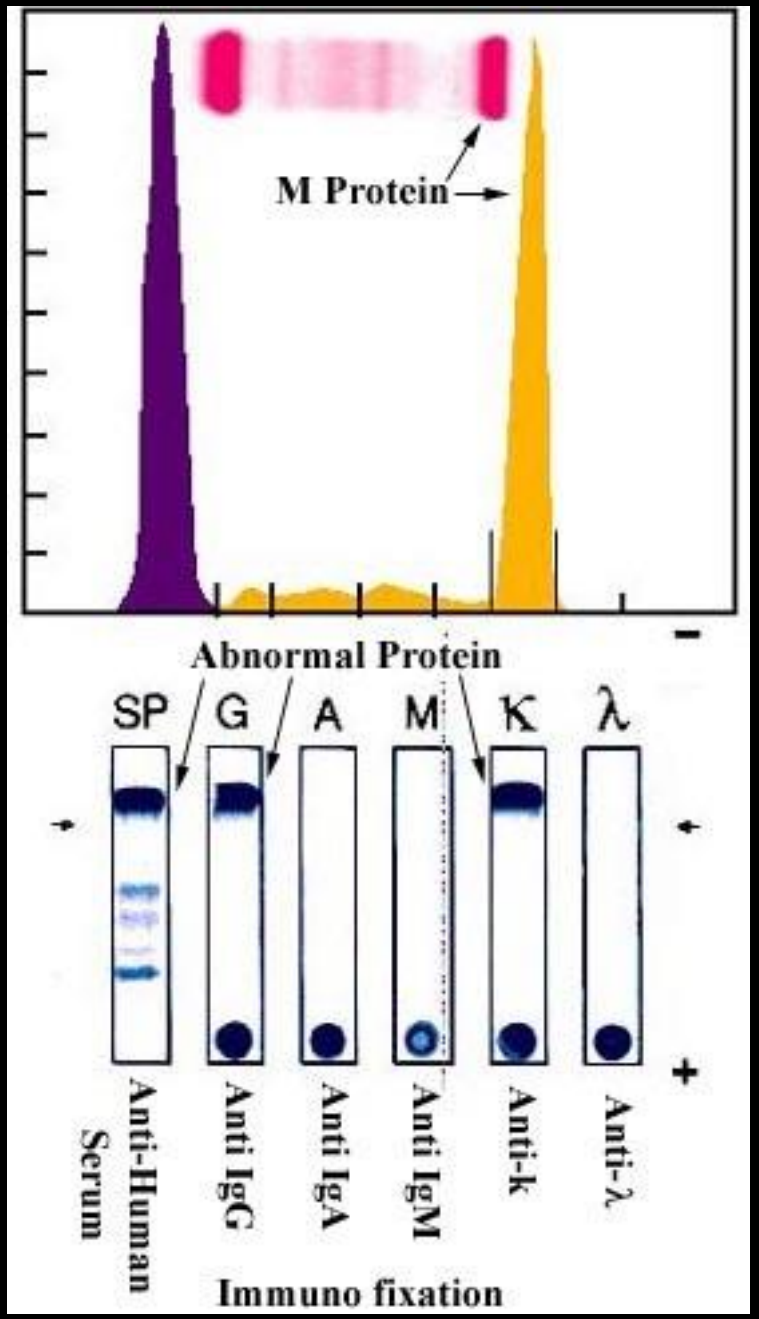
# Thrombocytopenia

- If thrombocytopenia is isolated and the blood film and physical examination are unremarkable then a bone marrow examination may not be necessary.
- If patient is asymptomatic then monitoring with serial blood counts may be all that is required.
- Most patients with isolated mild thrombocytopenia do not develop clinical disease but of those that do, the commonest group of diseases that develop is autoimmune in origin.
- Consider HIV and Hepatitis C as an underlying cause of a low platelet count without other explanation.

# Case - Paraprotein

- 60 year old woman
- Presents with back pain following a recent fall
- FBC, U+E, LFT, CRP, calcium, SPEP
- XR spine

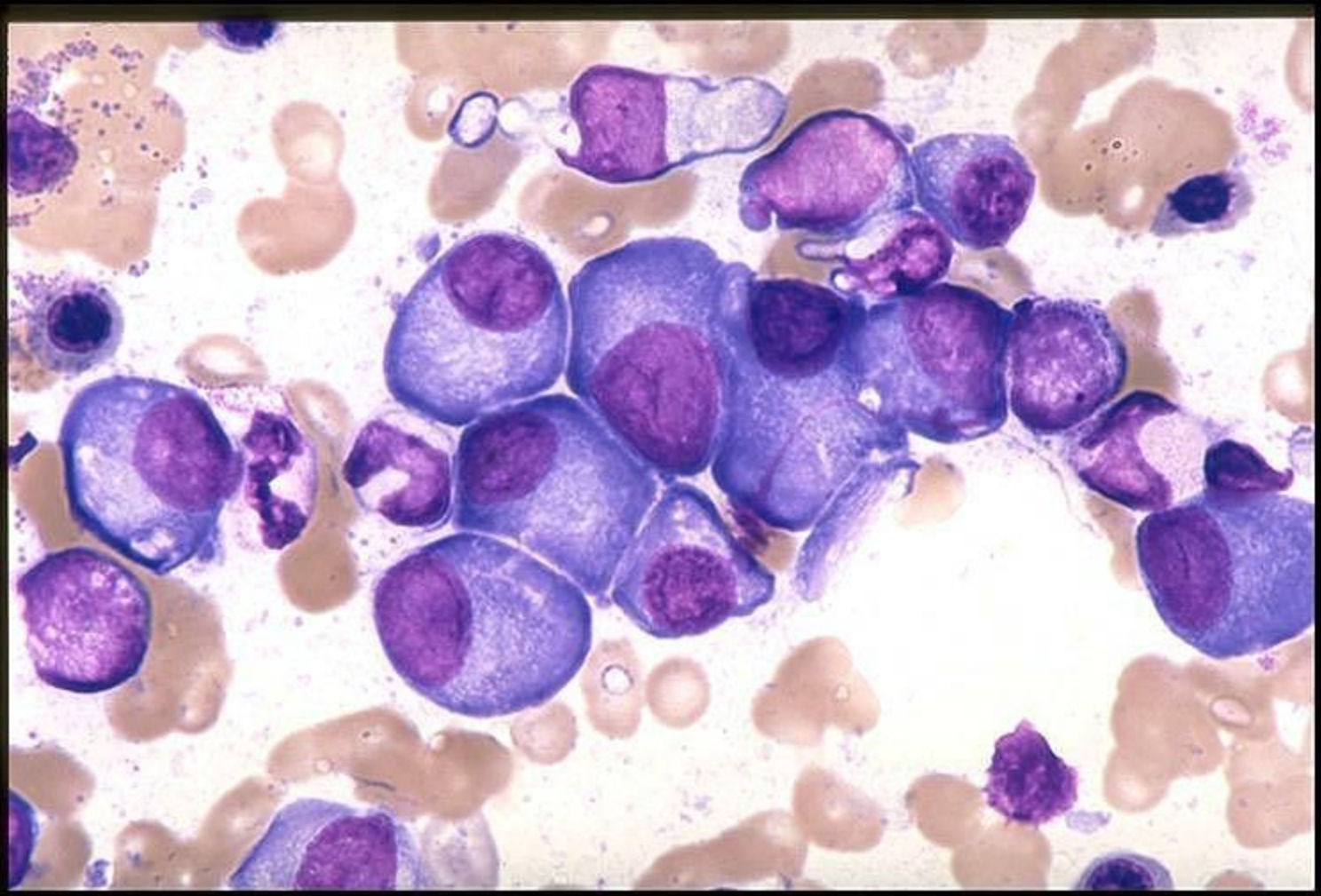

Alb
Alb α1 α2 β γ
α1
α2
β
γ


M Protein
Abnormal Protein
SP
G
A
M
K
λ
Anti-Human Serum
Anti IgG
Anti IgA
Anti IgM
Anti-k
Anti-λ
Immuno fixation

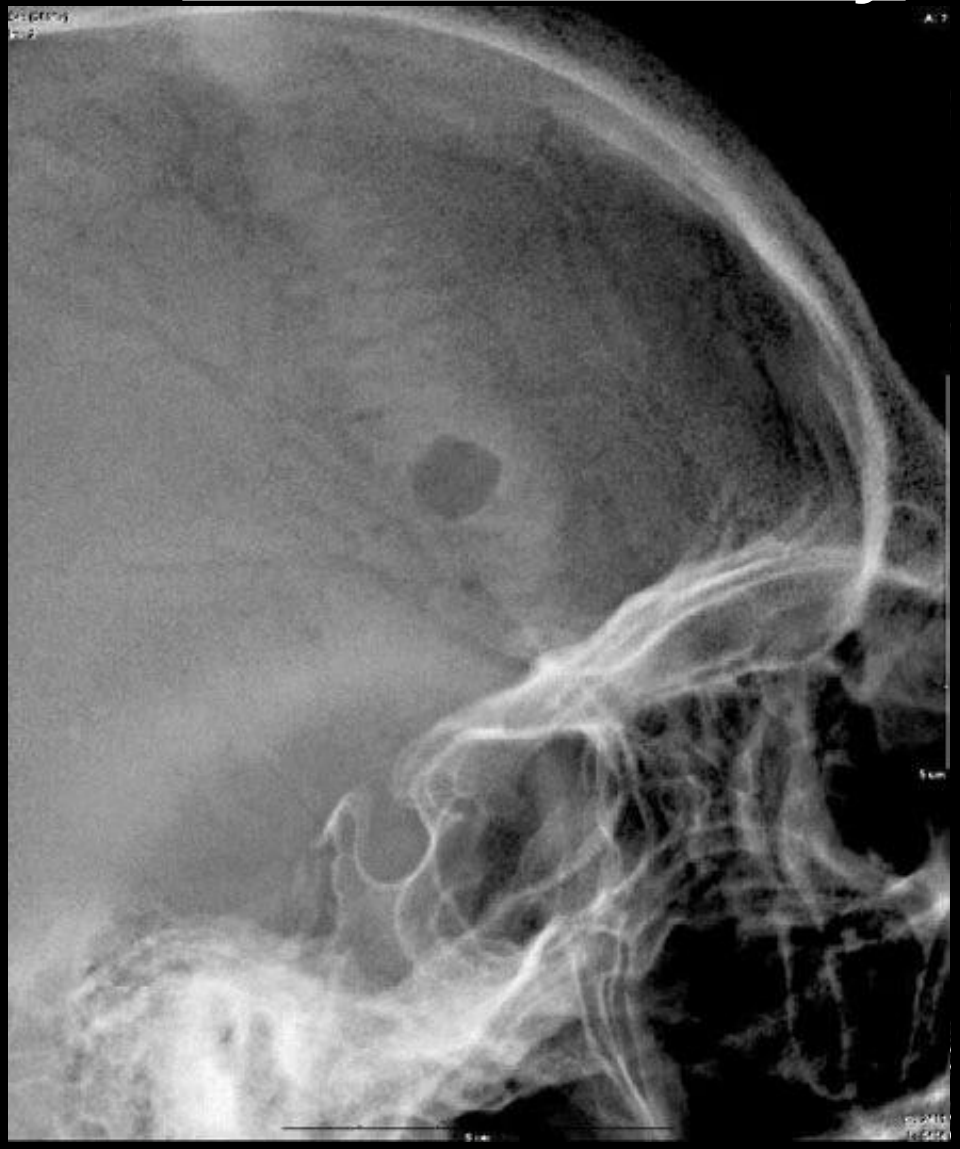
# Results 60 year woman with back pain

- FBC - normal
- Renal function, calcium - normal
- IgG kappa paraprotein 8 g/L
- IgA and IgM normal

- Spinal XR - “osteopenia, crush fracture L4”



# Skeletal survey



# Assessment of Paraprotein

- Does the patient have symptoms?
- Does the patient have clinical signs (e.g. nodes)?
- How high is the paraprotein concentration?
- What sort of paraprotein is it?:
  - IgA / IgG ~ myeloma
  - IgM / IgG ~ lymphoma
- Are the other Igs suppressed?
- Is the blood count normal?
- Are the renal function and calcium normal?

**Most paraproteins are discovered incidentally and do not mean that the patient has a malignancy (they usually represent MGUS)**

# MYELOMA & MGUS - Diagnosis

| | MYELOMA | MGUS |
|---|---|---|
| **Bone marrow plasma cells** | **> 10% on aspirate** | **<10% on aspirate** |
| **Serum paraprotein** | **Variable concentration** | **IgG usually < 20 g/l<br>IgA usually < 10 g/l** |
| **BJP** | **> 50% of cases** | **Rare** |
| **Immune paresis** | **> 95% of cases** | **Rare** |
| **Lytic bone lesions** | **Often present** | **Absent** |
| **Symptoms** | **Frequent** | **Absent** |
| **Anaemia** | **Frequent** | **Absent** |
| **Hypercalcaemia** | **May be present** | **Absent** |
| **Renal impairment** | **May be present** | **Absent** |

# Monoclonal Gammopathy of Undetermined Significance (MGUS)

- Monoclonal gammopathy found in:
  - 1% of people > 50 yrs
  - 10% of people > 80 yrs
- Clinical features of MGUS
  - No symptoms / signs
  - Incidental chance finding
  - ~ 10% will develop myeloma
- How to monitor?
  - 6 monthly FBC, U/E, calcium, protein electrophoresis and paraprotein quantitation.
  - Refer to haematology if Hb falling, urea or calcium rising, paraprotein rising, bone pain, lymphadenopathy

# Polyclonal Hypergammaglobulinaemia

- The finding of raised globulins without a monoclonal band is not an indication of myeloma.

- Causes of polyclonal ↑ γ globulins:
  - Chronic infection
  - Chronic liver disease
    - Cirrhosis
    - Autoimmune hepatitis
  - HIV infection
  - Connective tissue disease (Sjogren's syndrome, SLE, RA)
  - Angioimmunoblastic lymphadenopathy
  - Tropical splenomegaly syndrome