Anaemia 1

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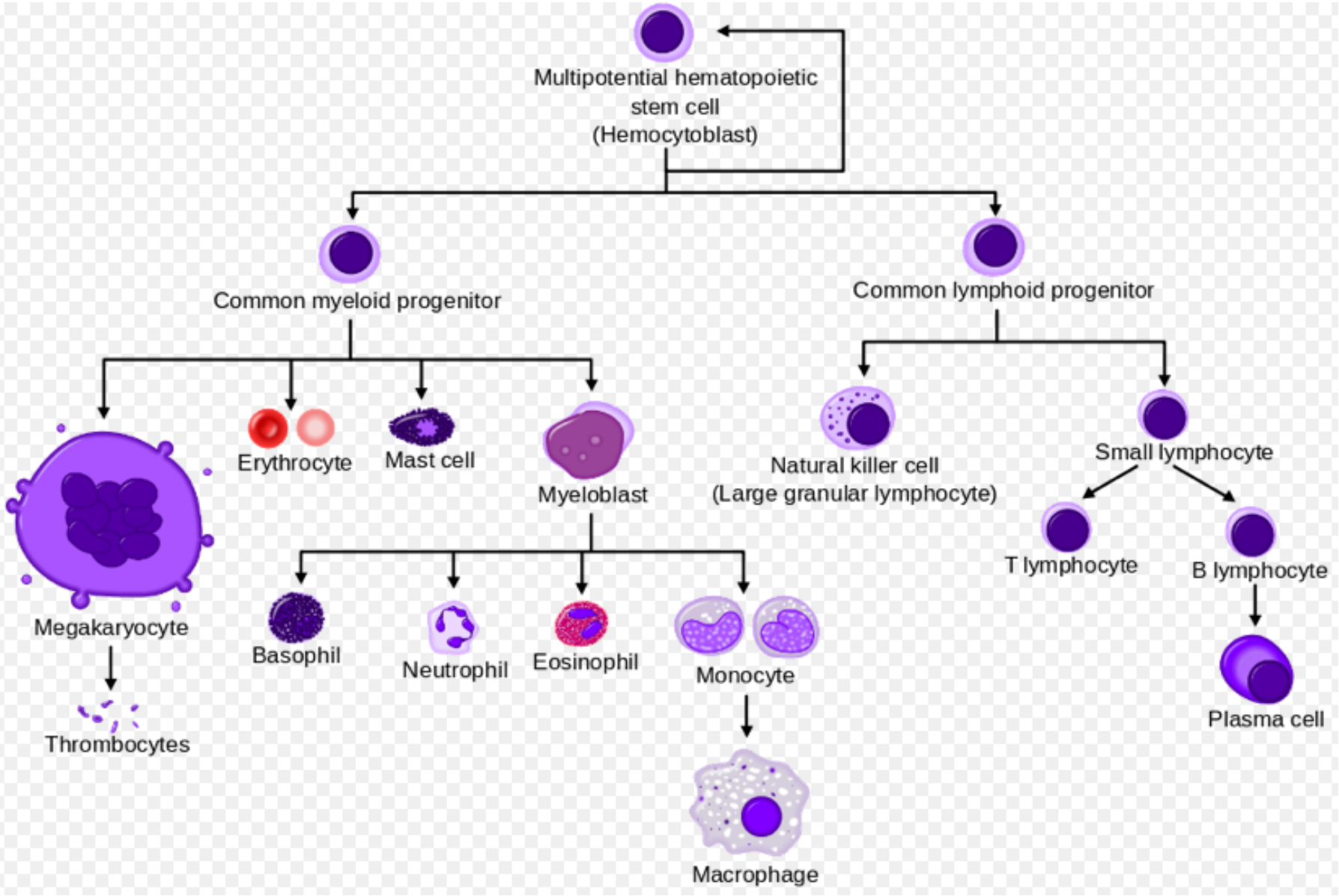
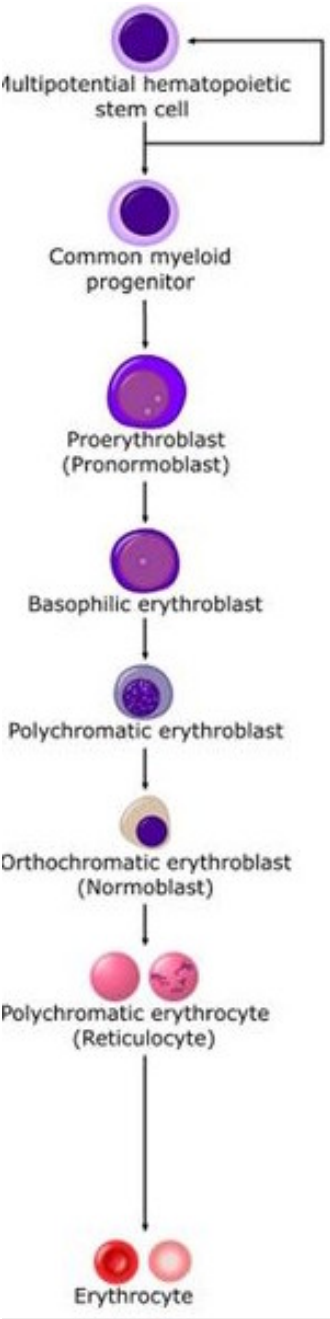
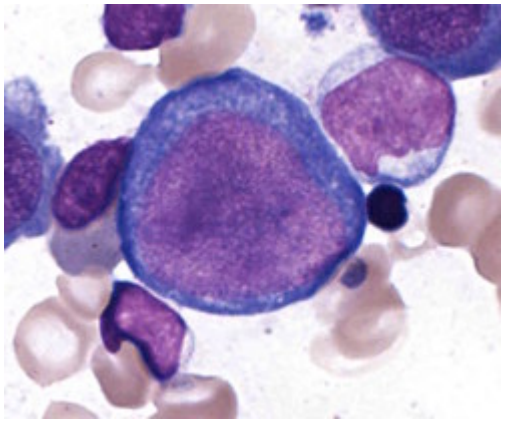
Overview

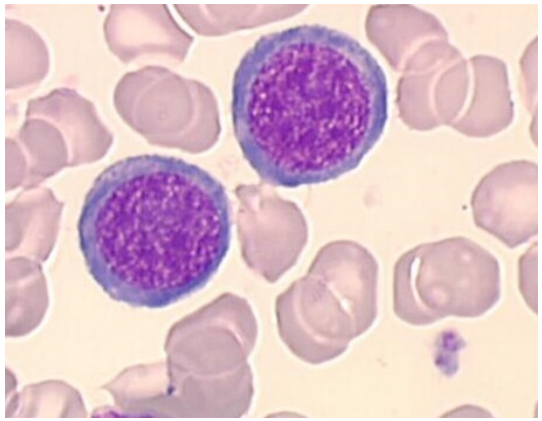
- Anaemia 1
  - Haematological disorders

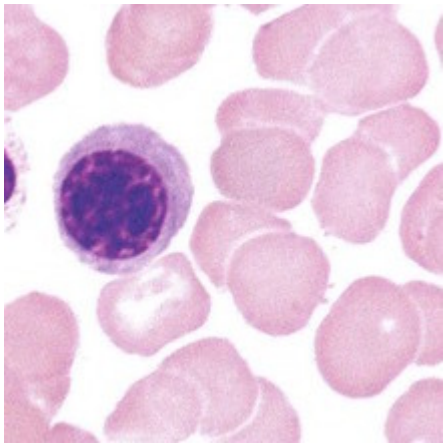
- Anaemia 2
  - Non-haematological disorders

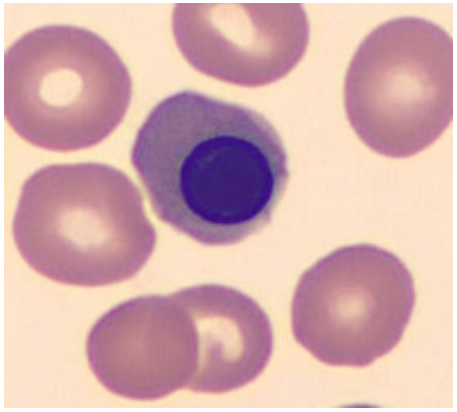

Multipotential hematopoietic stem cell (Hemocytoblast)
Common myeloid progenitor
Common lymphoid progenitor
Erythrocyte
Mast cell
Myeloblast
Natural killer cell (Large granular lymphocyte)
Small lymphocyte
Megakaryocyte
Thrombocytes
Basophil
Neutrophil
Eosinophil
Monocyte
T lymphocyte
B lymphocyte
Plasma cell
Macrophage

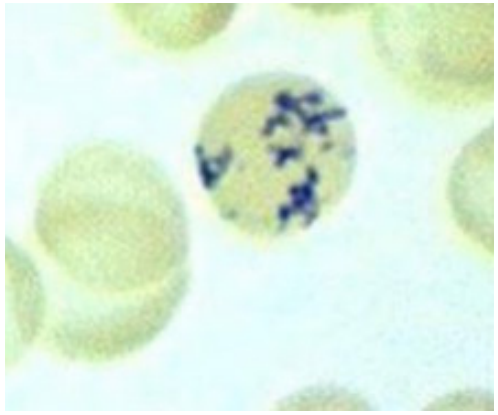

Multipotential hematopoietic stem cell
Common myeloid progenitor
Proerythroblast (Pronormoblast)
Basophilic erythroblast
Polychromatic erythroblast
Orthochromatic erythroblast (Normoblast)
Polychromatic erythrocyte (Reticulocyte)
Erythrocyte

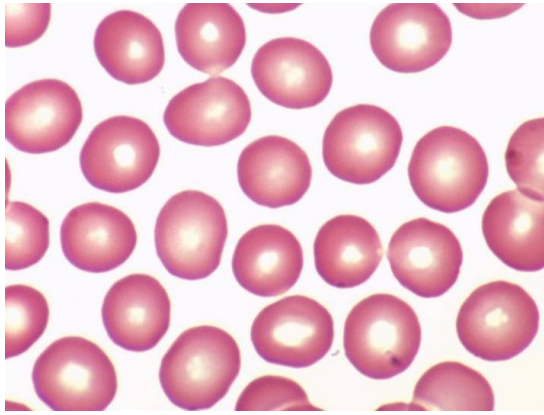




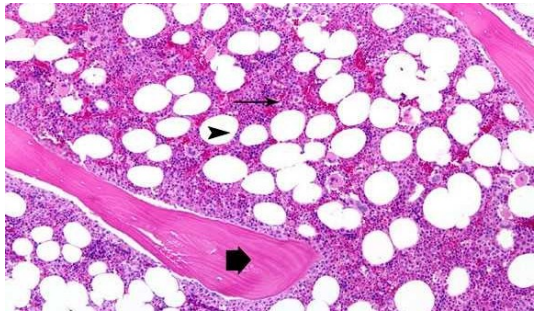








Erythroid homeostasis



Bone marrow

Substrates: Iron, folate, vitamin B12

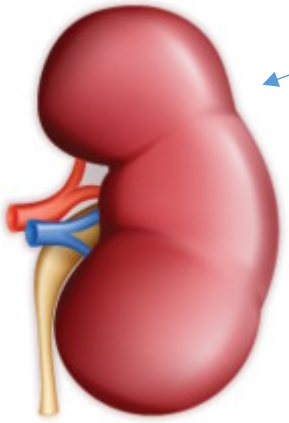
Globin chain synthesis

Red cell mass

Destruction in spleen (~1% per day)

Lung function

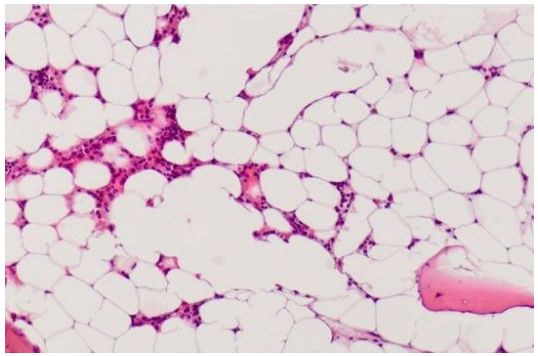
Atmospheric O_2 levels



Organ oxygenation: Peritubular capillary cells of the kidney

EPO

Causes of anaemia



Bone marrow failure

Substrate deficiency:
Iron, folate, vitamin B12

Globin chain synthesis abnormality

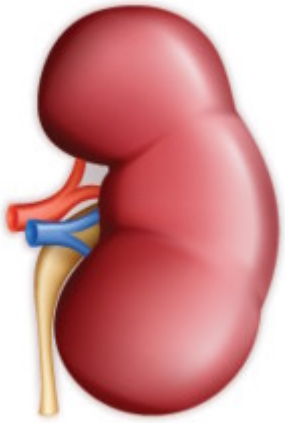
Red cell mass

Blood loss

Intravascular haemolysis

Increased destruction in spleen

Organ oxygenation:
Peritubular capillary cells of the kidney



EPO deficiency

Case 1

- 53 year old female
- PC: Fatigue
- Noticed decreased exercise tolerance over last 6 weeks. Breathless on walking up incline.
- O/E: Pallor of conjunctiva. No palpable hepatosplenomegaly or lymph nodes.

FBC

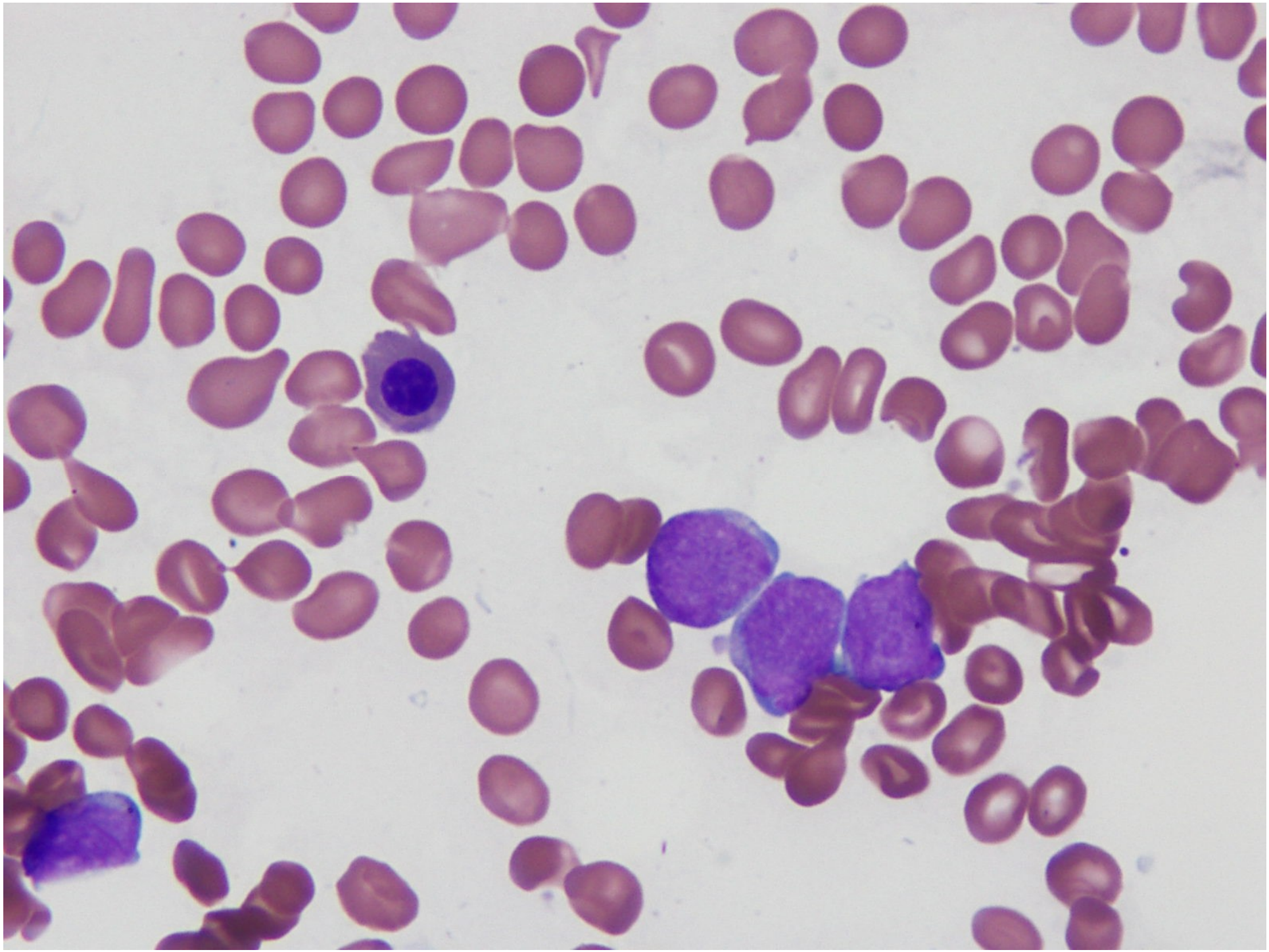
	Value	Reference
Haemoglobin	**78** g/L	120-160
WCC	**1.1** x 10^9/L	3.6-11
Platelets	**20** x 10^9/L	150-400
Neutrophils	**0.11** x 10^9/L	1.8-7.5
MCV	**111.5** fL	82-98
Reticulocytes	**20** x 10^9/L	50-100

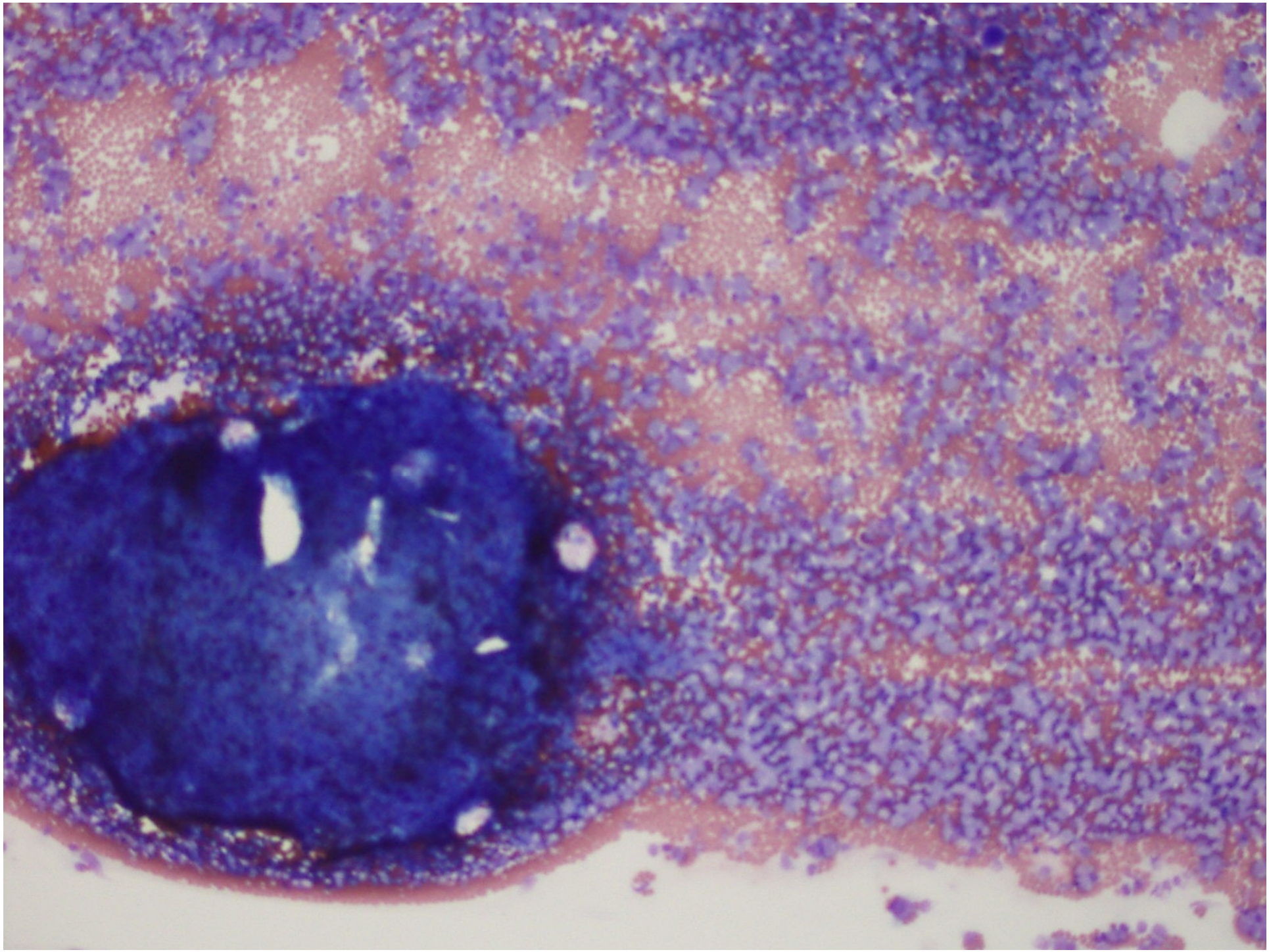
Blood film comment

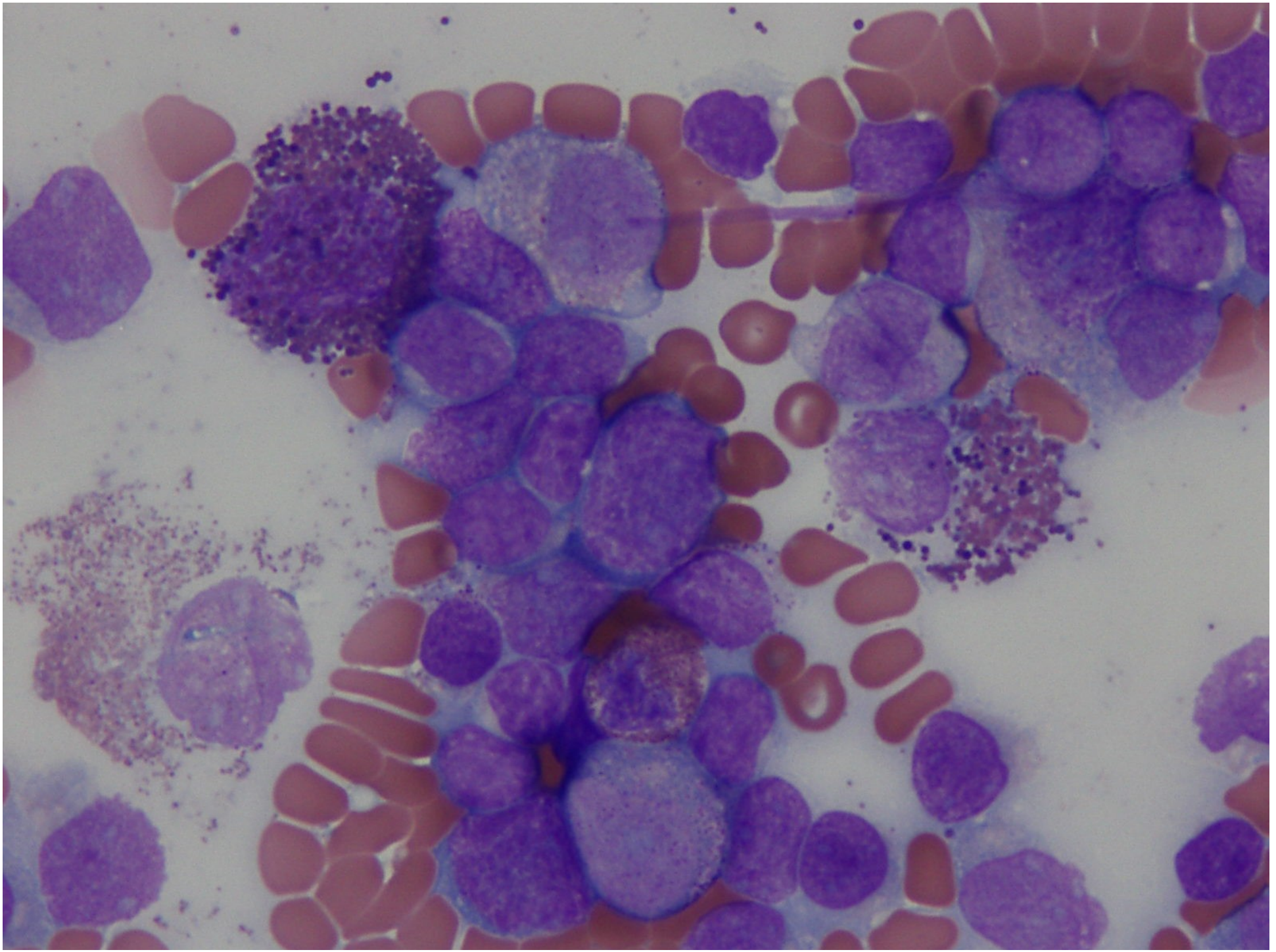
- “Leuco-erythroblastic blood picture with atypical/reactive lymphoid cells. Macrocytosis ++ and platelet count appears genuine.”

Differential Diagnosis

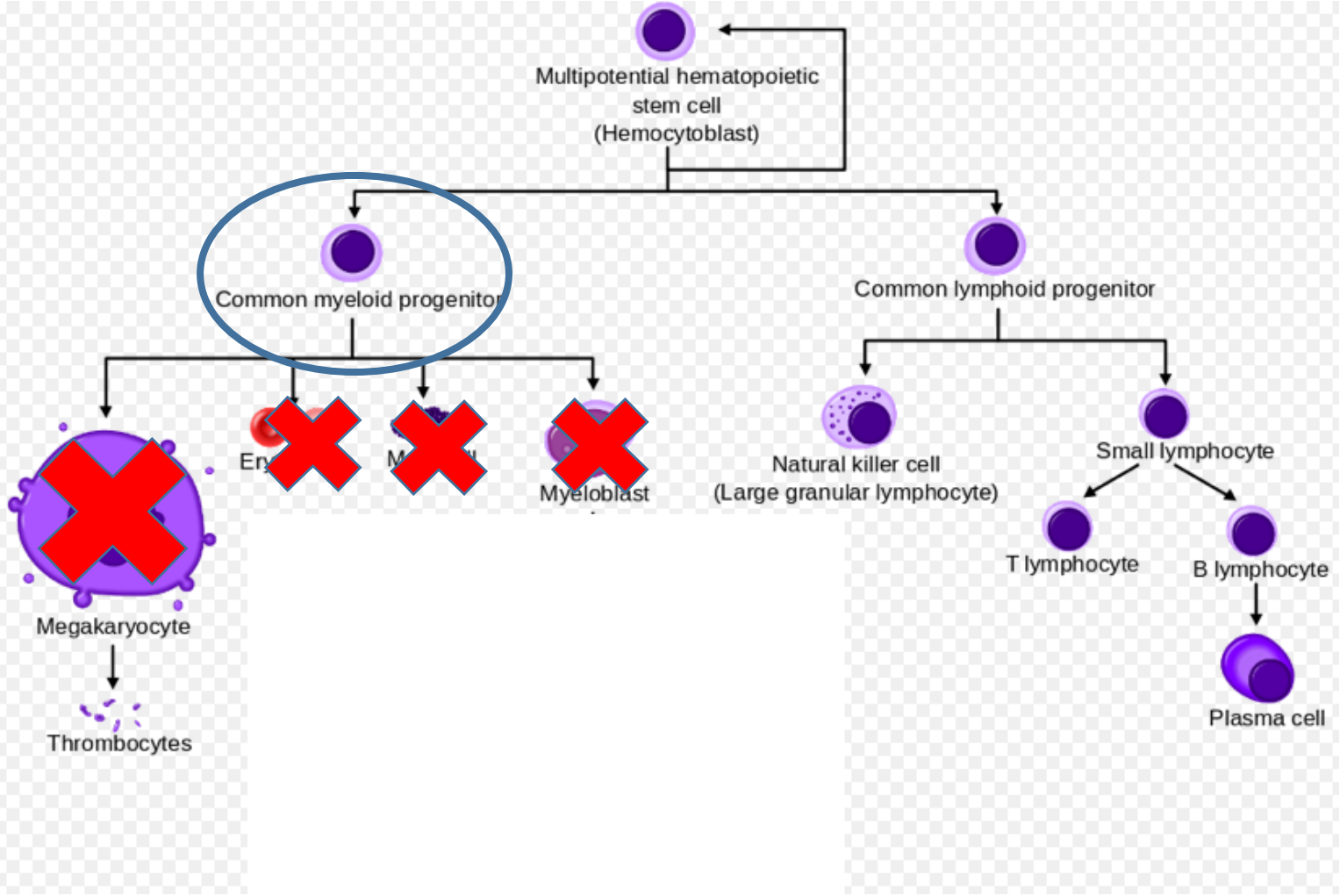
- Acute Leukaemia (Myeloid or Lymphoblastic)
- Myelodysplasia
- Myelofibrosis
- Other haematological malignancy with heavy bone marrow involvement
- Aplastic Anaemia
- ?Autoimmune
- B12/ Folate deficiency







Acute Myeloid Leukaemia



Acute Myeloid Leukaemia

- Fatigue
- New spontaneous bleeding/bruising
- Bone pains
- Rapid onset of symptoms

FBC

- Pancytopenia
- Peripheral blasts
- Leukoerythroblastic blood film

Action

- Urgent Haematology phone referral
- If any bleeding symptoms consider DIC: send clotting profile plus D-dimer

Treatment

- Induction chemotherapy
- Consider allogeneic stem cell transplant

Case 2

- 68 year male
- PC: FU for hypertension
- Feels well. No recent infections.
- PMH: Hypertension
- DH: Ramipril, simvastatin
- O/E: Nil to find

FBC

	Value	Reference
Haemoglobin	**108** g/L	120-160
WCC	**1.6** x 10^9/L	3.6-11
Platelets	**90** x 10^9/L	150-400
Neutrophils	**0.6** x 10^9/L	1.8-7.5
MCV	97 fL	82-98
Reticulocytes	**45** x 10^9/L	50-100

Film comment

- “Anaemia first noted in 2011. Normochromic and progressive. Anisocytosis with tear-drop poikilocytes as well as dysplastic changes in granulocytes (hypogranulation, pseudo-Pelger forms and paramyeloid cells.”

Differential diagnosis

- Myelodysplasia
- Acute Leukaemia
- Bone marrow infiltration (e.g. myelofibrosis, lymphoma, myeloma)
- Autoimmune
- B12/ Folate deficiency
- Infection

Further tests

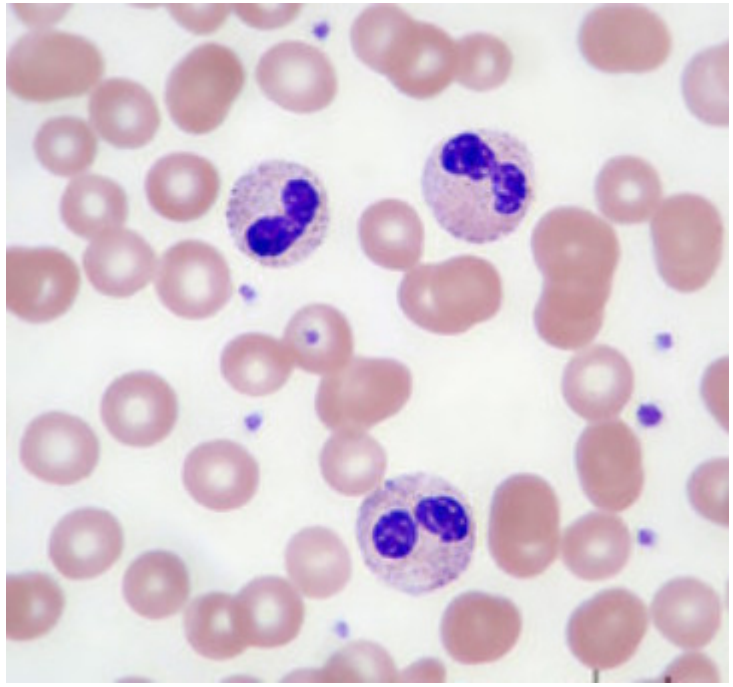
- B12 and folate
- TSH
- Ferritin
- Myeloma screen

Action

- Outpatient referral to Haematology

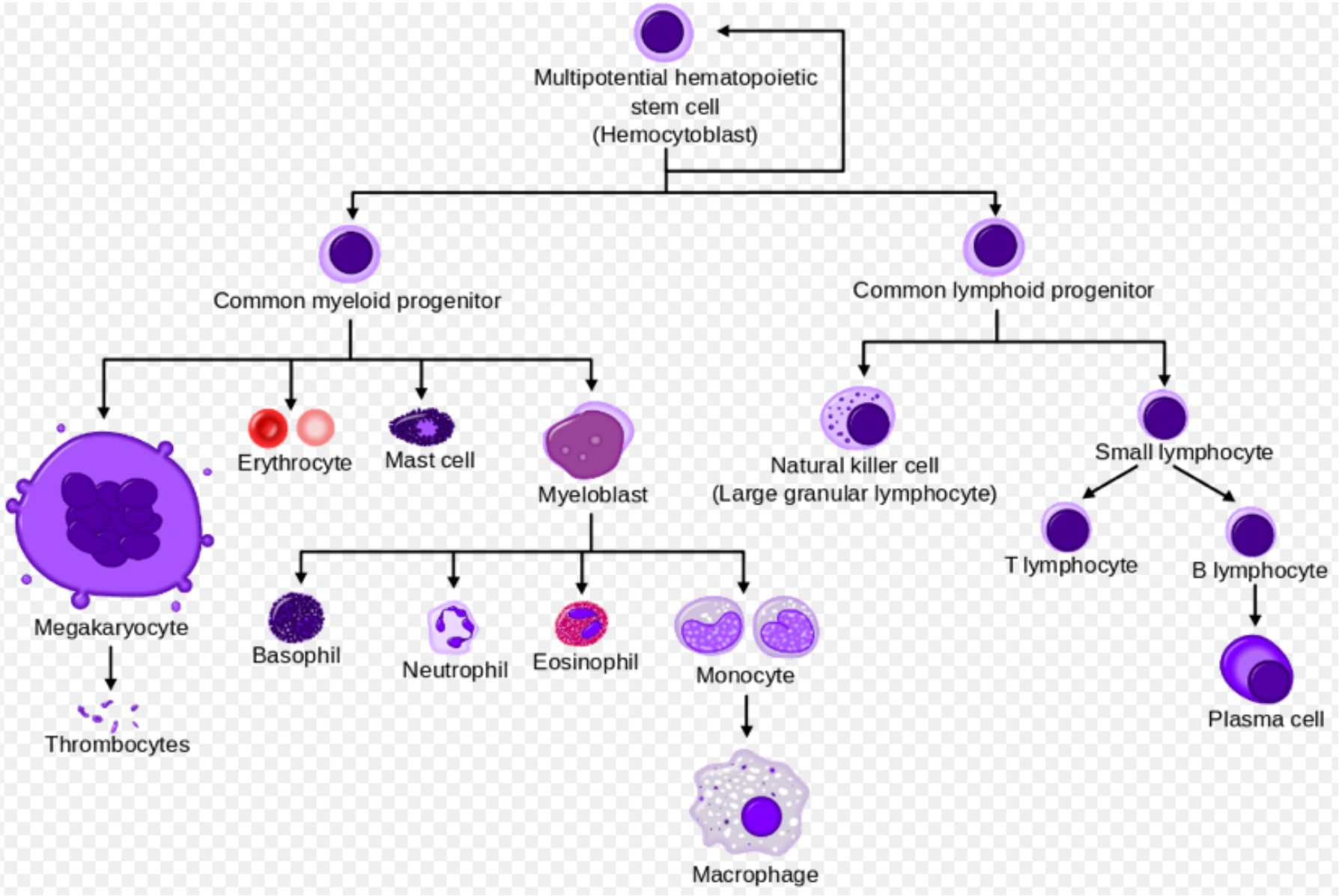
Further tests

- Bone marrow biopsy
- Cytogenetics



Myelodysplastic Syndrome

- Refractory Anaemia (RA)
- Refractory Anaemia with Ringed Sideroblasts (RARS)
- Refractory Cytopenia with Multilineage Dysplasia (RCMD)
- Refractory Anaemia with Excess Blasts (RAEB)
  - 1: 5-9% blasts on BMA
  - 2: 10-19% blasts on BMA
- Chronic Myelomonocytic Leukaemia (CMML)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Neutrophil
Eosinophil
Monocyte
T lymphocyte
B lymphocyte
Plasma cell
Macrophage

Prognosis

ble 5. Revised International Prognostic Scoring System (IPSS-R) for myelodysplastic syndromes [8]

gnostic characteristics	Points						
	0	0.5	1	1.5	2	3	4
ogenetic risk category[a]	Very good		Good		Intermediate	Poor	Very p
sts in bone marrow, %	≤2		>2%–5%		5%–10%	>10%	
emoglobin, g/dl	≥10		8–<10	<8			
telet count, $\times 10^9$/l	≥100	50–<100	<50				
solute neutrophil count, $\times 10^9$/l	≥0.8	<0.8					

S-R risk group	Score	Median overall survival, years	Median time to 25% AML evolution, years
y low	≤1.5	8.8	NR
v	>1.5–3	5.3	9.4
ermediate	>3–4.5	3.0	2.5
gh	>4.5–6	1.6	1.7
y high	> 6	0.8	0.7

Treatment

- Low risk/intermediate 1: Supportive care
  - If symptomatic anaemia
    - Consider EPO +/- GCSF
    - Red blood cell transfusions
  - PRN antibiotics
  - Monitor FBC

Treatment

- High risk
  - Azacitadine
  - Induction chemotherapy + allogeneic SCT if age < 65 yrs

Case 3

- 67 year old female
- PC: Increasing fatigue
- HPC: Non-specific, gradual onset. Complains of OA in hips and knees. High BMI.
- PMH: T2DM, hypertension
- DH: Citalopram, metformin, ramipril, analgesics

FBC

	Value	Reference
Haemoglobin	**104** g/L	120-160
WCC	8.2 x 10^9/L	3.6-11
Platelets	270 x 10^9/L	150-400
Neutrophils	5.8 x 10^9/L	1.8-7.5
MCV	**99** fL	82-98
Reticulocytes	51 x 10^9/L	50-100

Differential

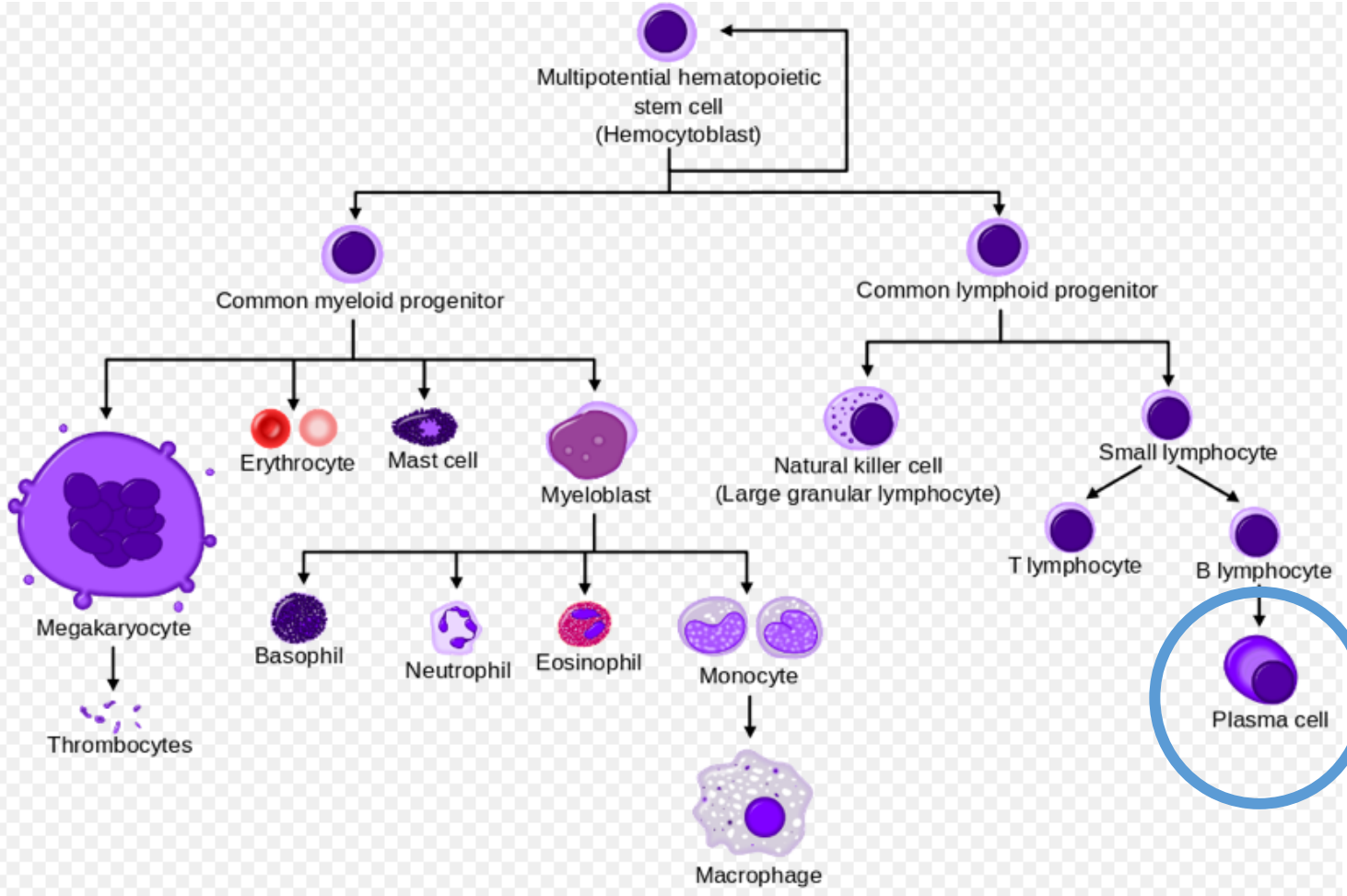
- B12, folate deficiency
- IDA
- Anaemia of chronic disease
- Hypothyroidism
- Myelodysplasia
- Bone marrow infiltration (e.g. myelofibrosis, lymphoma, myeloma)

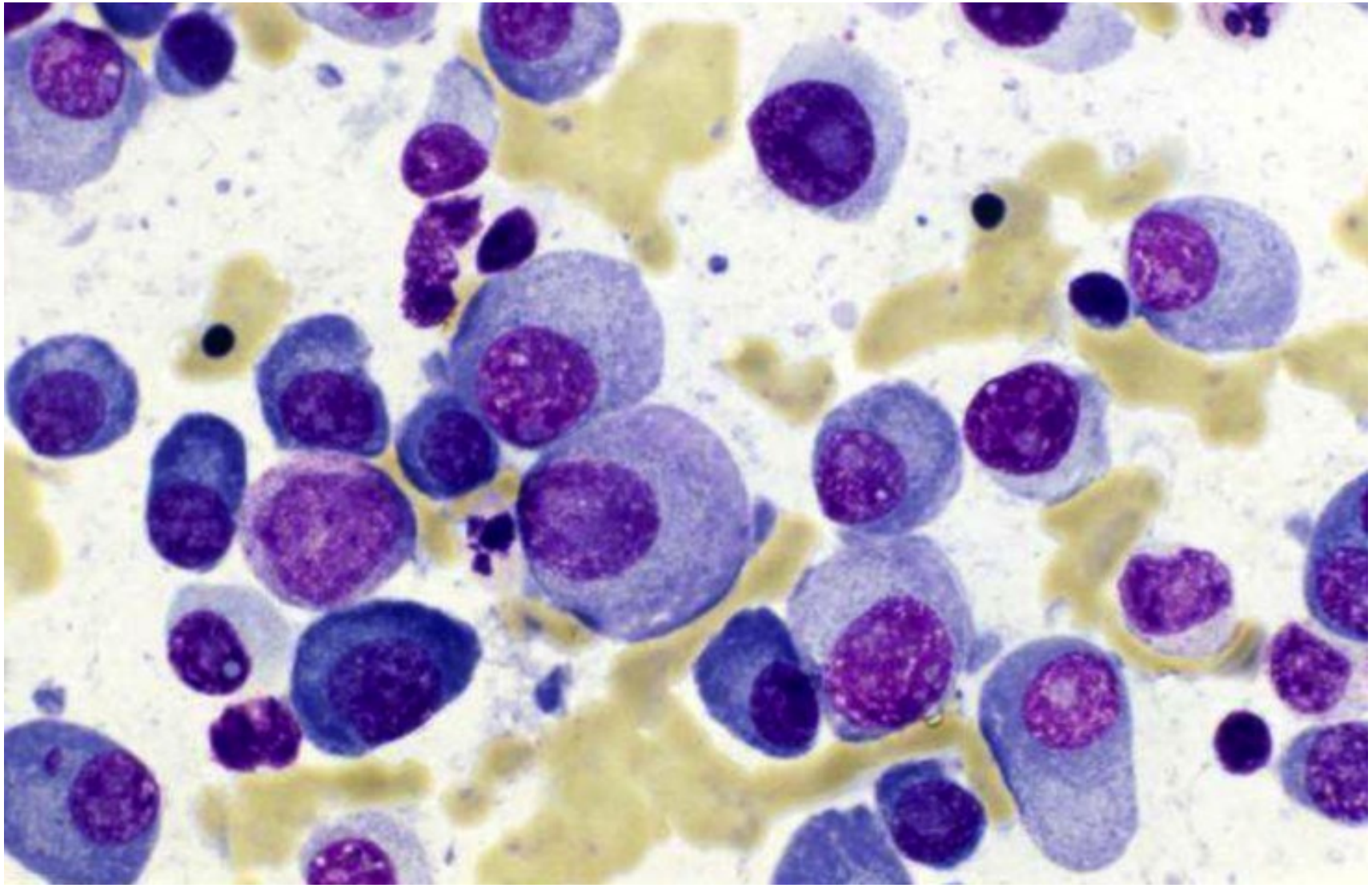
Further blood tests

- U&Es normal
- ALT 16, Bilirubin 4, ALP 93, Albumin 43 g/L, Total protein 81 g/L
- Ferritin, B12, folate normal
- CRP normal

- Calcium normal
- Serum protein electrophoresis: Band protein monoclonal band 15 g/L
- Bence-Jones Protein negative

Multiple Myeloma

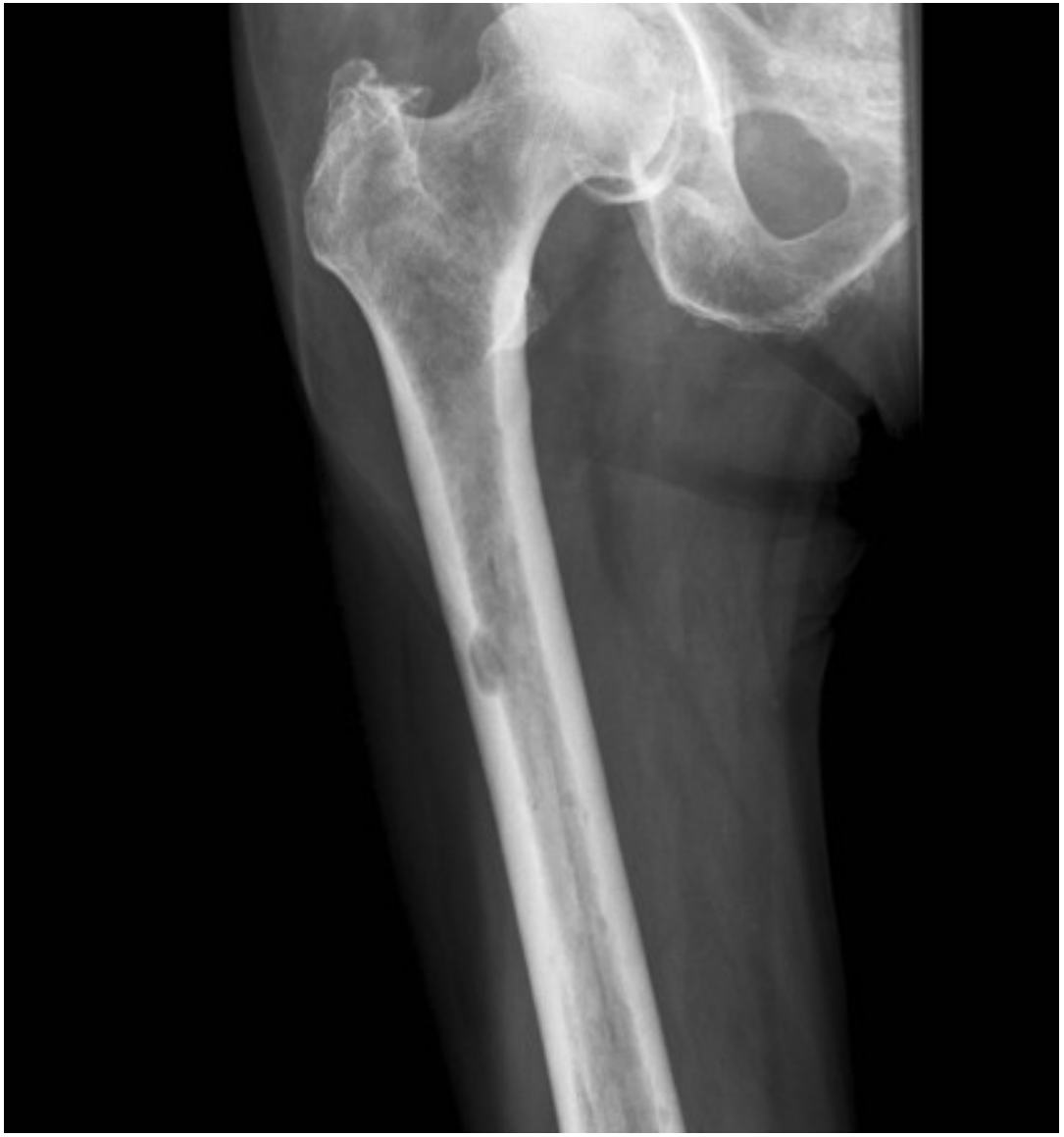




Multiple Myeloma

- Suspect:

- **C**alcium: High calcium
- **R**enal: New impairment
- **A**naemia: Unexplained
- **B**one pains



Action

- Refer to Haematology
- Treatment involves several therapies managed as outpatient

Monoclonal Gammopathy of Uncertain Significance (MGUS)

- Underlying plasma cell dyscrasia
- Low probability of progression to symptomatic myeloma: 5% in 10 years
- Risk stratify based on paraprotein level, Ig type, light chain ratio and age.
- Can be monitored in community

Summary

- Systematic approach to diagnosis
- Recognise red flag signs
- Always assess for splenomegaly and lymphadenopathy
- Recognise utility of reticulocyte count in diagnosing bone marrow failure
- Appropriate referral to Haematology