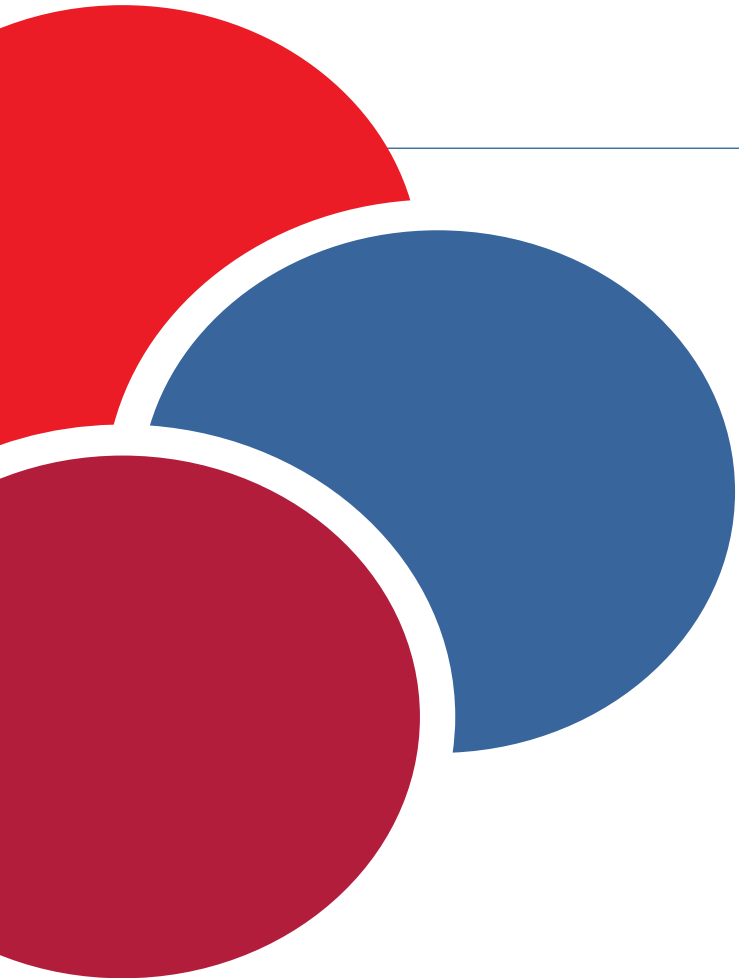




Case 1

Presented by Dr Alesia Khan

Consultant Haematologist

Leeds Teaching Hospital Trust



**The Leeds
Teaching Hospitals**
NHS Trust



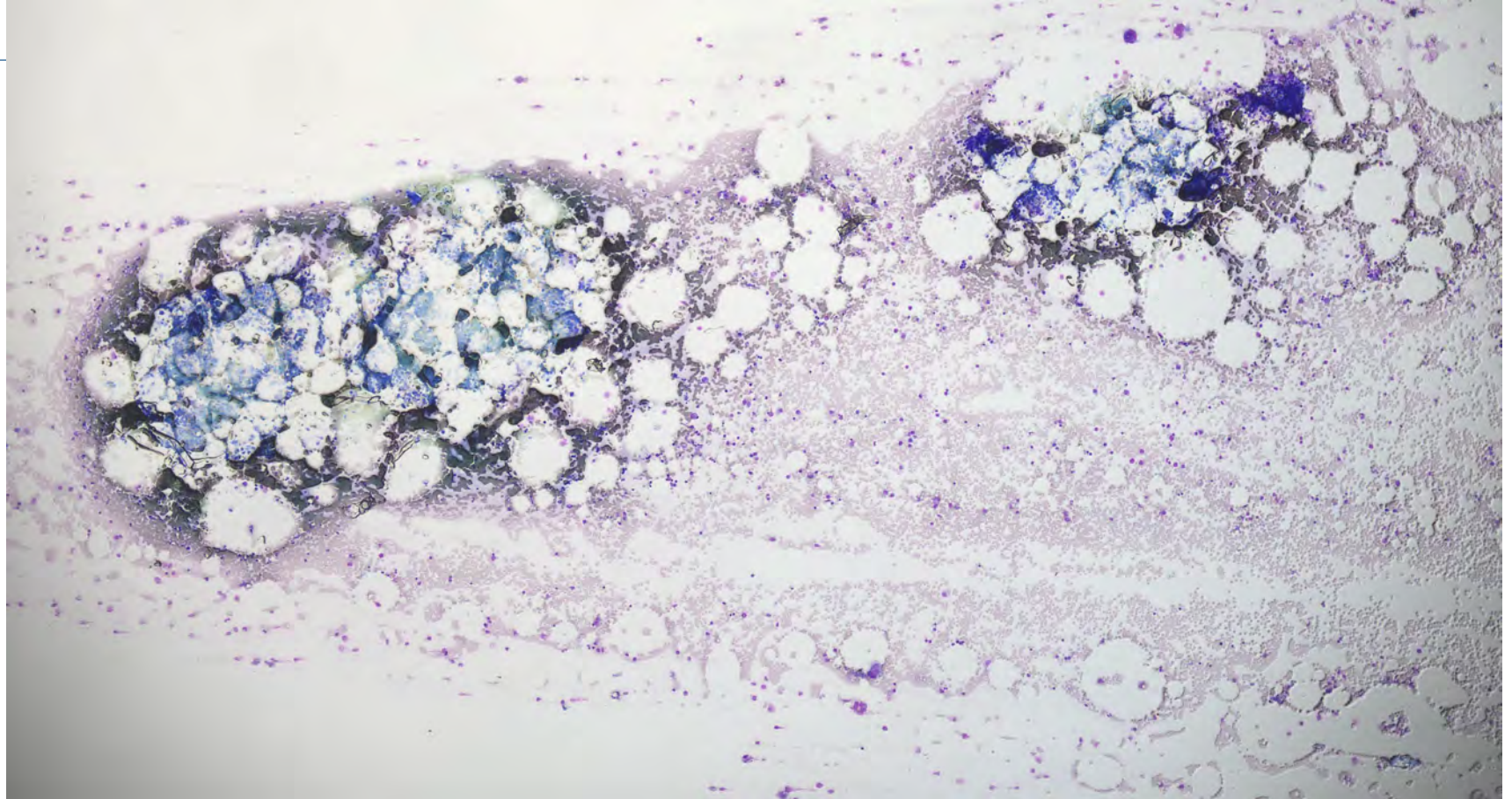
Conflicts of Interest

- AOP – educational support
- GSK – honorarium
- Novartis – honorarium & educational support

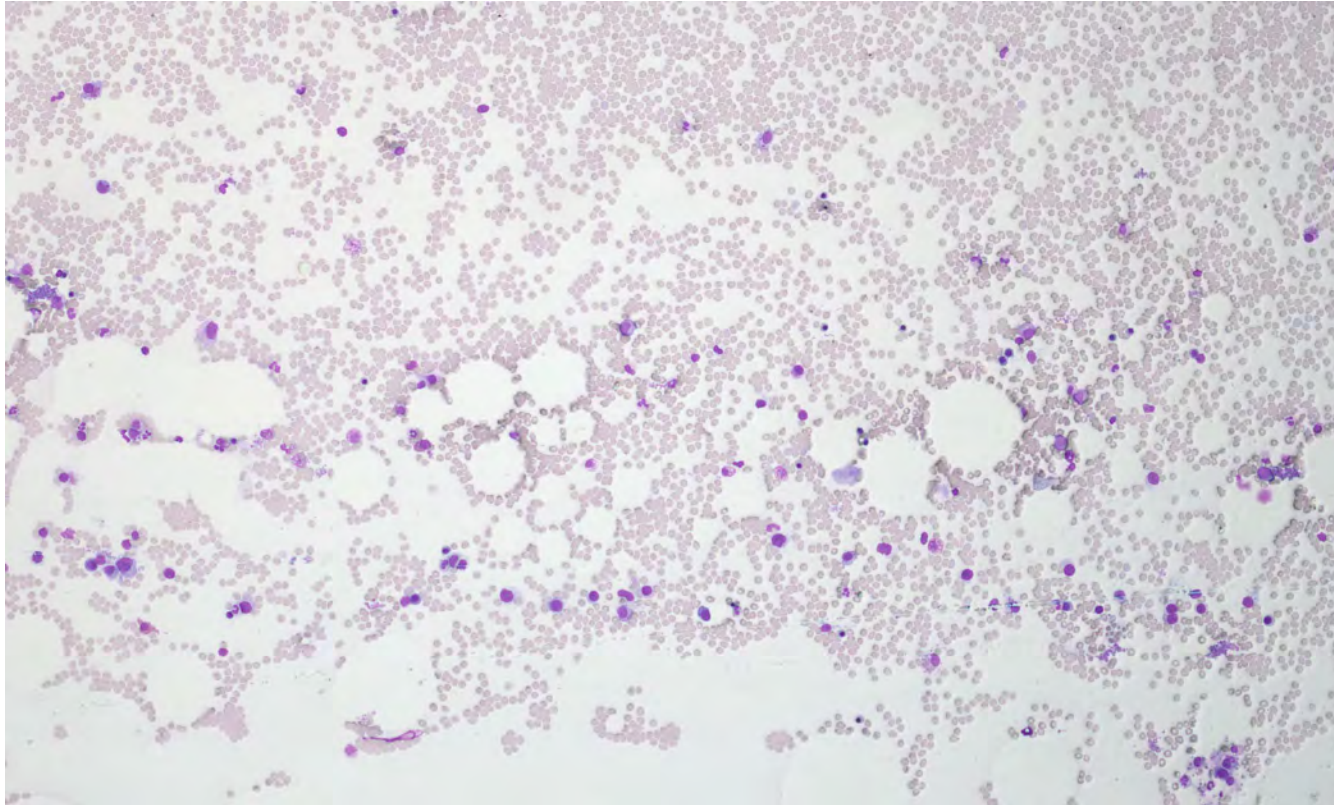
Case 1

- 73 year old gentleman.
- PMH: Hypertension and TY2DM.
- Presents with pancytopenia and bone pain
- Hb 98g/dL, WCC 2.3×10^9 , Plt 94×10^9 .

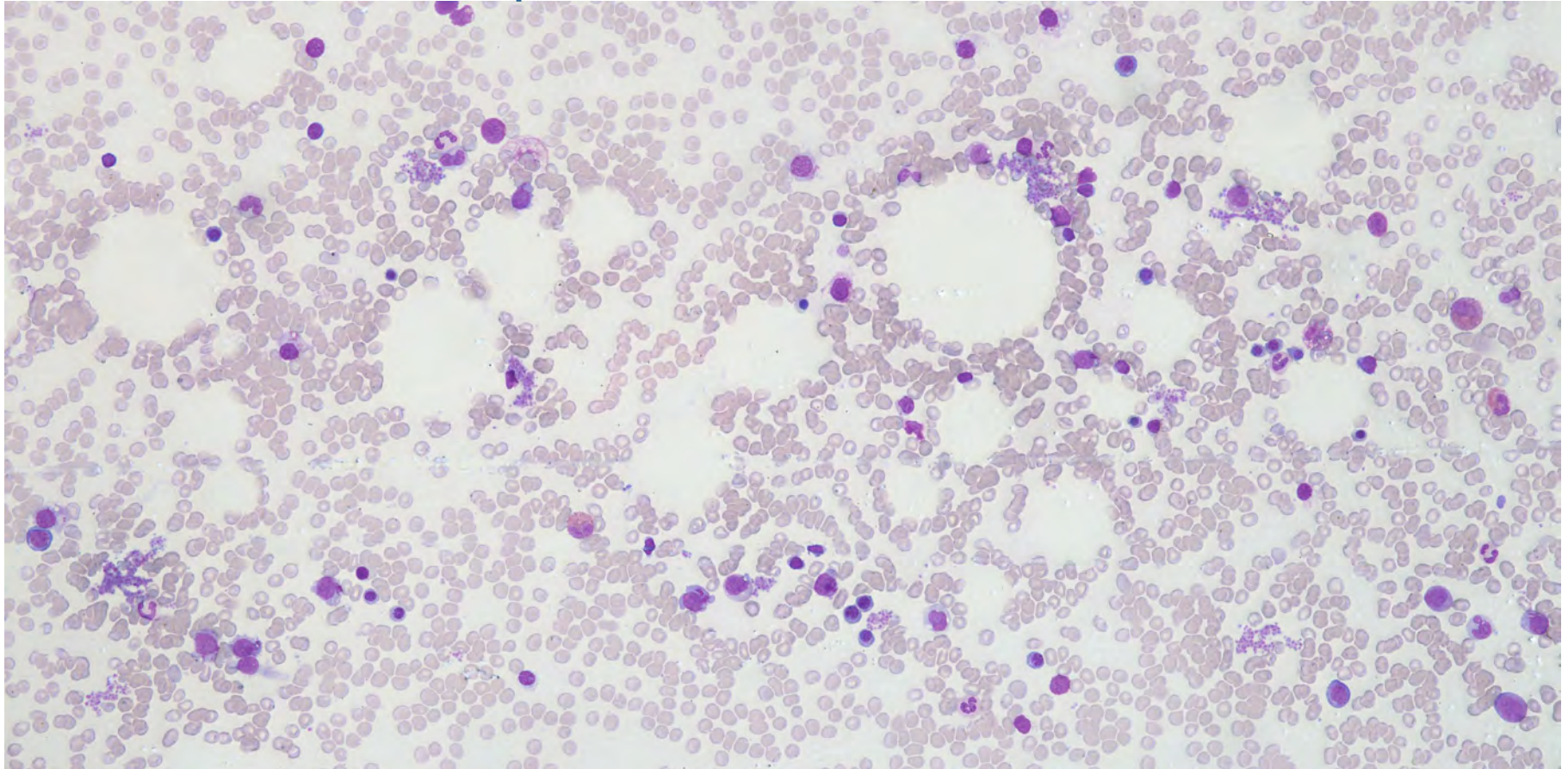
Bone marrow aspirate x 2.5



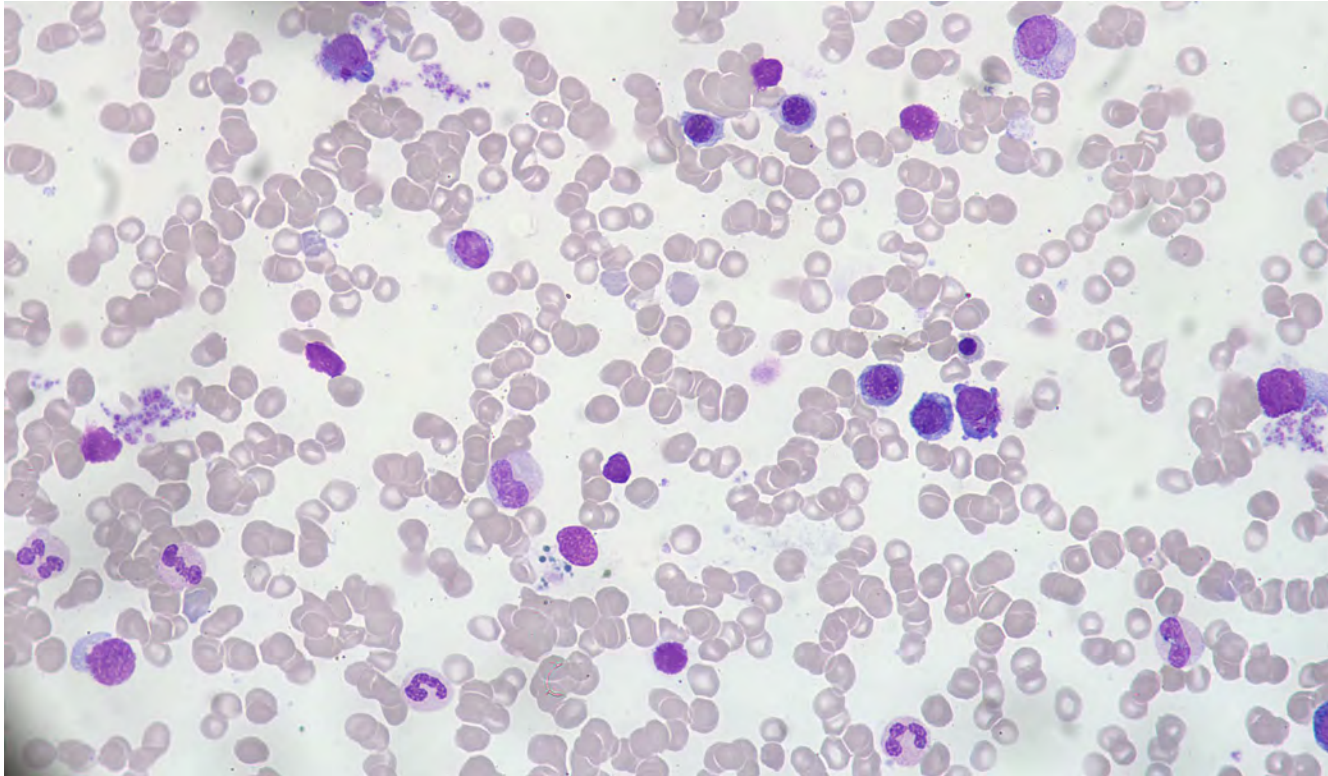
Bone marrow aspirate x 4



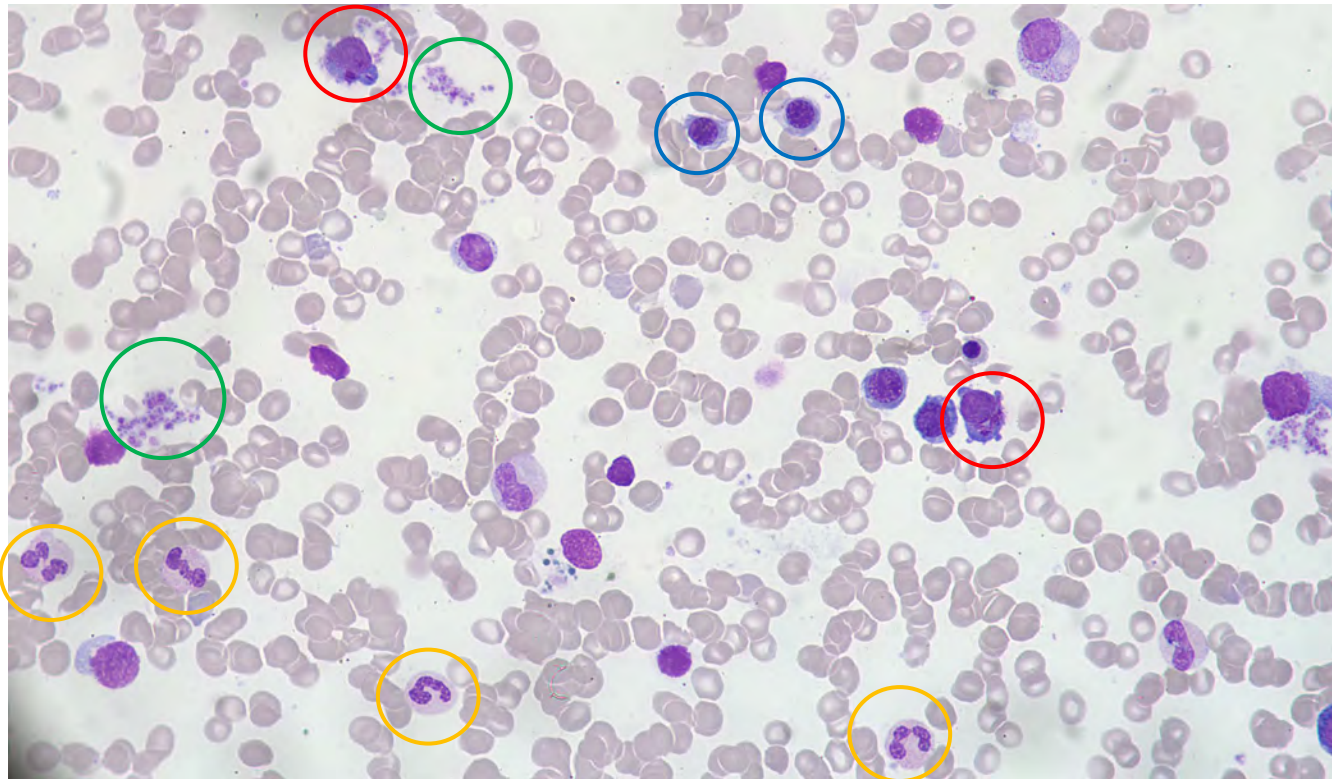
Bone marrow aspirate x 10



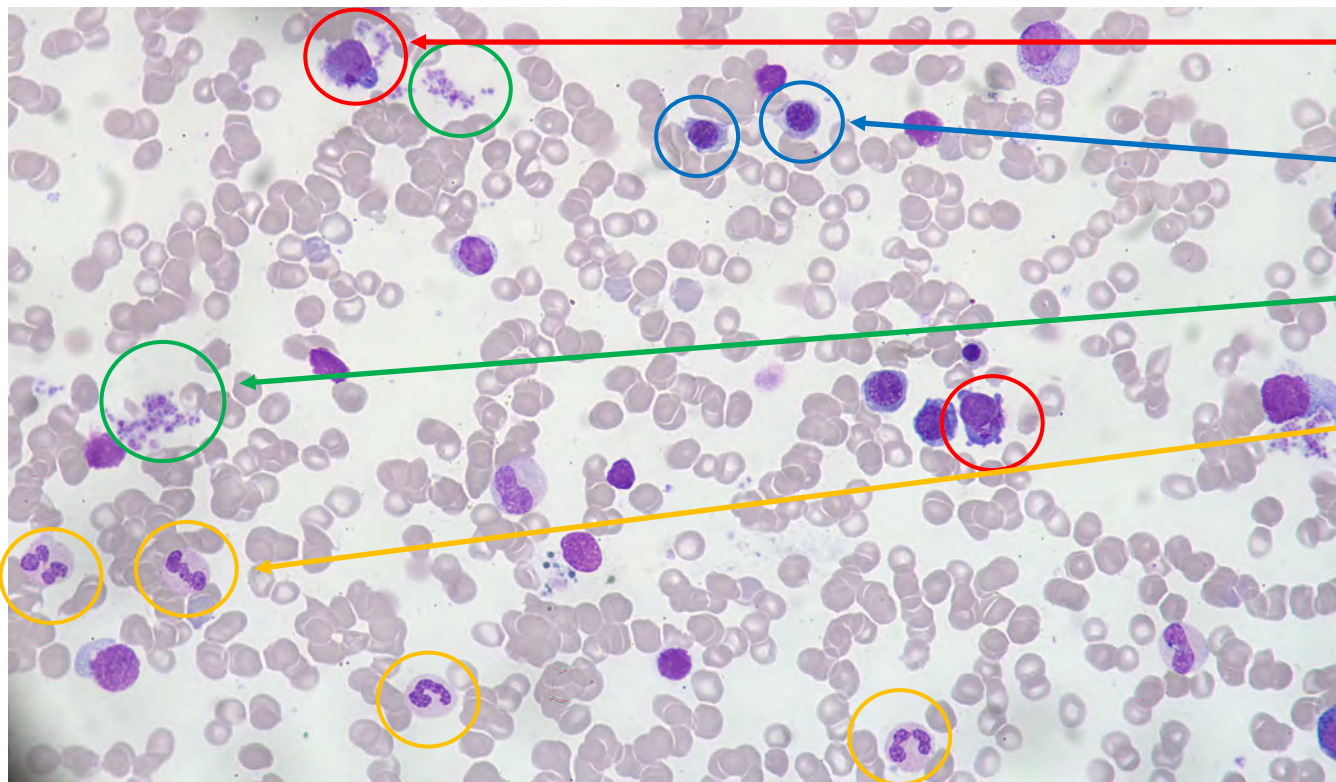
Bone marrow aspirate x 20



Bone marrow aspirate x 20



Bone marrow aspirate x 20



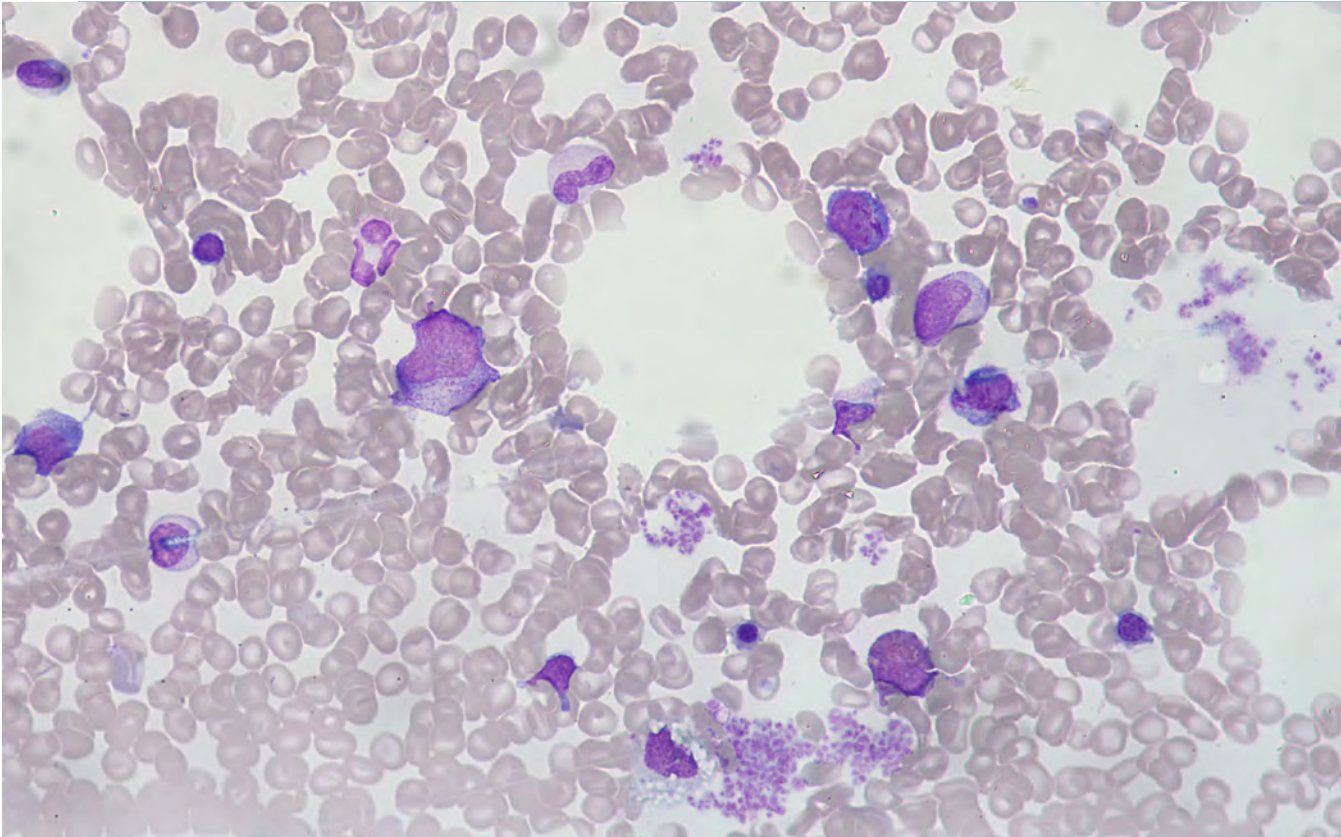
Scattered atypical cells

Erythroid precursors

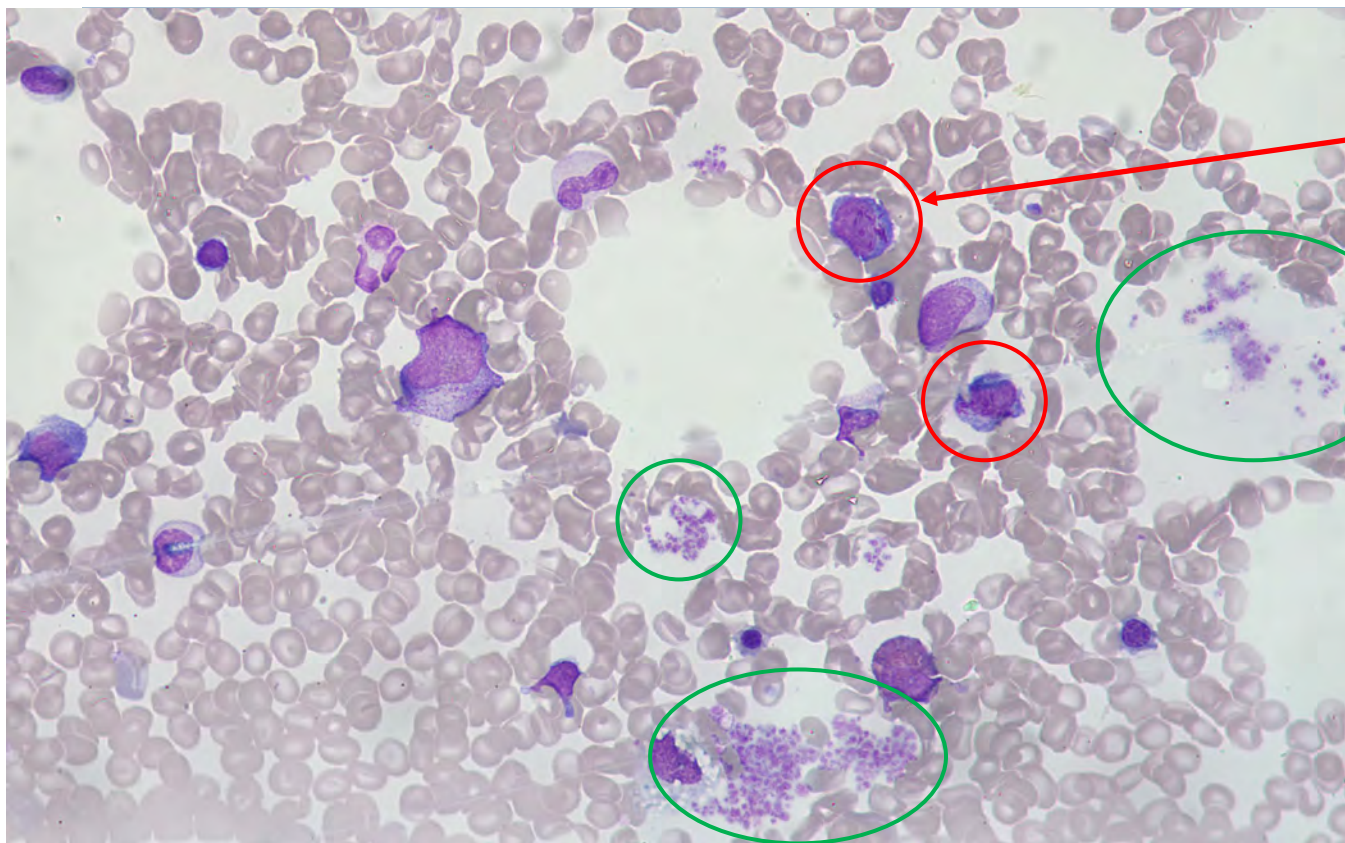
Scattered platelet drifts

Maturing granulocytes

Bone marrow aspirate x 40



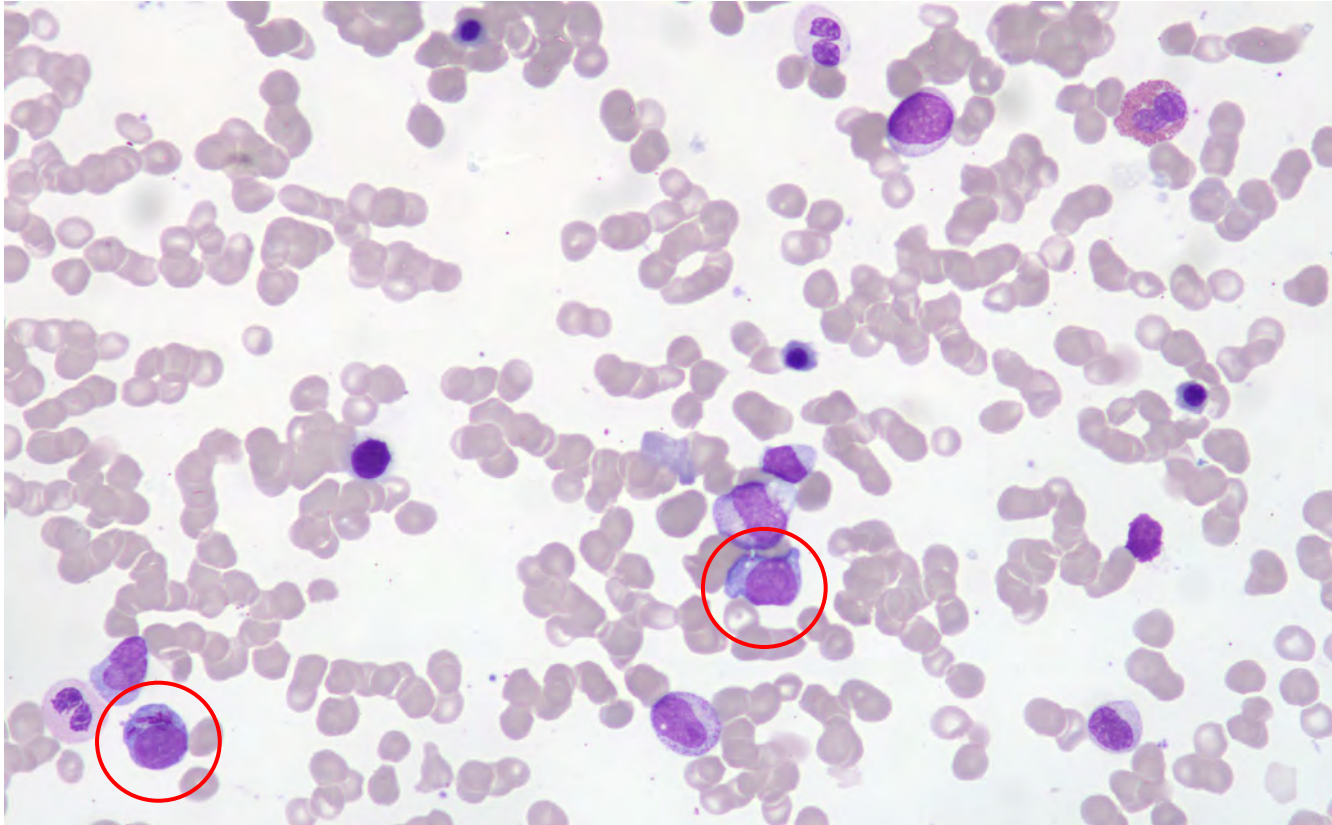
Bone marrow aspirate x 40



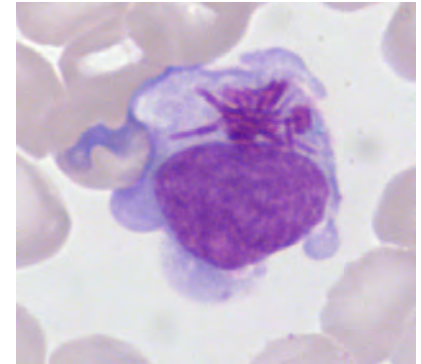
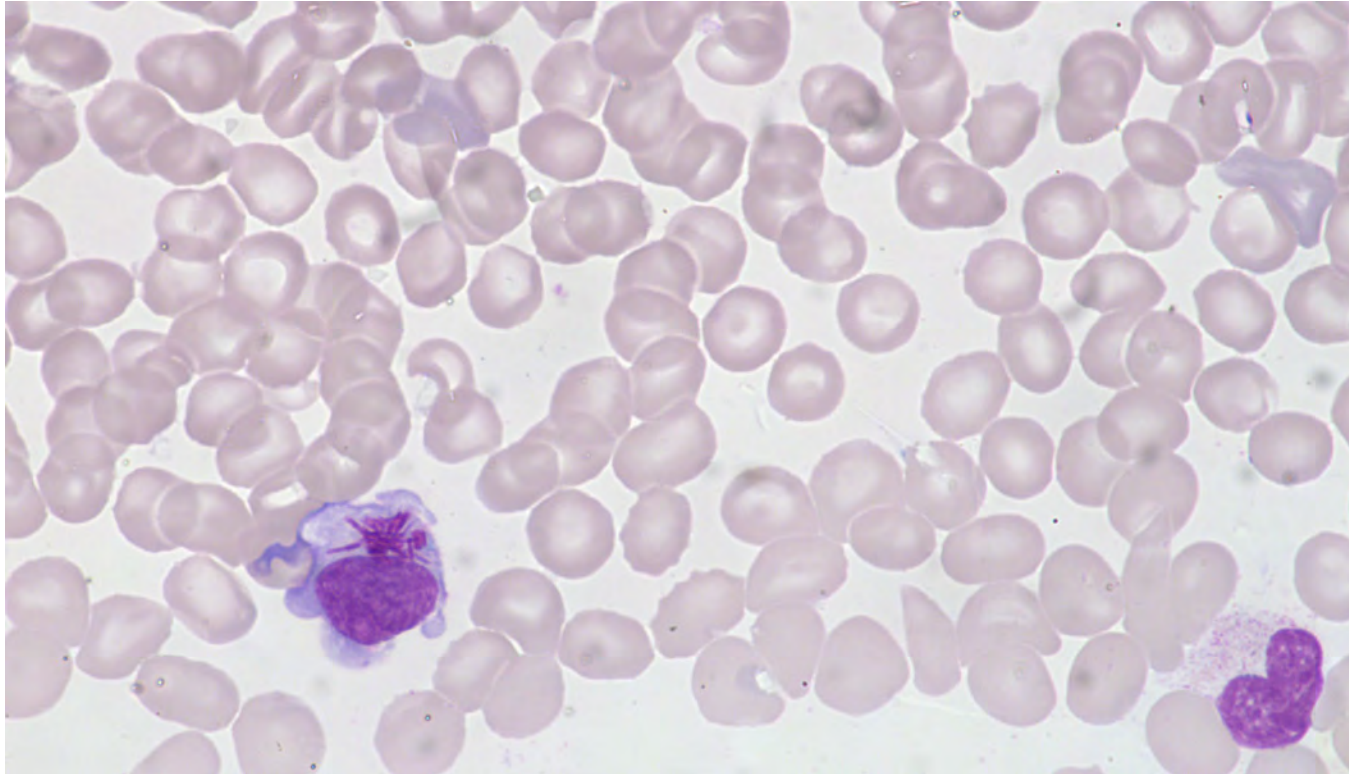
Scattered atypical cells

Scattered platelet driffts

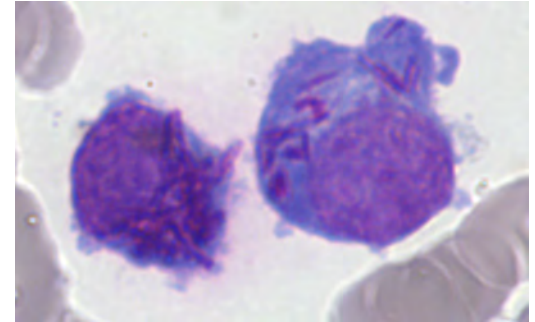
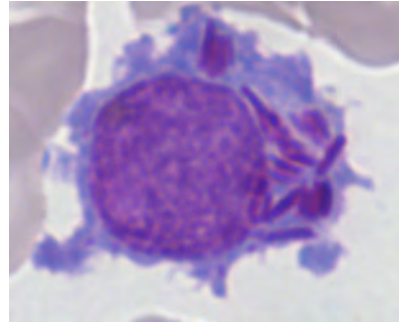
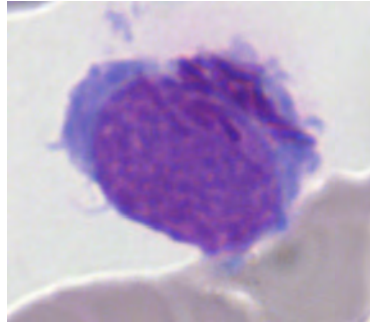
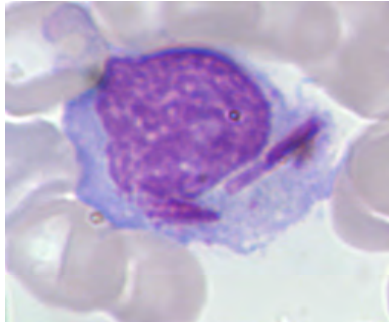
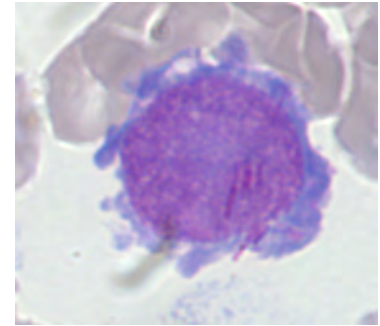
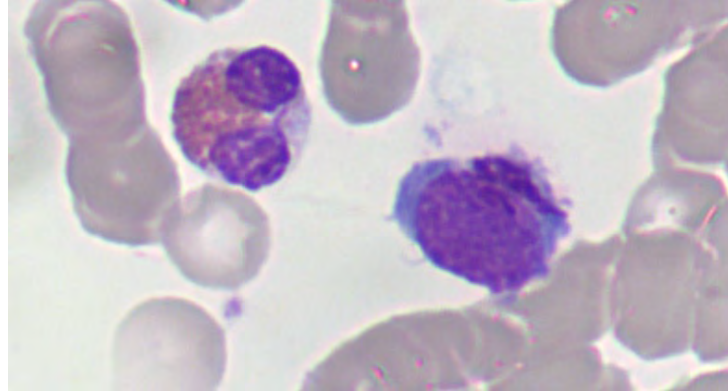
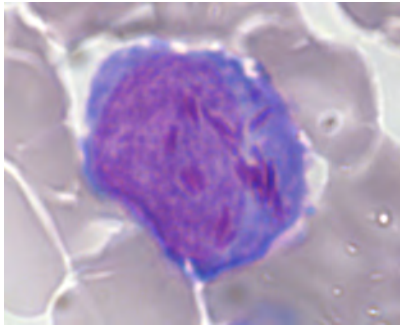
Bone marrow aspirate x 40



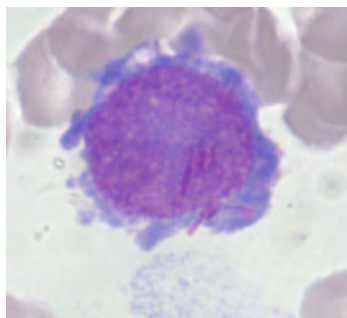
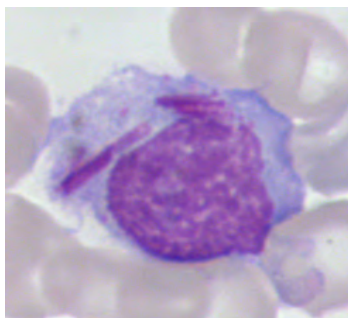
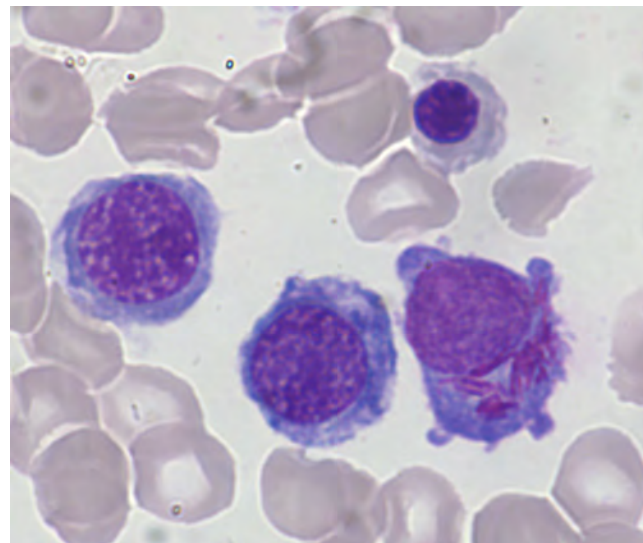
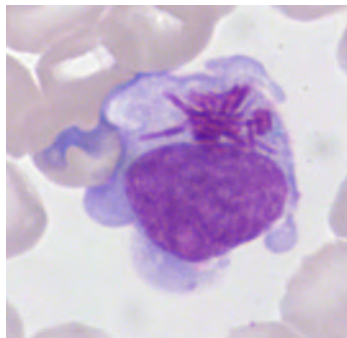
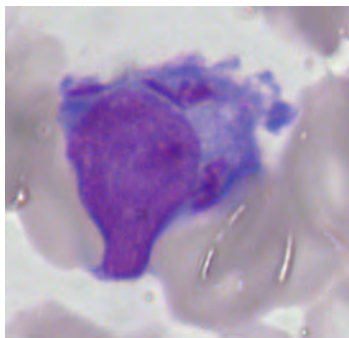
Bone marrow aspirate x 100



High power magnification of cells



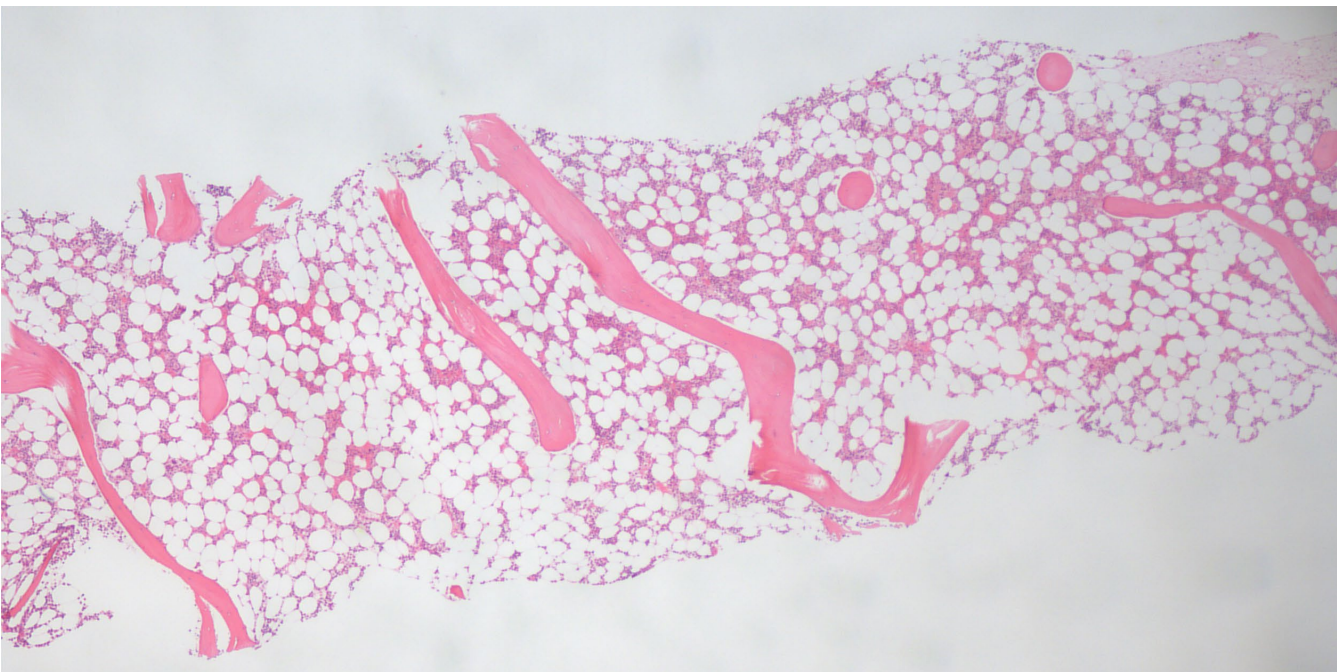
High power magnification of cells



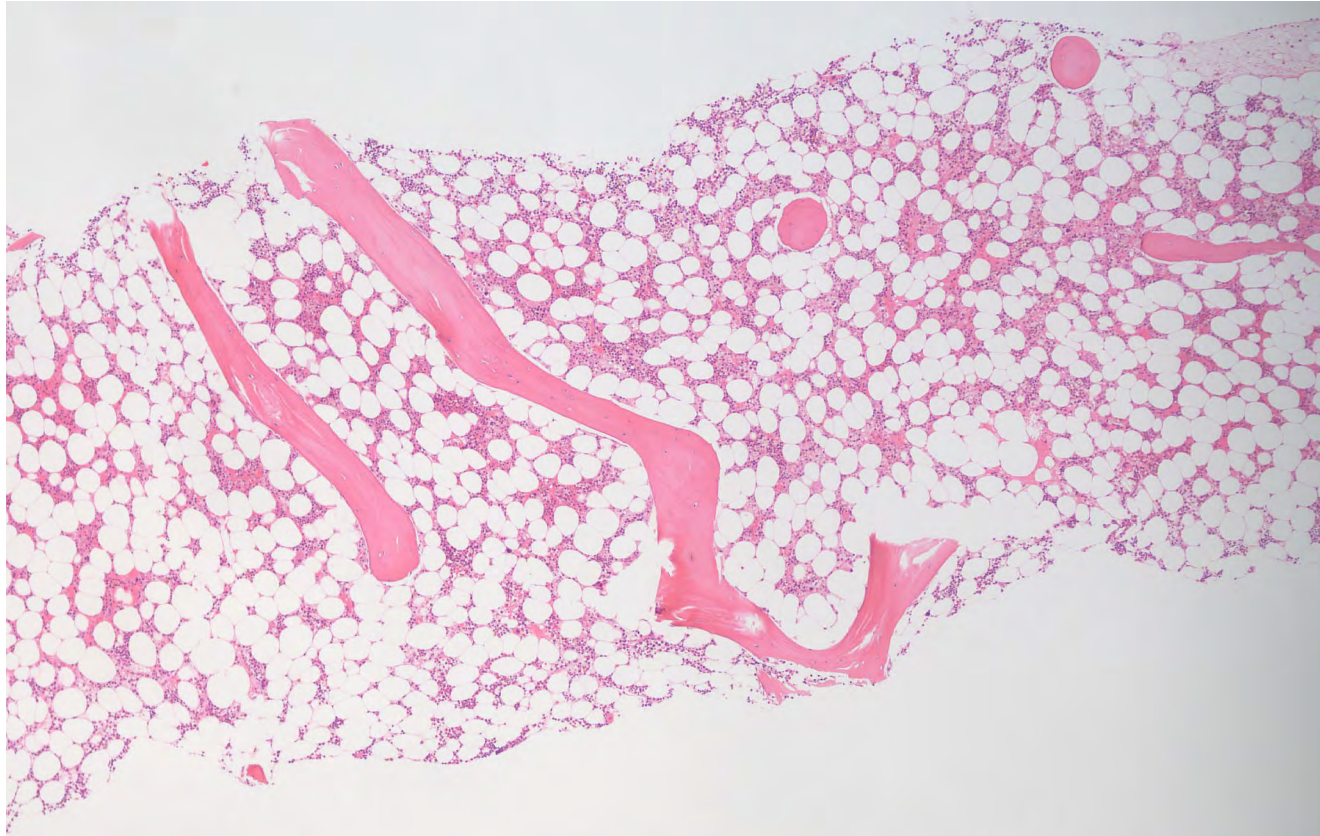
What do you think the diagnosis is?

- a) Accelerated phase myelofibrosis
- b) Acute Promyelocytic Leukaemia
- c) Acute myeloid leukaemia with NPM1 mutation.
- d) Plasma cell myeloma
- e) AML myelodysplasia related
- f) Lysosomal storage disorder

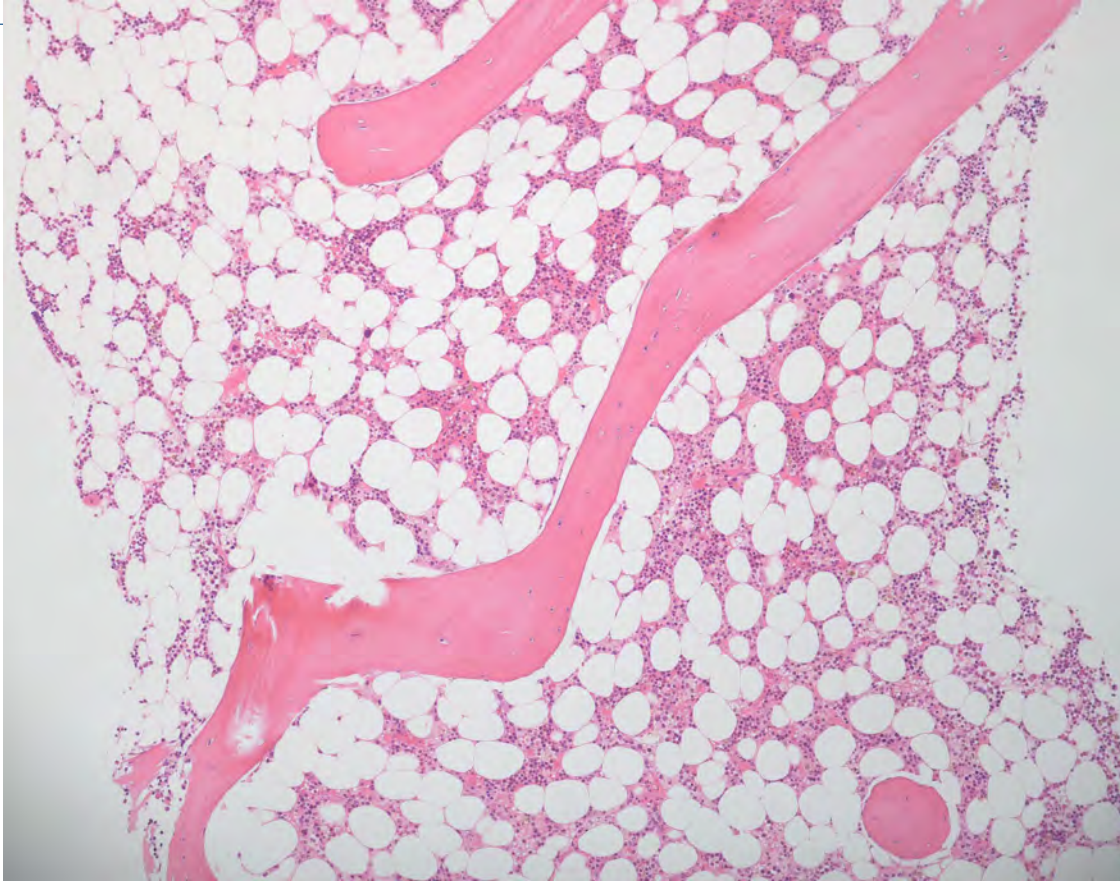
Trephine x 2.5



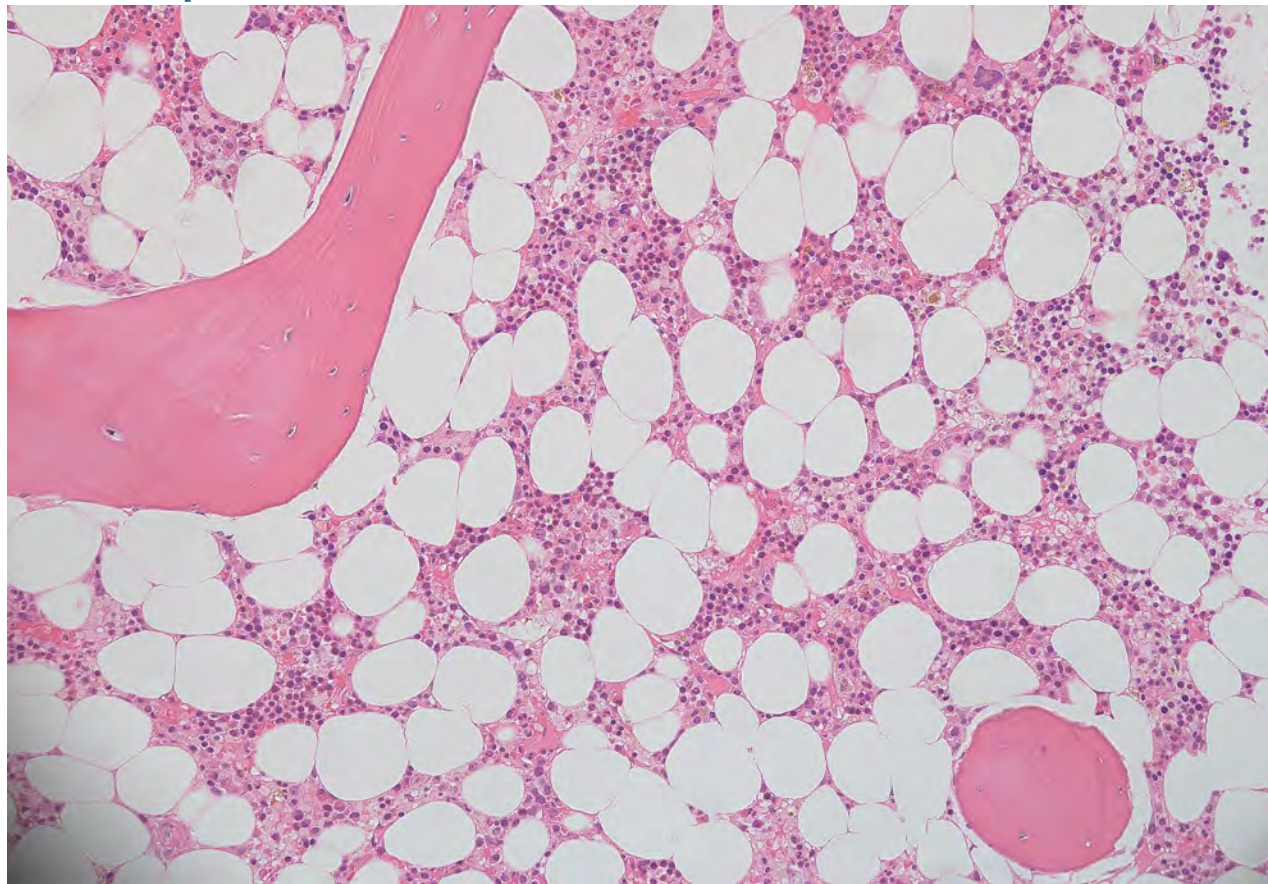
Trephine x 4

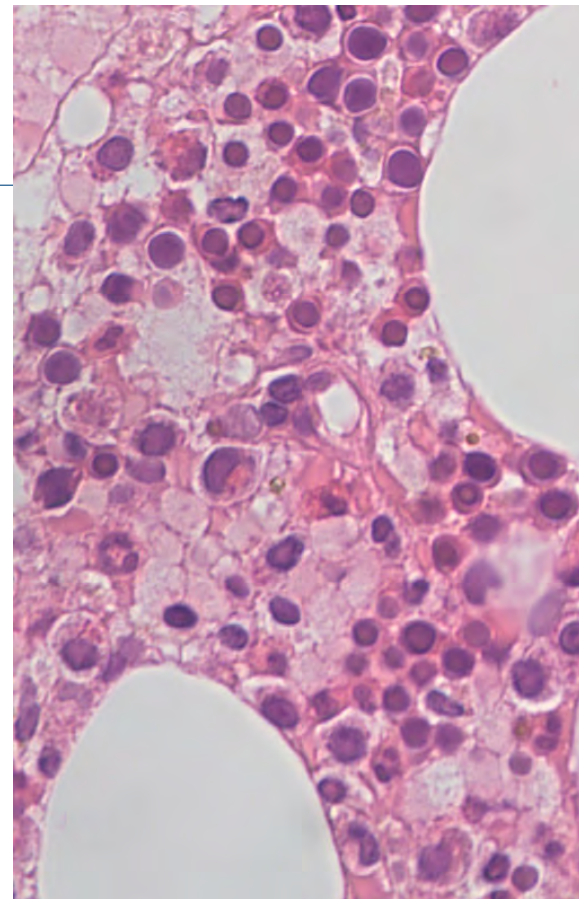
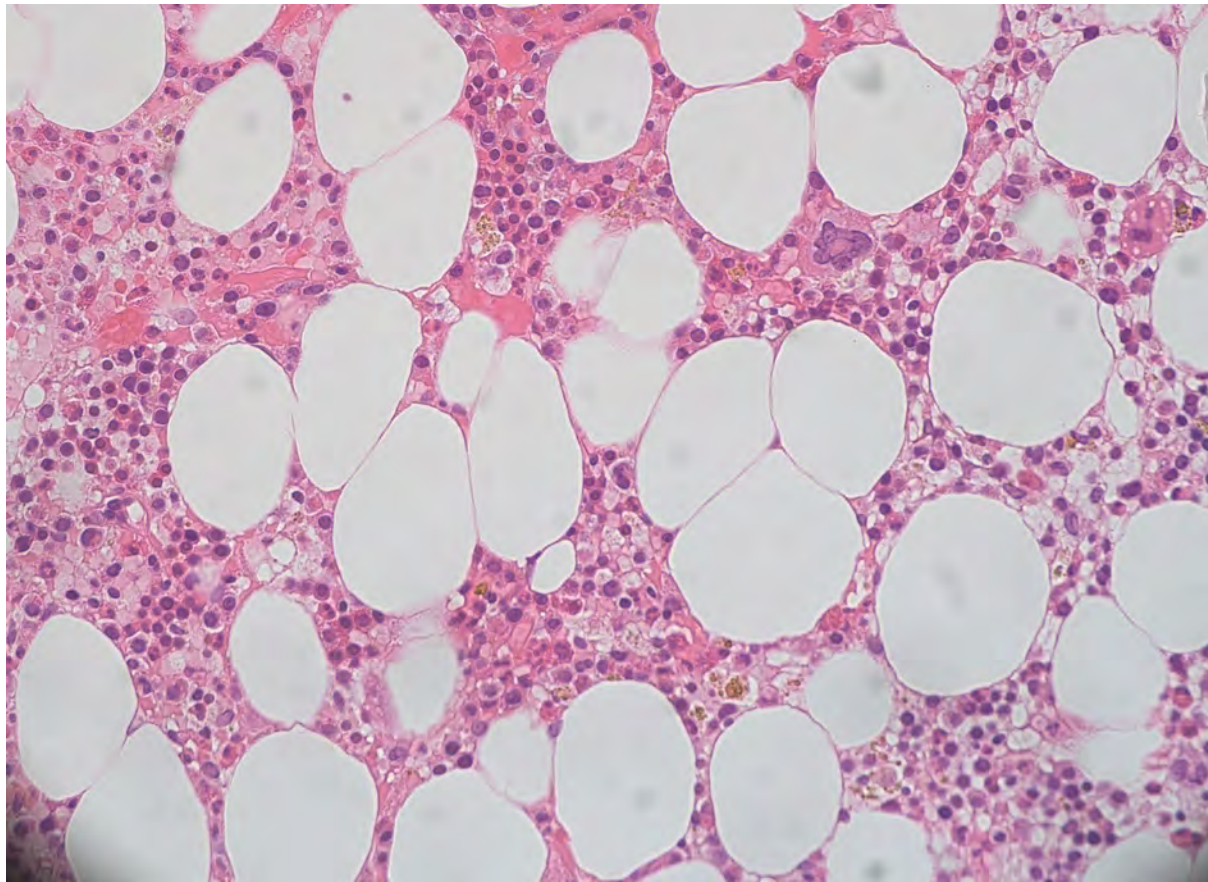


Trephine x 10

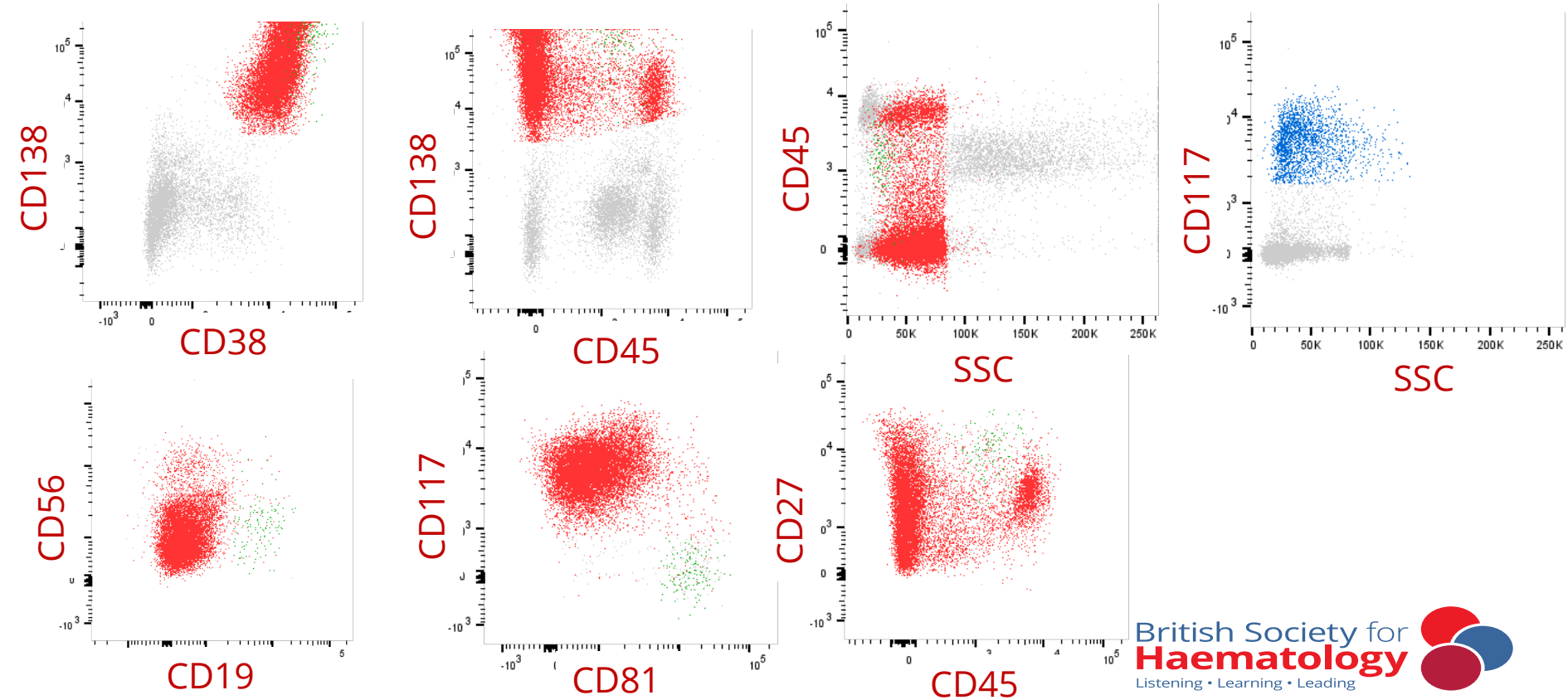


Trephine x 20





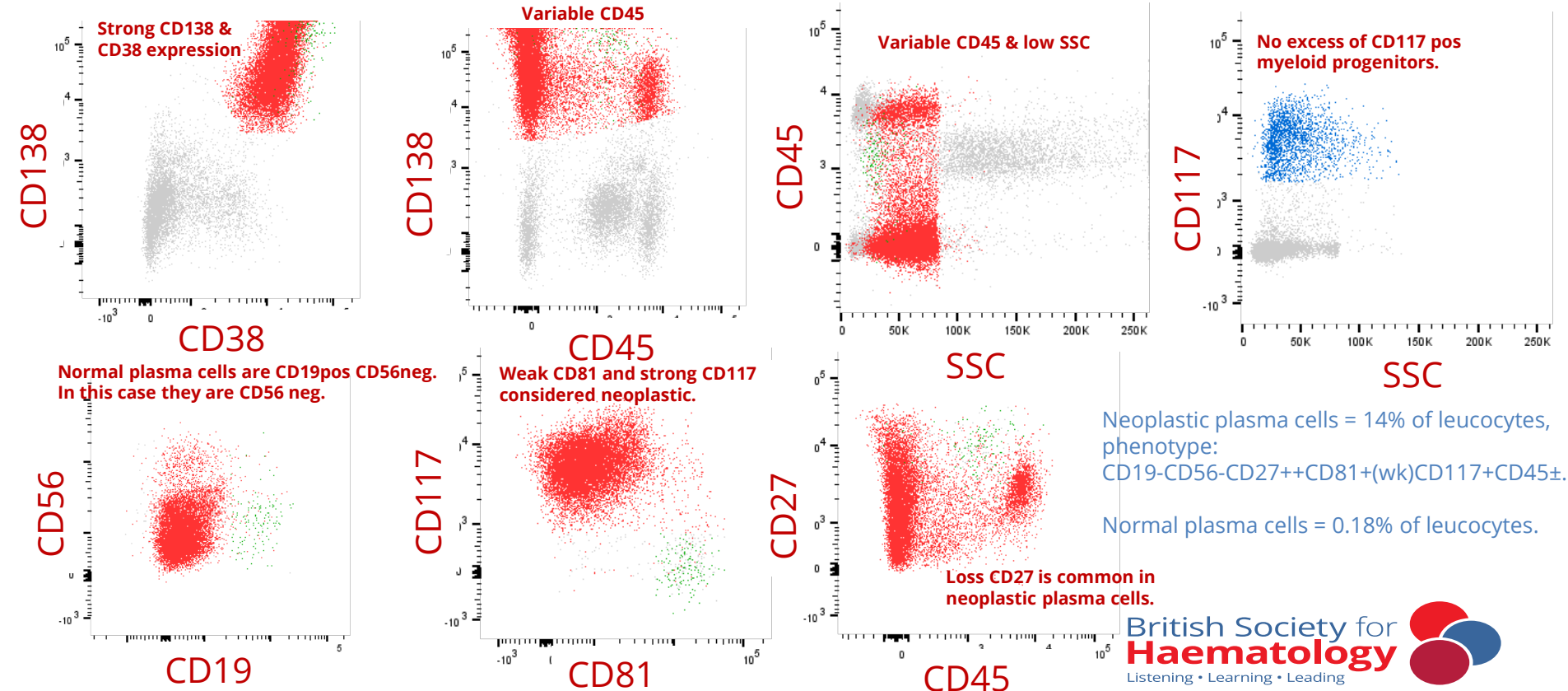
Flow Cytometry



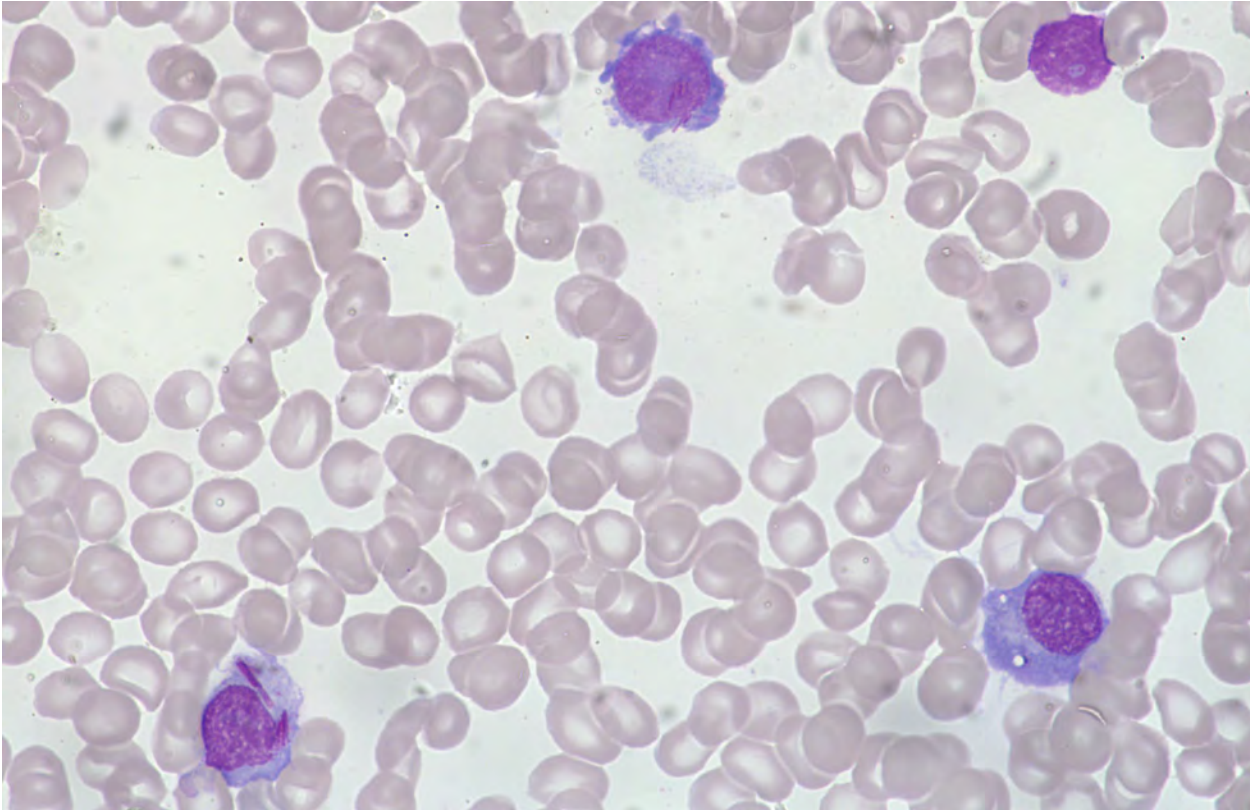
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- a) Accelerated phase myelofibrosis
- b) Acute Promyelocytic Leukaemia
- c) Acute myeloid leukaemia with NPM1 mutation.
- d) Plasma cell myeloma
- e) AML myelodysplasia related
- f) Lysosomal storage disorder

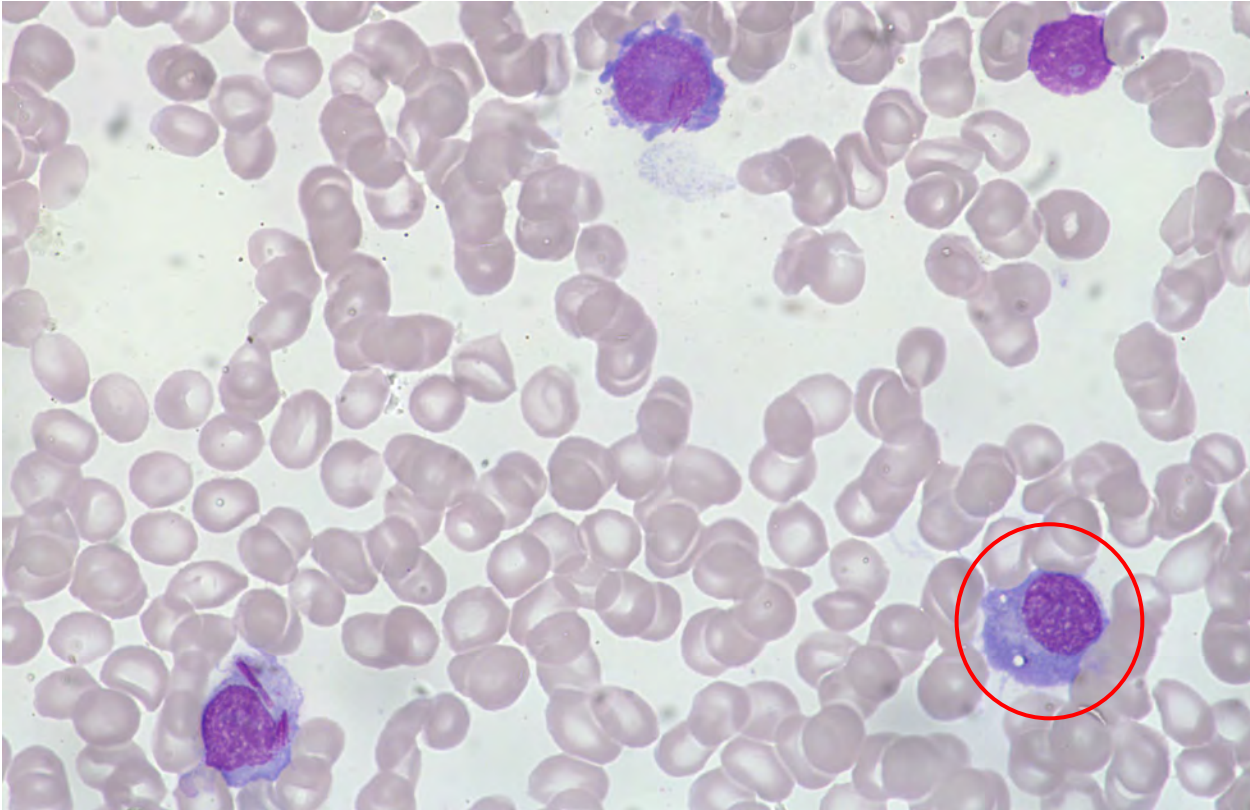
Flow Cytometry

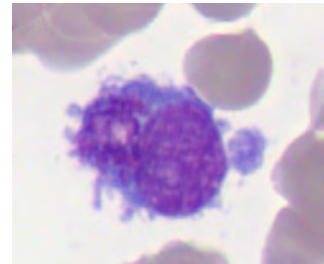
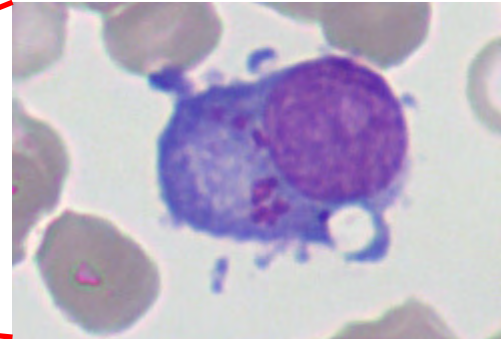
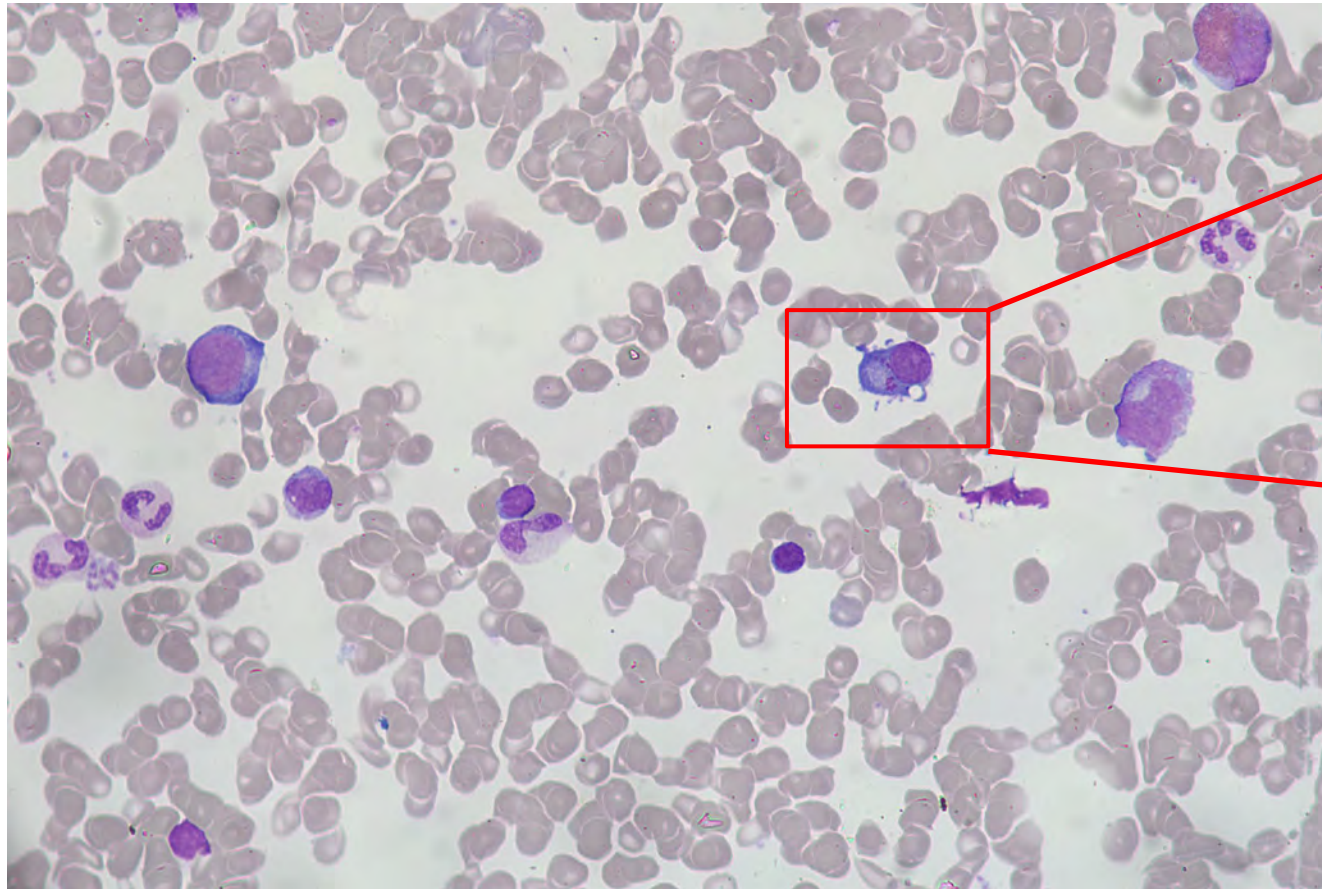


Bone marrow aspirate x 40

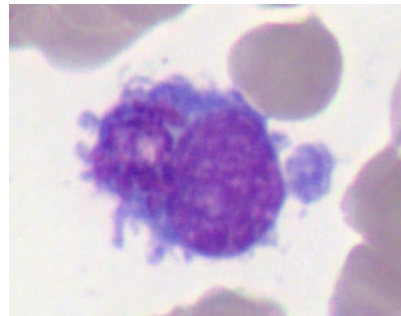
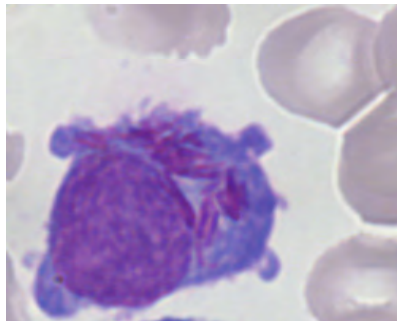
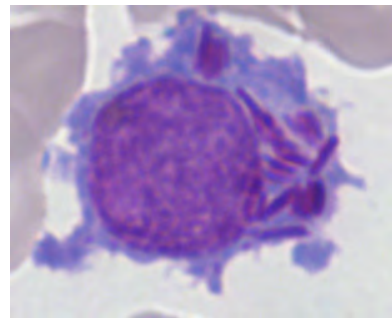
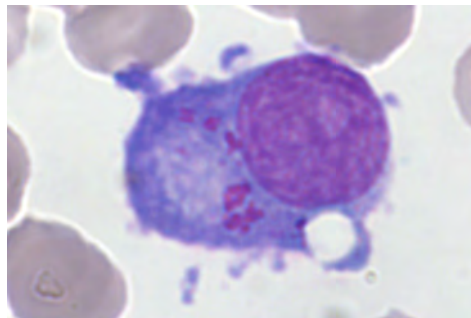
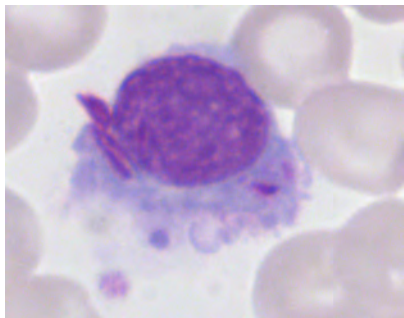


Bone marrow aspirate x 40



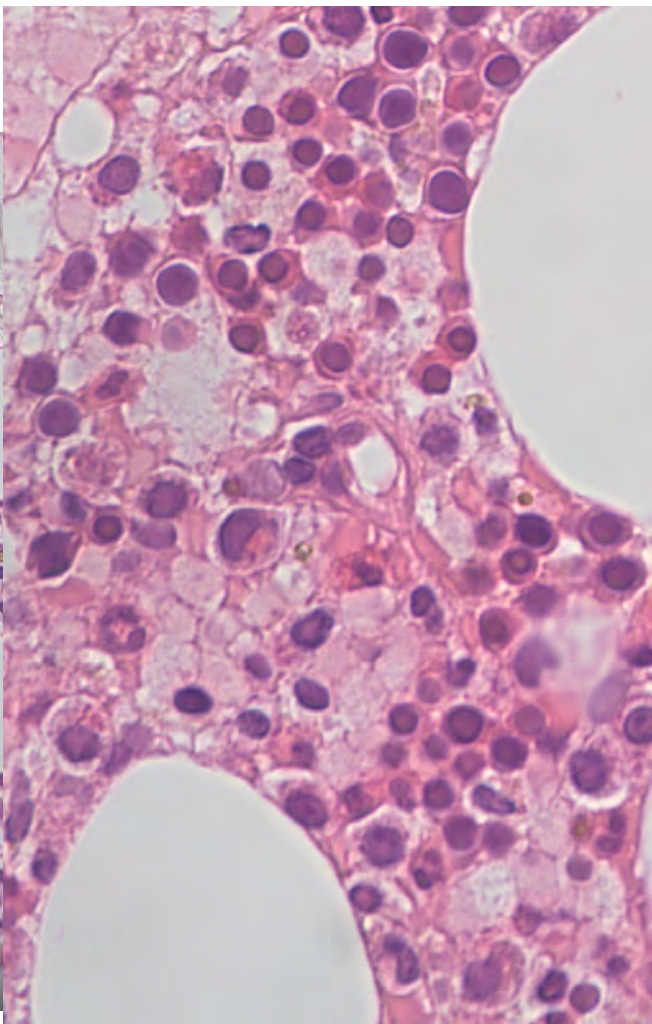
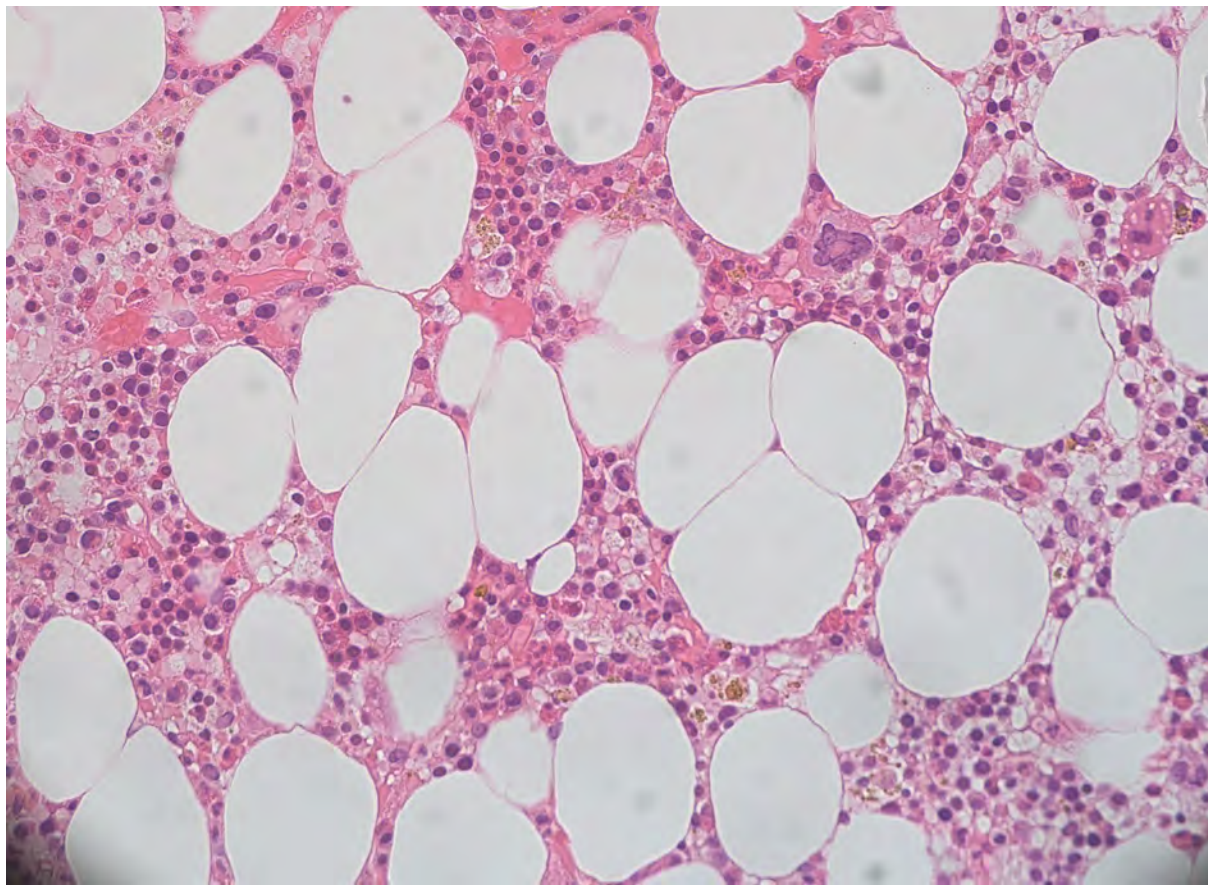


Plasma cell morphology

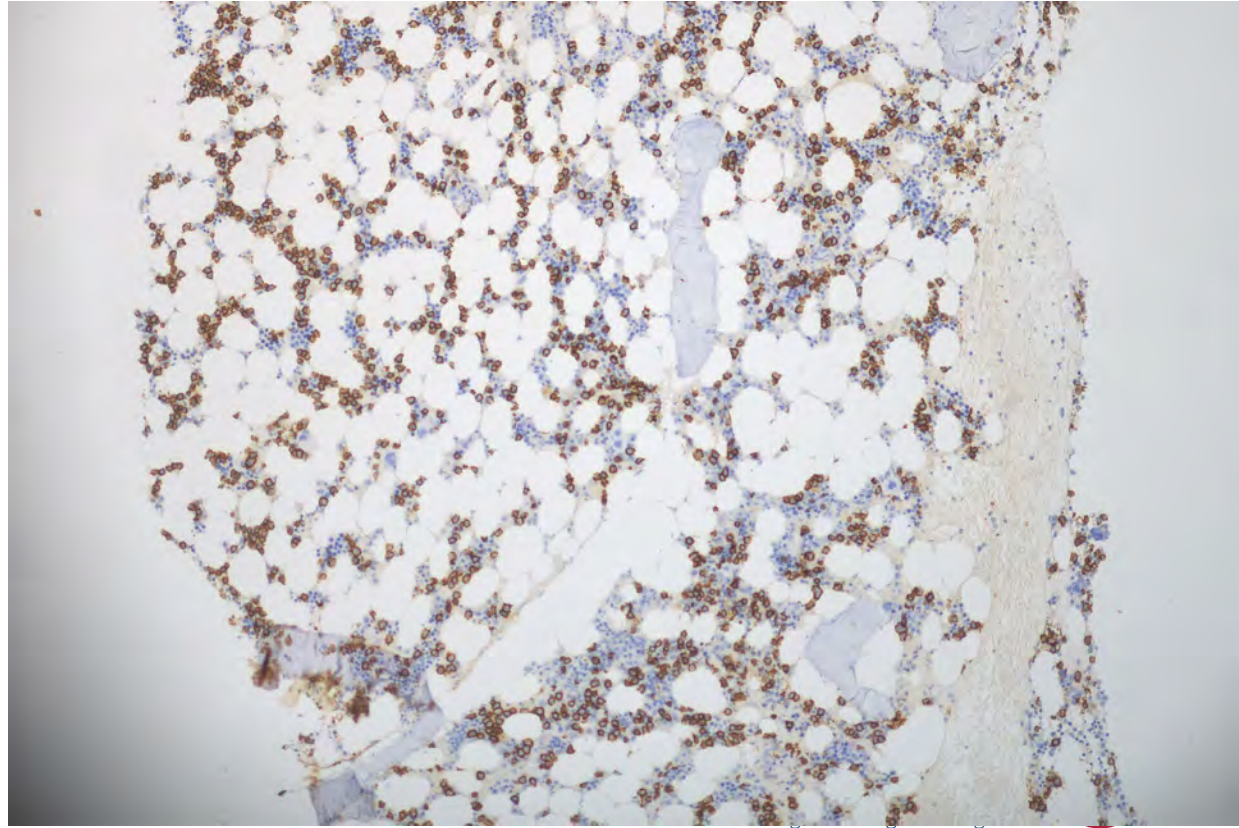


Diagnosis

Plasma cell myeloma



CD138



Results – MLPA

- MLPA performed on DNA from CD138-selected plasma cells
 - No copy number abnormalities detected with probes covering relevant regions of 1p, 1q, 5q, 9p, 9q, 12p, 13, 14, 15, 16q and 17p.
- so no evidence to suggest hyperdiploidy

Results – FISH

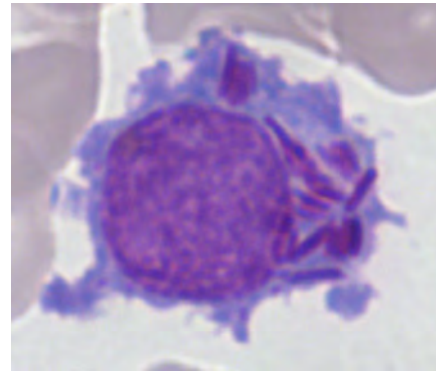
- FISH analysis of 100 CD138+ selected plasma cells.
- No evidence of IGH, IGH::CCND1, IGH::FGFR3, IGH::MAF or IGH::MAFB rearrangement.
- Additional IGH signal has been noted at a low level (between 5-17%), but this could represent low level rearrangement or an additional copy of chromosome 14.

Additional investigations

- Serum electrophoresis:
 - IgG Kappa monoclonal band 28g/L
- Low dose CT-PET
 - Lytic lesions in skull and both femur

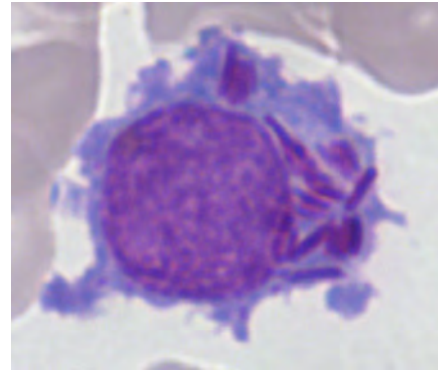
What would you call the inclusions?

- a) Russell bodies
- b) Auer rod-like inclusions
- c) Dutcher bodies
- d) Mott cells



What do you think the inclusions are composed of?

- a) Crystalline inclusions
- b) Immunoglobulin inclusions
- c) Lysosomes
- d) Viral particles



The history of Auer rods

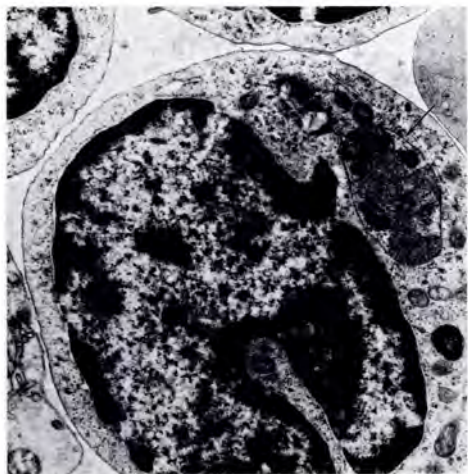


Fig. 3. Electron micrograph of bone marrow lymphoblast showing large inclusion body (arrow) bound by a single membrane, and containing numerous doughnut-shaped particles. $\times 30,100$.

- Brunning et al. Blood **1974** 44 (5): 735–741.
 - ‘Unusual basophilic inclusions’ described in 4 patients with Down’s syndrome and leukaemia.
- Siskind. Am J Clin Pathol. **1986** Aug;86(2):261-3.
 - ‘*Peculiar Cytoplasmic Inclusions in Cells of Acute Lymphoblastic Leukemia.*’
 - ‘*intrigued by the occurrence of "virus-like" particles (VLPs) in leukemic lymphoblasts.*’

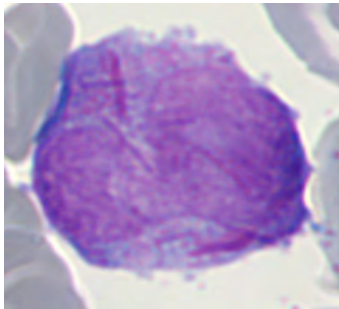
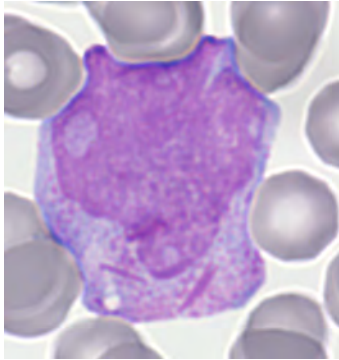


What are Auer rods...?

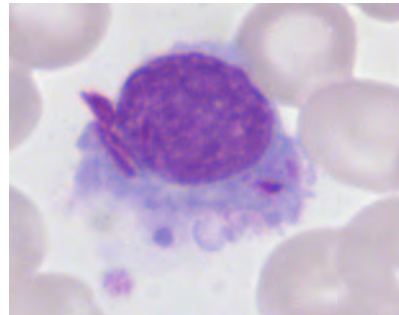
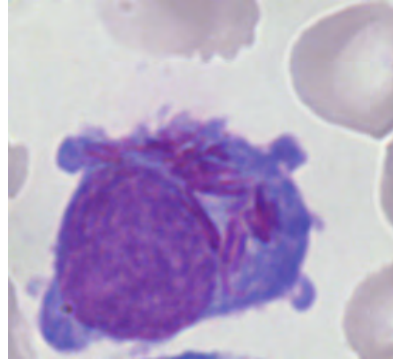
- Composed of fused lysosomes.
- Lysosomes are cellular organelles containing enzymes for breaking down waste and debris → fuse together.
- Contain azurophilic granules, inc peroxidase & other lysosomal enzymes.
- Typically seen in myeloid blast cells.
- They are **not** immunoglobulin inclusions even when seen in plasma cells.

Auer rods and 'Auer rod-like'....

Auer rods in myeloid blasts

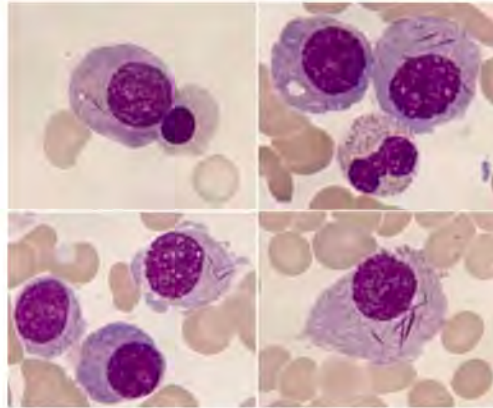


Auer rod-like in plasma cells



Auer-rod like inclusions in the literature

IgG Multiple myeloma with pseudo-Auer inclusions



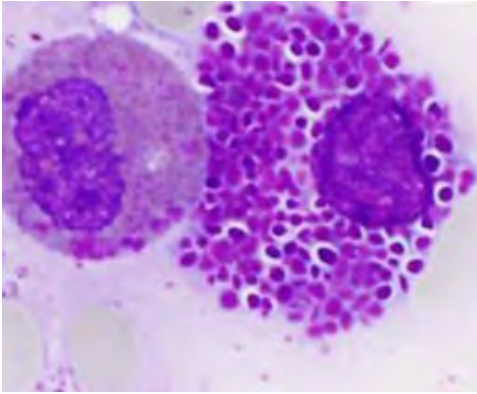
- Rare – reported in sporadic case reports over the decade.
- Significance is unclear



The bone marrow smear from a 63-year-old-female with IgG Kappa MM progressed from 15-year-long MGUS, displayed 52% plasma cells. The image shows plasma cells with intracytoplasmic Auer-like inclusions composed of cristallized protein that were seen in less than 1% of plasma cells.

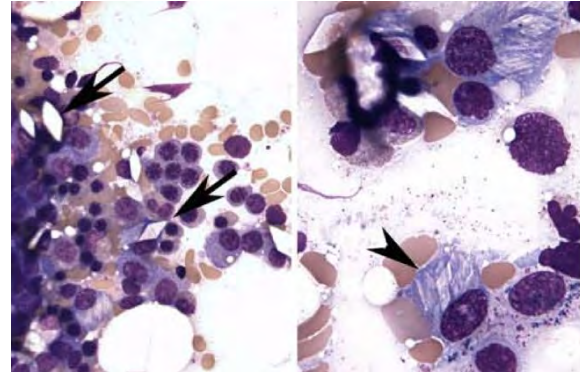
Sample type: Bone marrow smear
Stain type: May-Grünwald-Giemsa
Author/s: Ricardo Bernal Ruiz
Work centre: Hospital Universitario Virgen del Rocío, Sevilla

Other unusual inclusions....



Cytoplasmic azurophilic granules

- Thought to be immunoglobulin

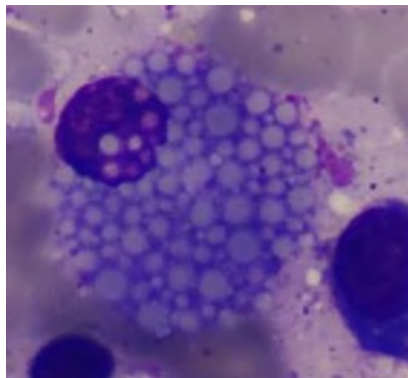


Crystalline inclusions

- Thought to be immunoglobulin

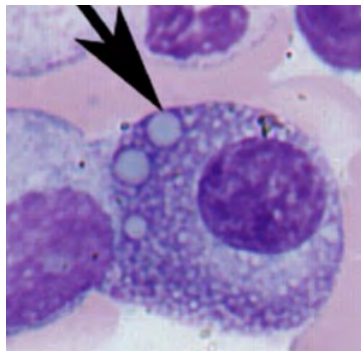


Other unusual inclusions....



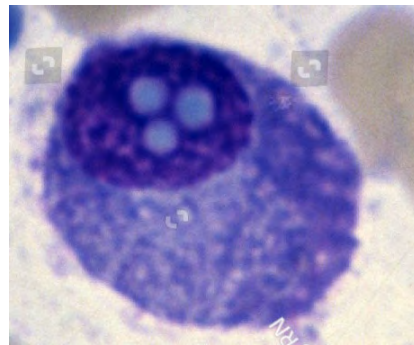
Mott cells

- ‘Bunch of grapes’
- Numerous Russell bodies ***filling the cytoplasm***
- Occur in a number of conditions.



Russell bodies

- Intracytoplasmic inclusion which is clearly ***seen in cytoplasm.***



Dutcher body

- Intracytoplasmic inclusion ***overlying the nucleus*** but still in the cytoplasm



References

1. Metzgeroth et al. Ann Hematol. 2003 Jan;82(1):57-60.
2. Shi M et al. Blood (2016) 127 (8): 1073.
3. Matoso A et al. Diagn Pathol (2010) 5, 6.
4. Maslak Blood 2009 ASH image bank Russell-bodies-1.
5. Brunning et al. Blood 1974 44 (5): 735–741.
6. Siskind. Am J Clin Pathol. 1986 Aug;86(2):261-3.
7. Jakob N et al . eJHaem.2020;1:6–7



Acknowledgments

- Rachel Brown and Linda Barton, Co-chairs.
- Richard Leach, HMDS.
- Anne O'Connor, BSH.
- BSH speaker team.
- Martin Waterhouse & Michael Hale, Scanning.
- Roger Owen, HMDS.