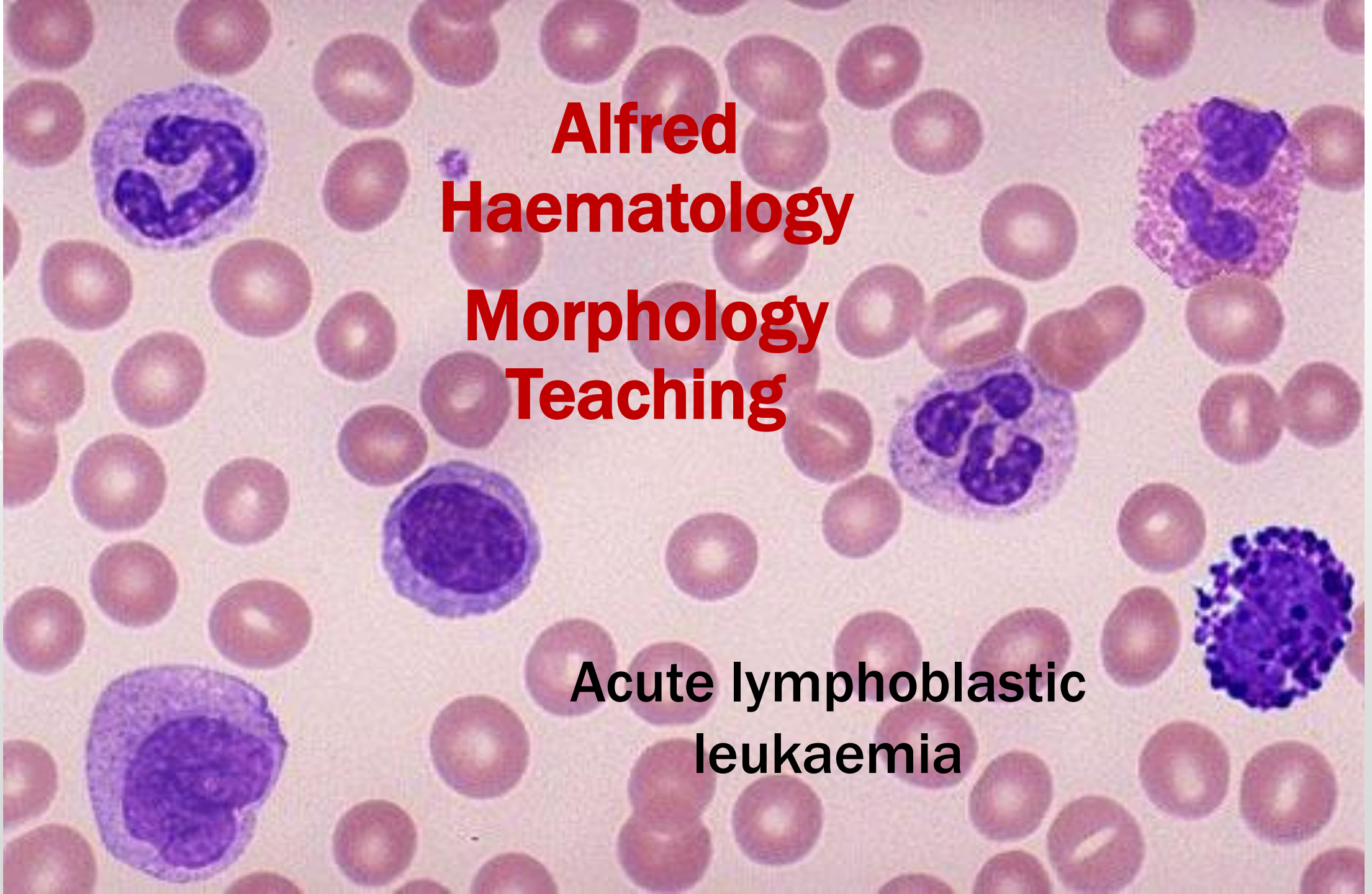
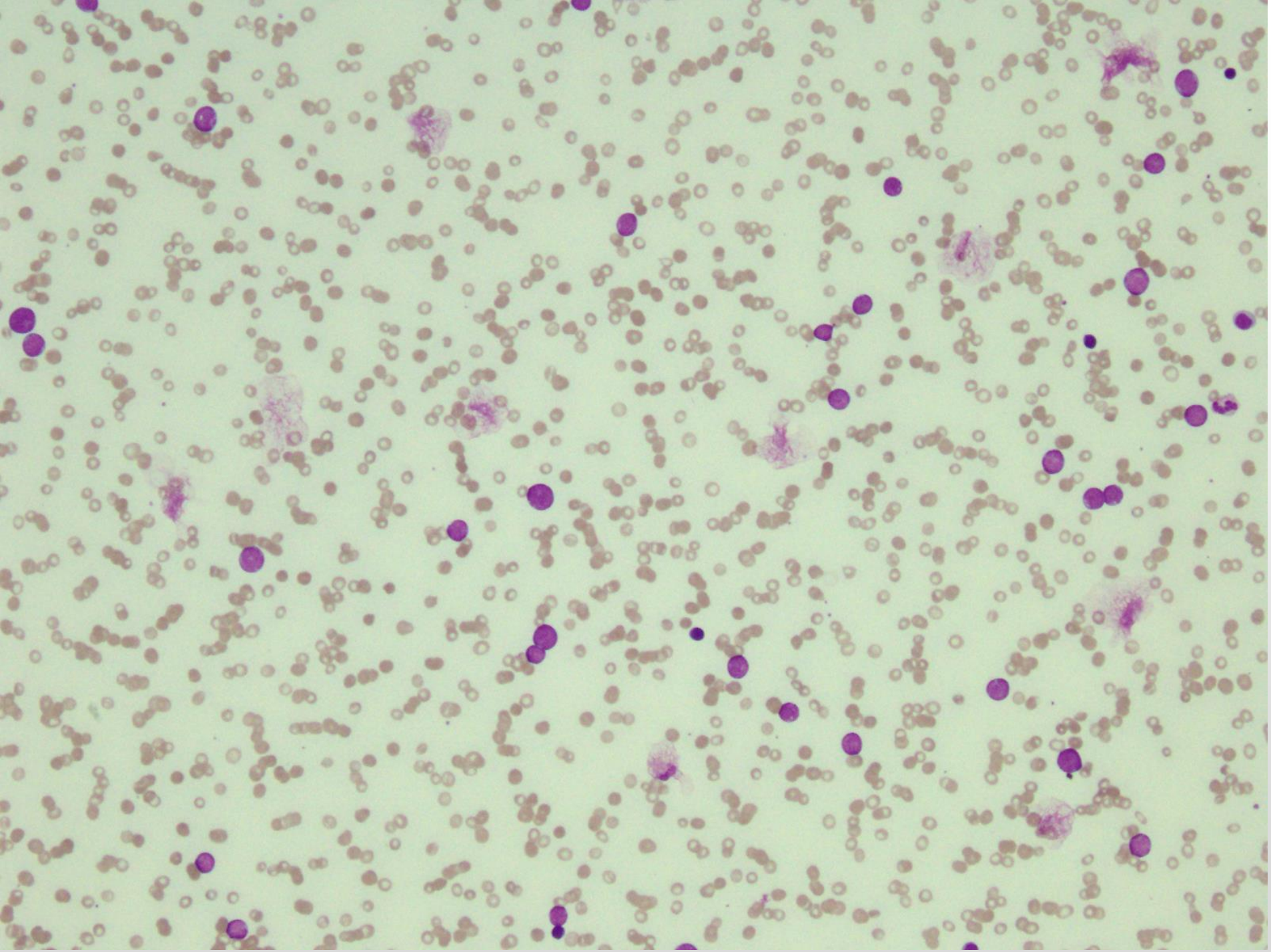

Alfred
Haematology
Morphology
Teaching
Acute lymphoblastic
leukaemia

Case 1: A worrying paediatric film

4 yo girl

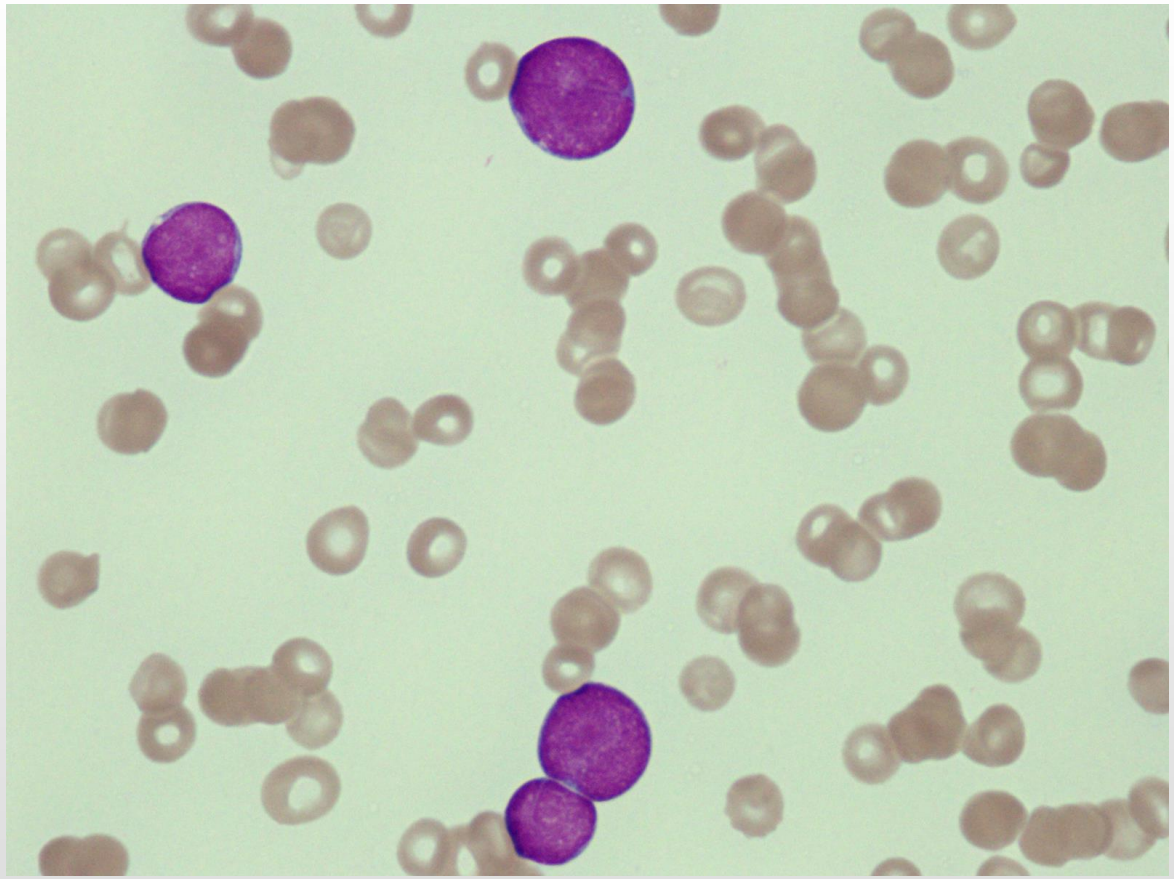
- Abdominal pain & refusing to walk
- In Emergency, possible appendicitis?

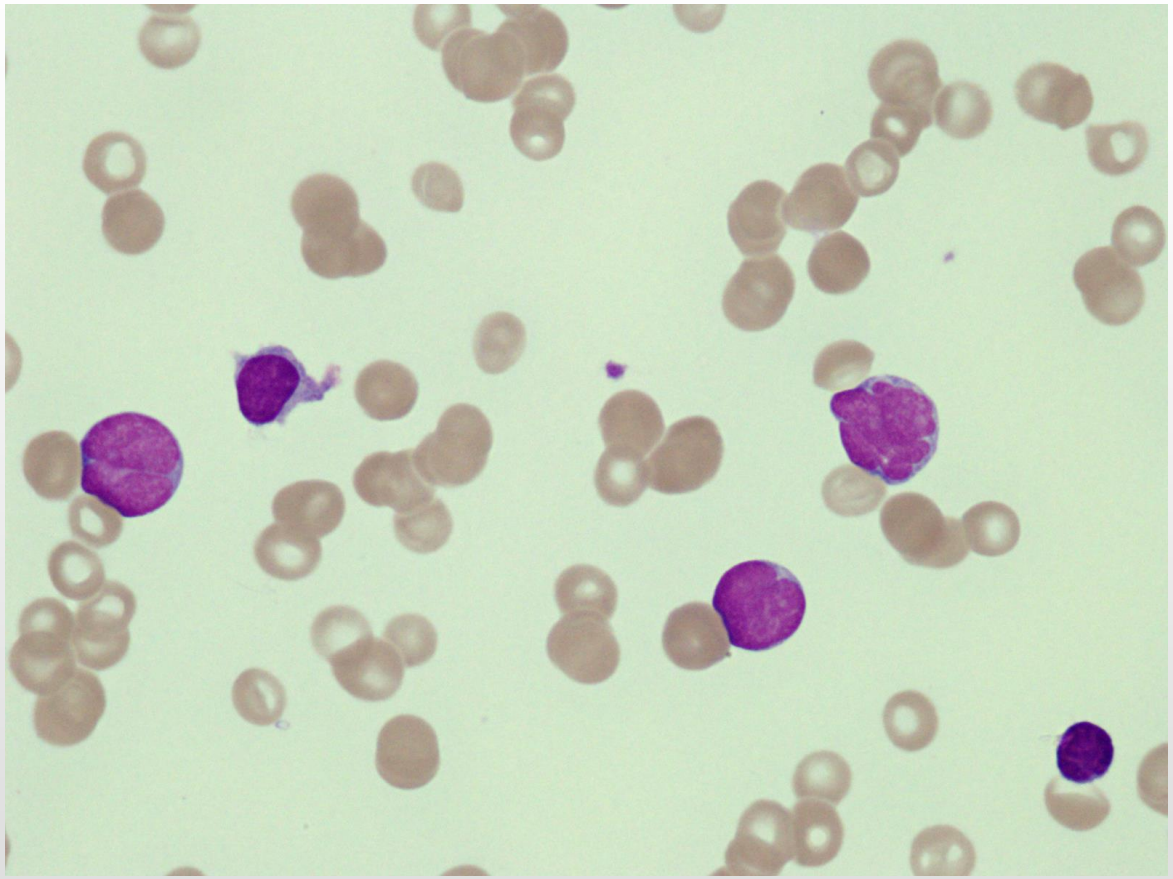
- Unexpected FBE parameters!
  - Hb 43 g/L (110-140)
  - WCC 21.43 x 10^9/L (5.5-15.5)
    - Neut 0.00 x 10^9/L
  - Platelets 16 x 10^9/L



What cells are most prominent in the white cell differential?

What diagnosis should we consider?





Blasts: Medium-sized, pleomorphic (but less so than myeloid blasts). Nuclear morphology variable here; some nuclei are lobulated or clefted. Very high nuclear/cytoplasmic ratio. No Auer rods or granules, although very little cytoplasm is visible.

Final diagnosis

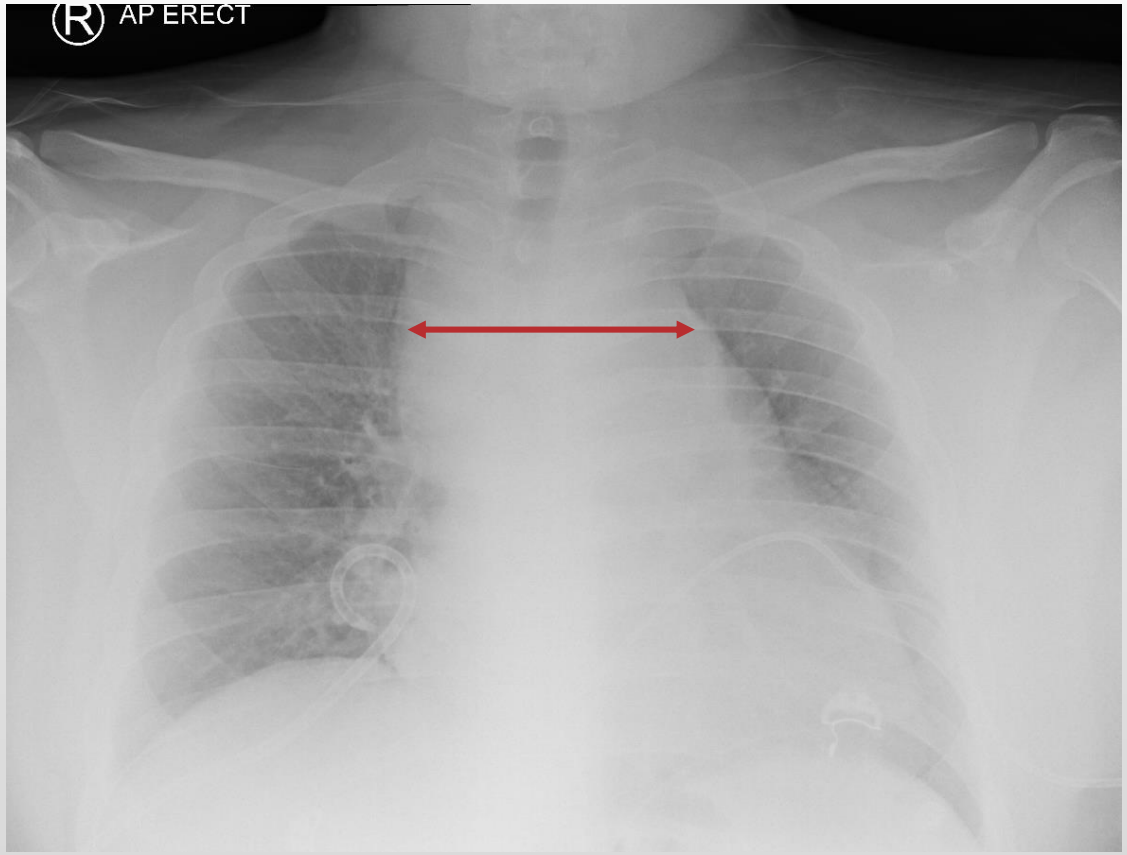
- Acute lymphoblastic leukaemia
- ALL comprises 70% of childhood leukaemia (Adults ~25%)
  - B-ALL 85%
  - T-ALL 15%
- Patient referred to Monash Medical Centre for ongoing management

Case 2: When a blood film can give you the diagnosis before the surgeon

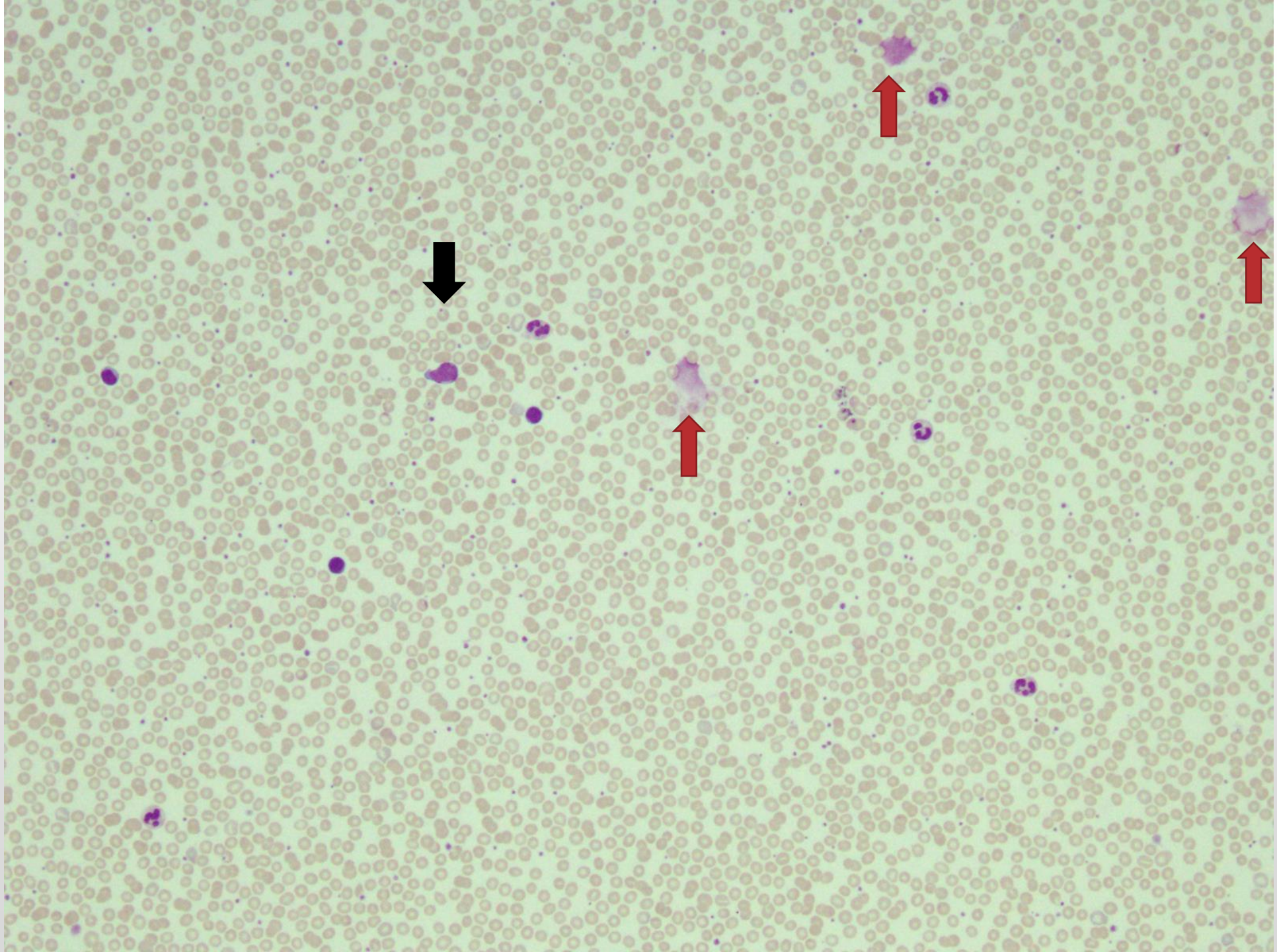
19 yo man

- Breathless
- Mediastinal mass, pleural fluid drained
- Referred to cardiothoracic surgery for biopsy of mass

- Hb 139 g/L (128-175)
- WCC 10.06 x 10^9/L (3.9-12.7)
- Platelets 234 x 10^9/L (150-396)
- No blast flag on analyser



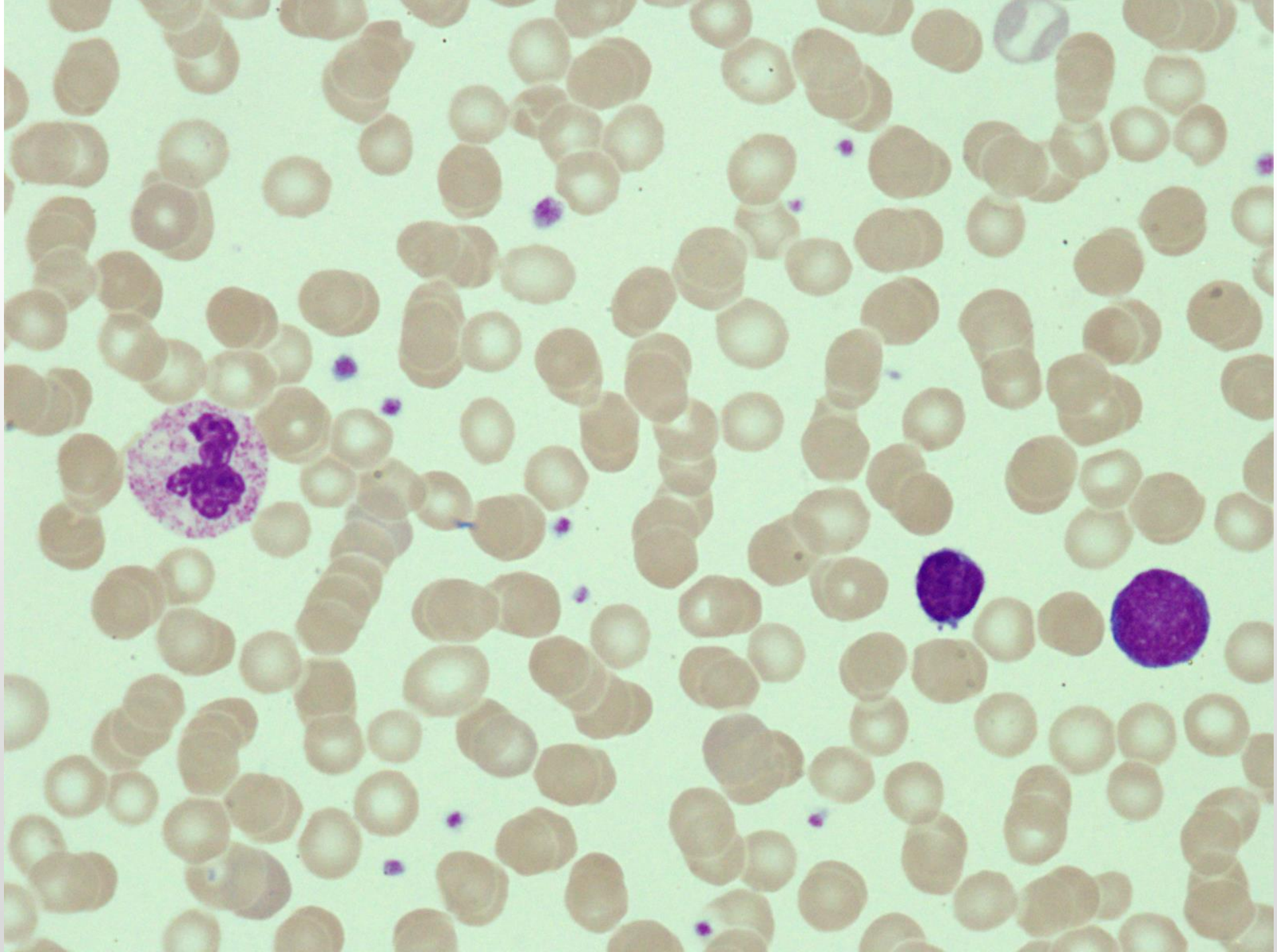
Widened mediastinum on chest Xray

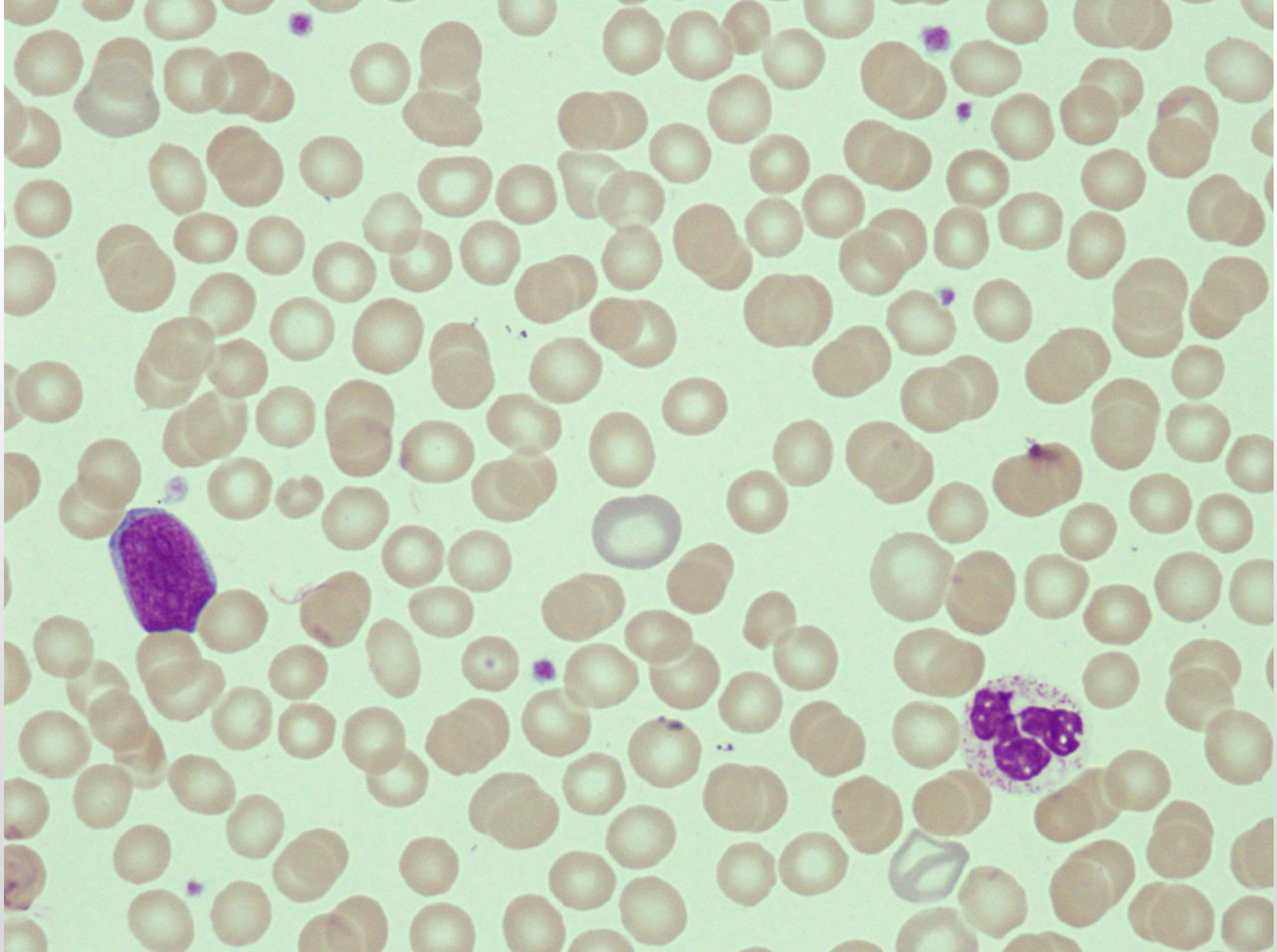


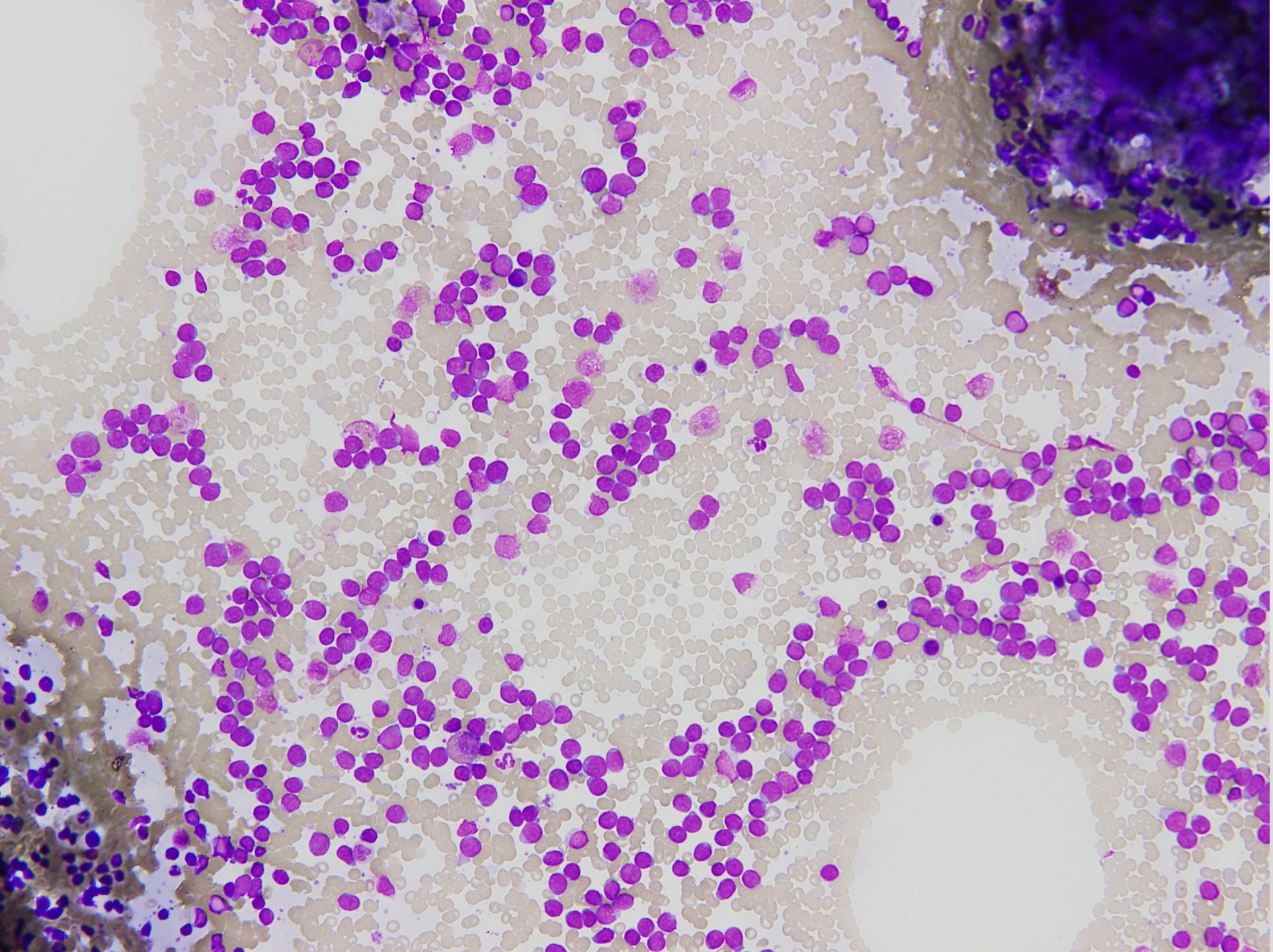
Blood film not normal despite normal counts and lack of blast flags

Smear cells raise suspicion of possible abnormal white cells

Atypical mononuclear cell, needs high power examination







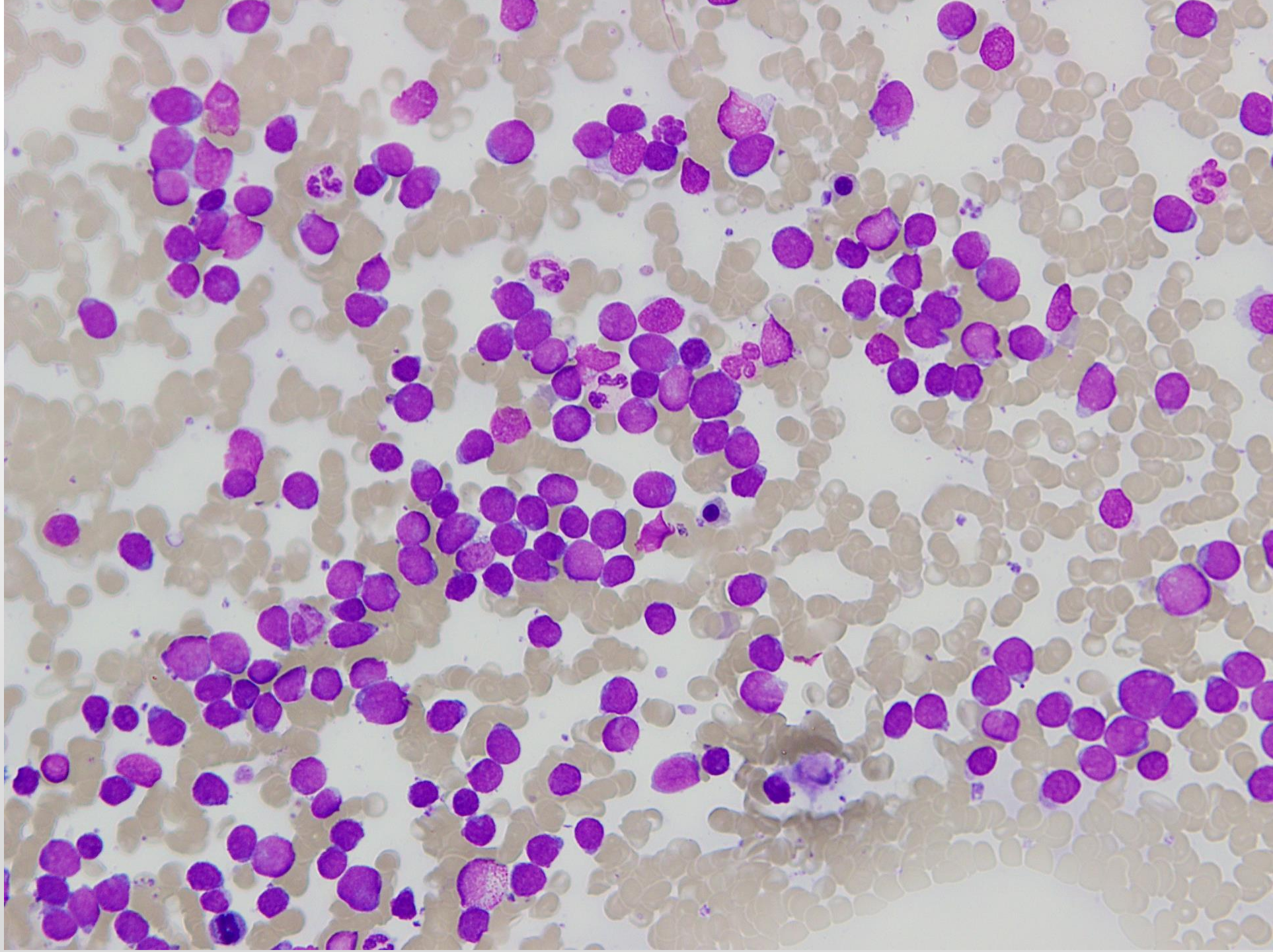
Bone marrow aspirate

Almost all cells the same

Minimal normal haematopoiesis

97% blasts

Monomorphic
High nuclear/cytoplasmic ratio
No Auer rods



Additional investigations

Flow cytometry on blood & bone marrow confirmed blast lineage

- Blasts positive for:
  - T-cell markers: CD7, CD1a, CD4, CD5, intracellular CD3
  - TdT (marker of a precursor cell, not seen in mature T-cell disorders)
  - *Other markers: CD10, CD38, intracellular 79a*

Mediastinal mass biopsy

- T-lymphoblastic lymphoma

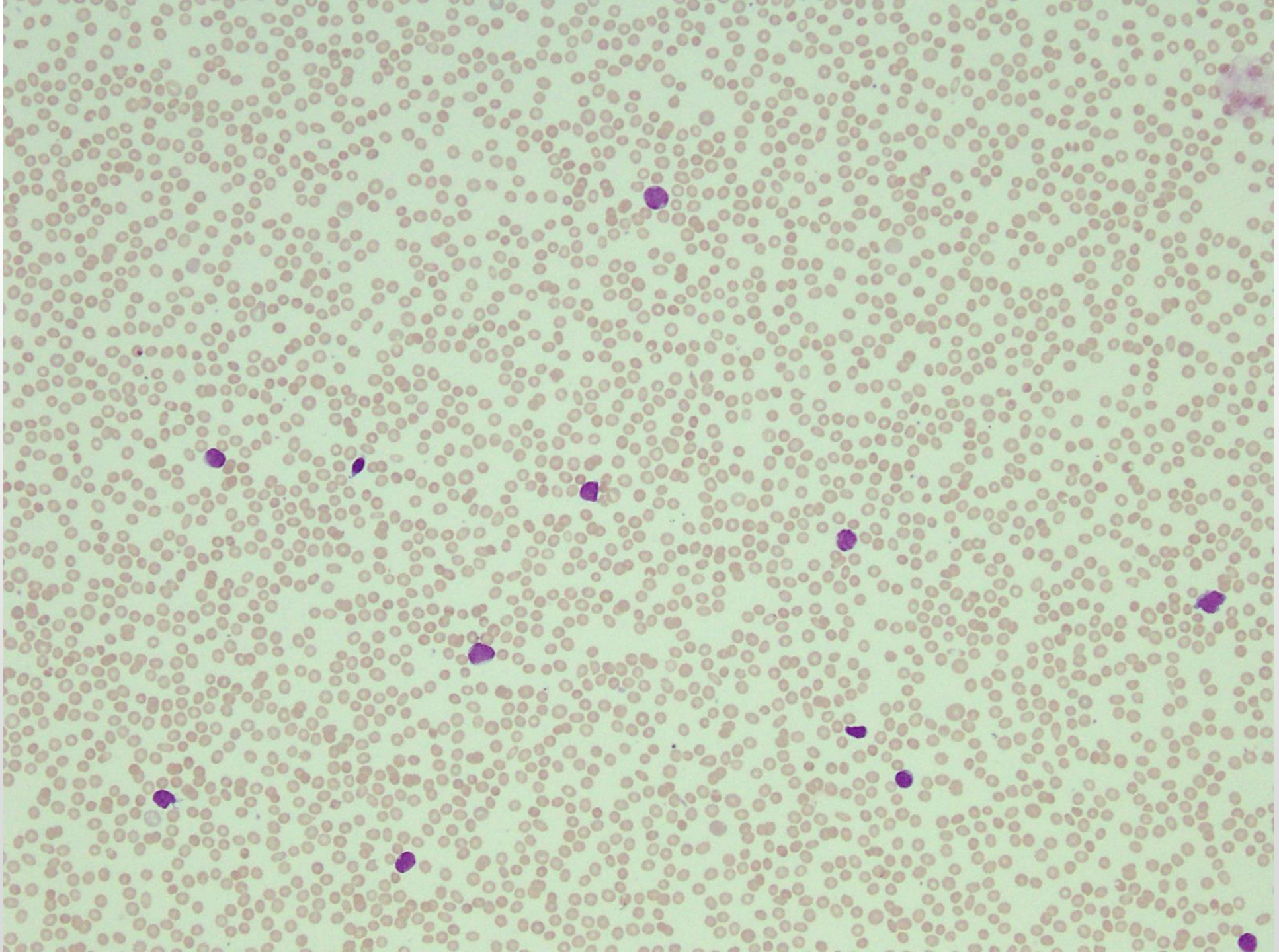
Final diagnosis

- T-cell acute lymphoblastic leukaemia/lymphoma

Case 3: Lymphoma or not lymphoma?

- 53 yo man
- 2 month history of lumps in neck and groin
- Lymph node biopsy at external pathology service showed "peripheral T-cell lymphoma"

- Hb 94 g/L (128-175)
- WCC 16.89 x 10^9/L (3.9-12.7)
  - Neutrophils 1.18 x 10^9/L
- Platelets 28 x 10^9/L (150-396)

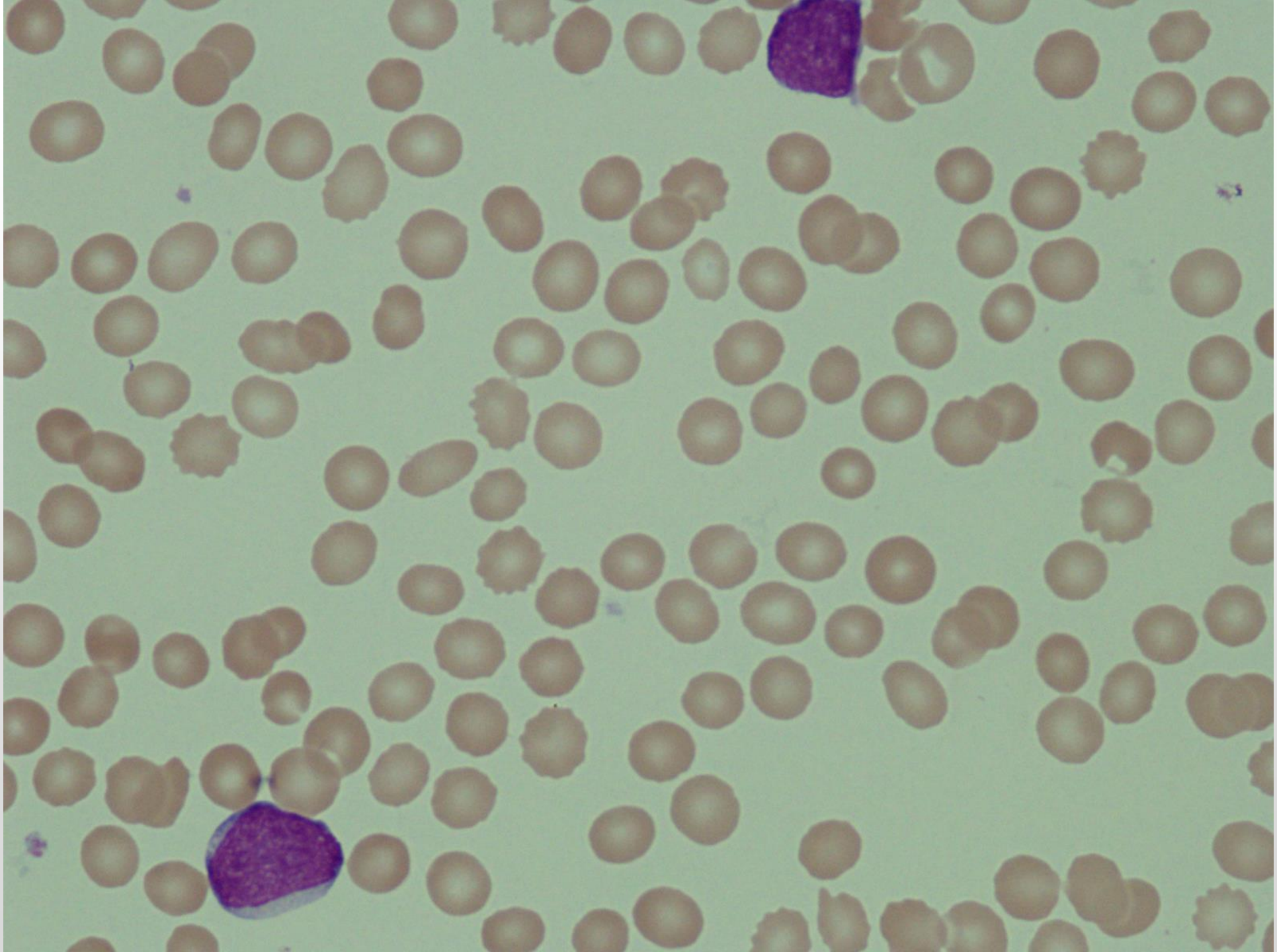


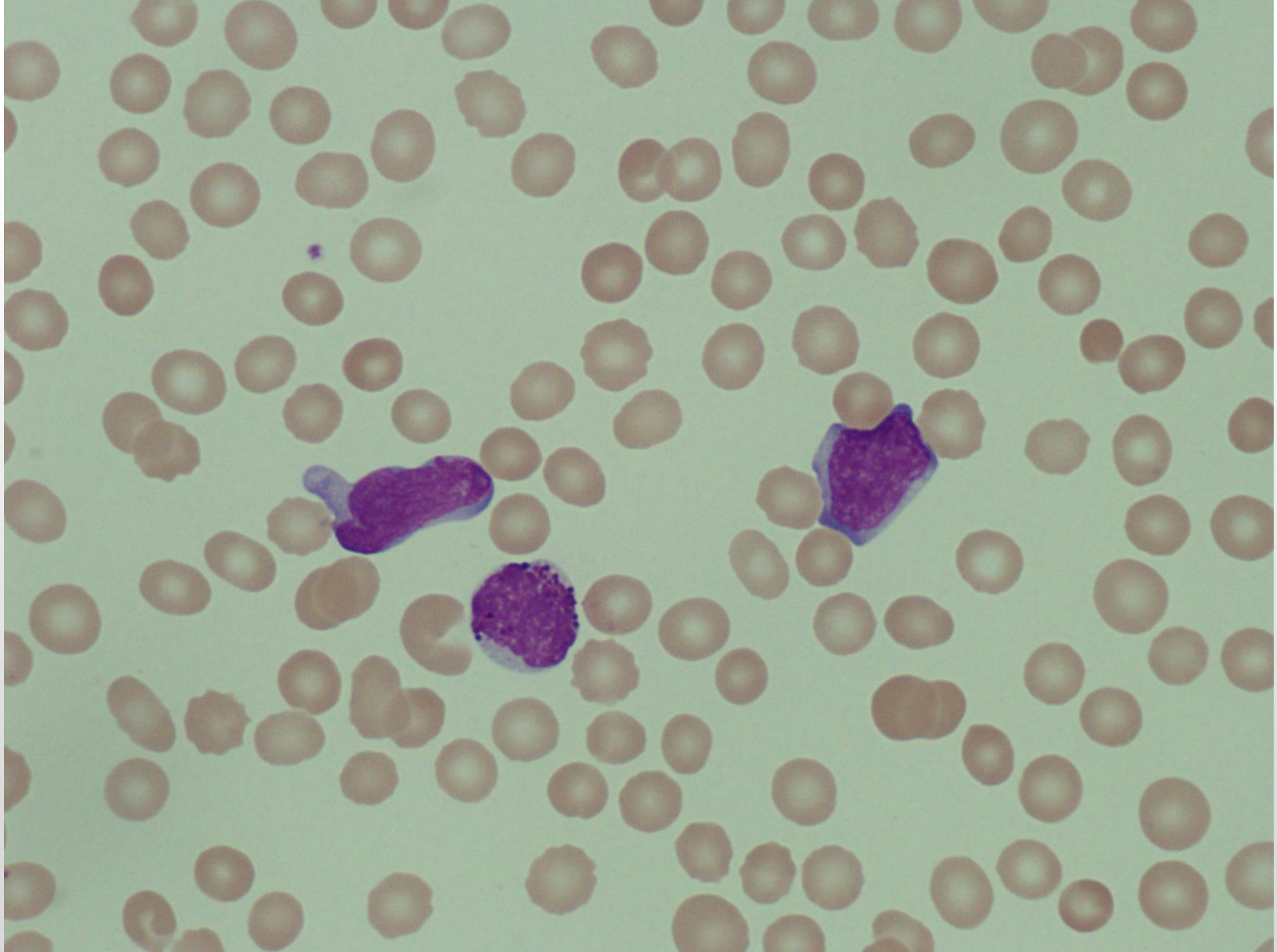
What white cells are most prominent here?

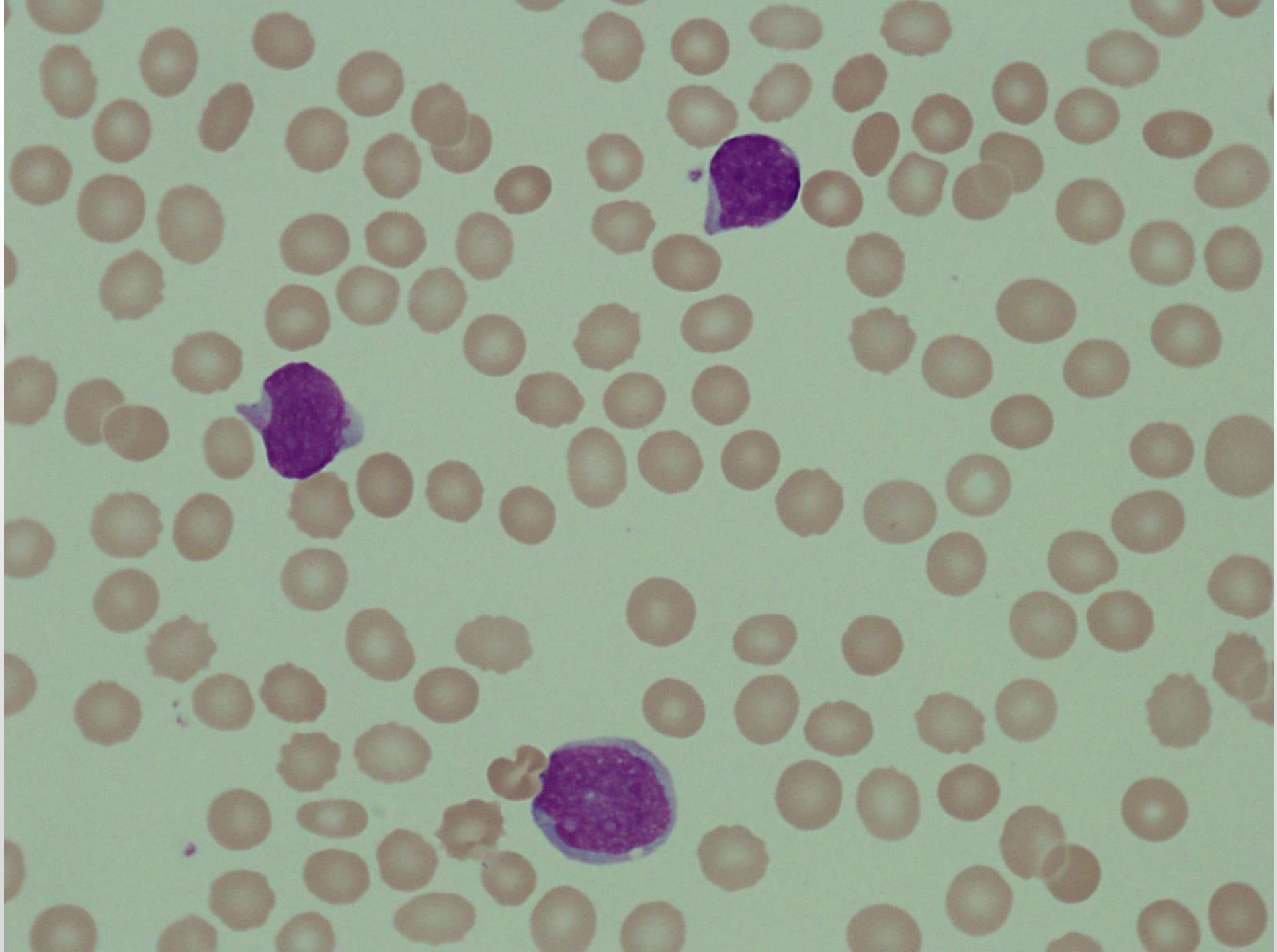
High power view
(always a good idea!)

What lineage are
these cells?

Are they lymphoma
cells?
Or not??







Flow gives the answer….

- Blasts positive for:
  - T-cell markers: CD7, CD5, intracellular CD3
  - CD34, TdT (markers of a precursor cell, not seen in mature T-cell disorders – so must be leukaemia)
  - *Other markers: CD38, intracellular 79a*
- Other T-cell markers such as CD4, CD8, CD2, CD1a not positive
- BUT the myeloid marker CD33 was positive
- This is a very immature type of T-ALL: ETP "early T-cell precursor" ALL. Genetic mutations causing this are more similar to those seen in AML than to other types of T-ALL.
- Prognosis similar to other types of T-ALL

- Biopsy results from the external lymph node reviewed
- Additional immunohistochemical stains performed
- Patient had T-cell acute lymphoblastic lymphoma – the same diagnosis as in the blood/bone marrow.

- NOTE: treatment of T-ALL and peripheral T-cell lymphoma are VERY different & correct diagnosis is essential!

Moral of the story: Always have an FBE before having cardiothoracic surgery!
And trust your eyes, not the clinical note.

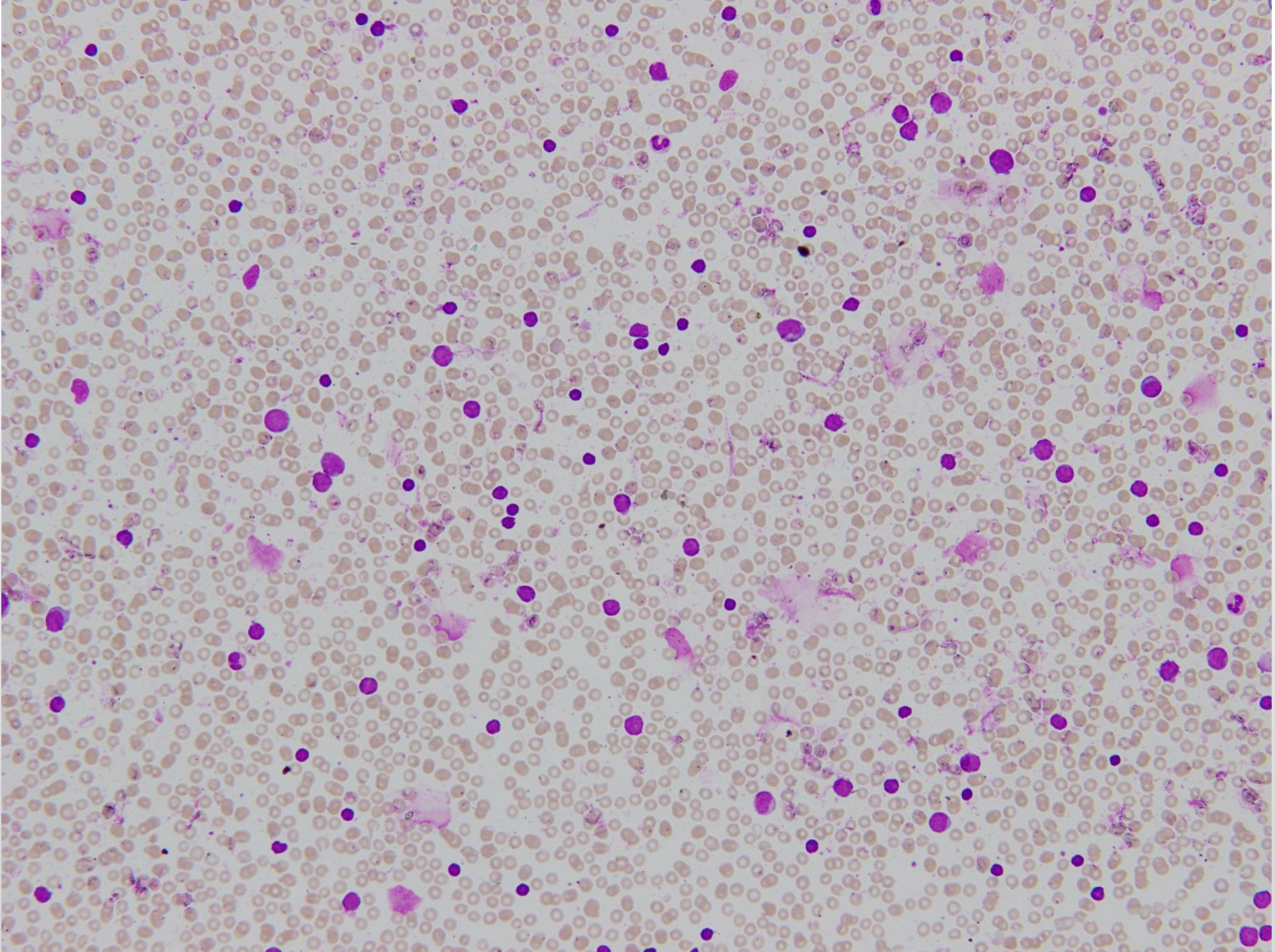
Final Diagnosis

- T-cell acute lymphoblastic leukaemia/lymphoma
- ETP subtype

Case 4: More than one type of blast?

- 50 yo man
- Presented to the Emergency Department with fever and leg swelling
- Blood film unexpectedly abnormal!

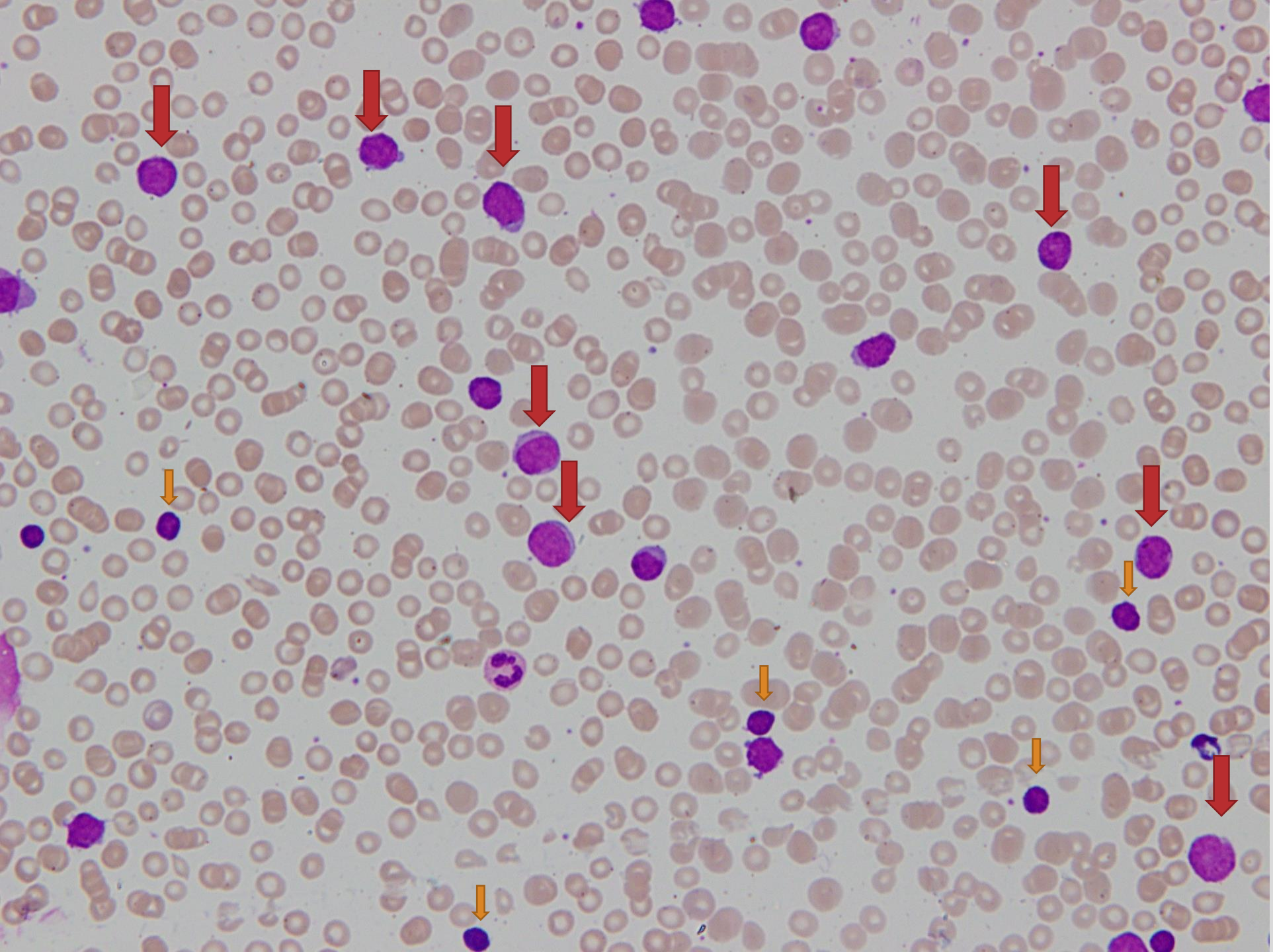
- Hb 94 g/L (128-175)
- WCC 141.71 x 10^9/L (3.9-12.7)
  - Neutrophils 2.83 x 10^9/L
- Platelets 114 x 10^9/L (150-396)



Marked leukocytosis

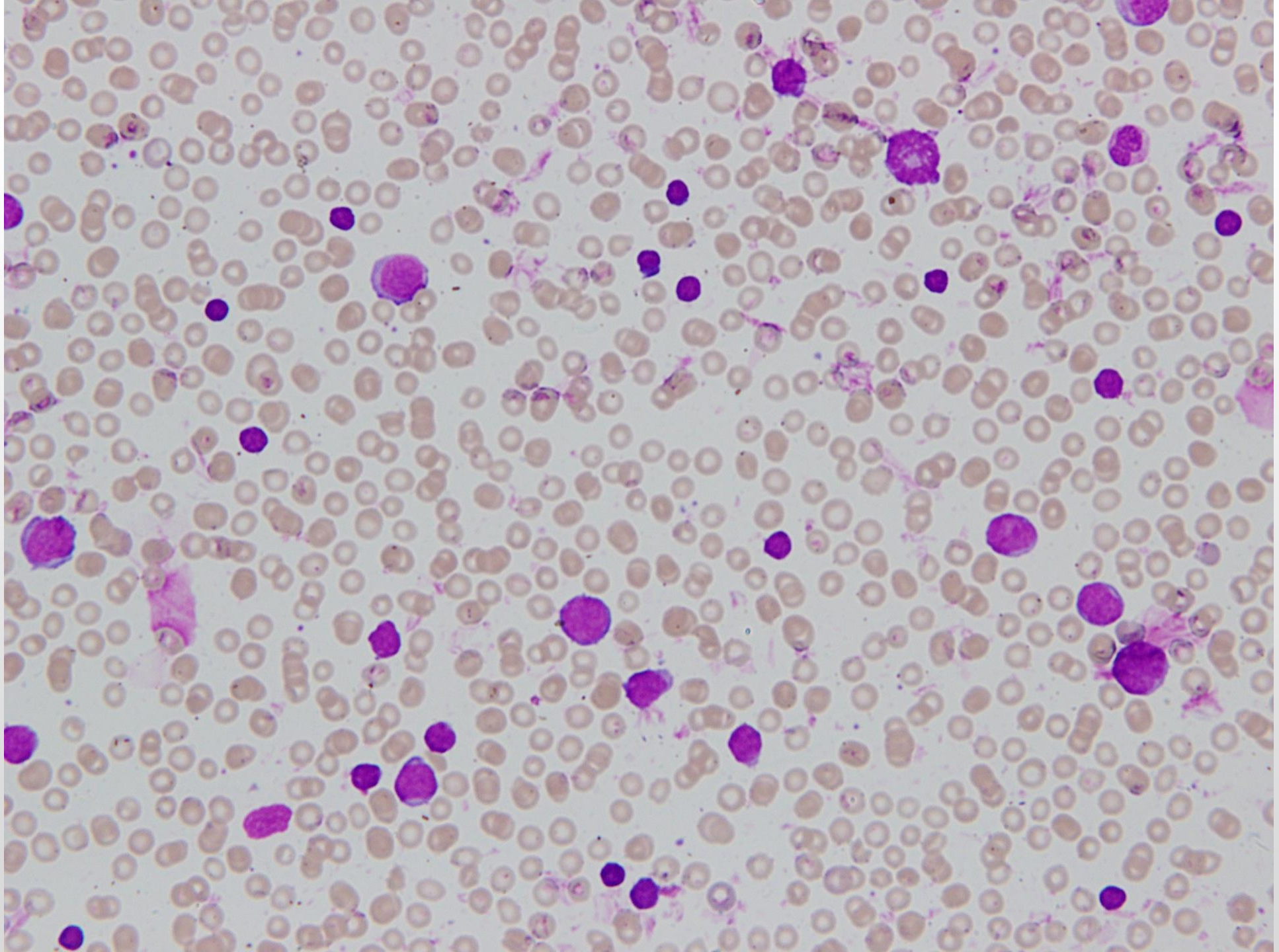
Smear cells

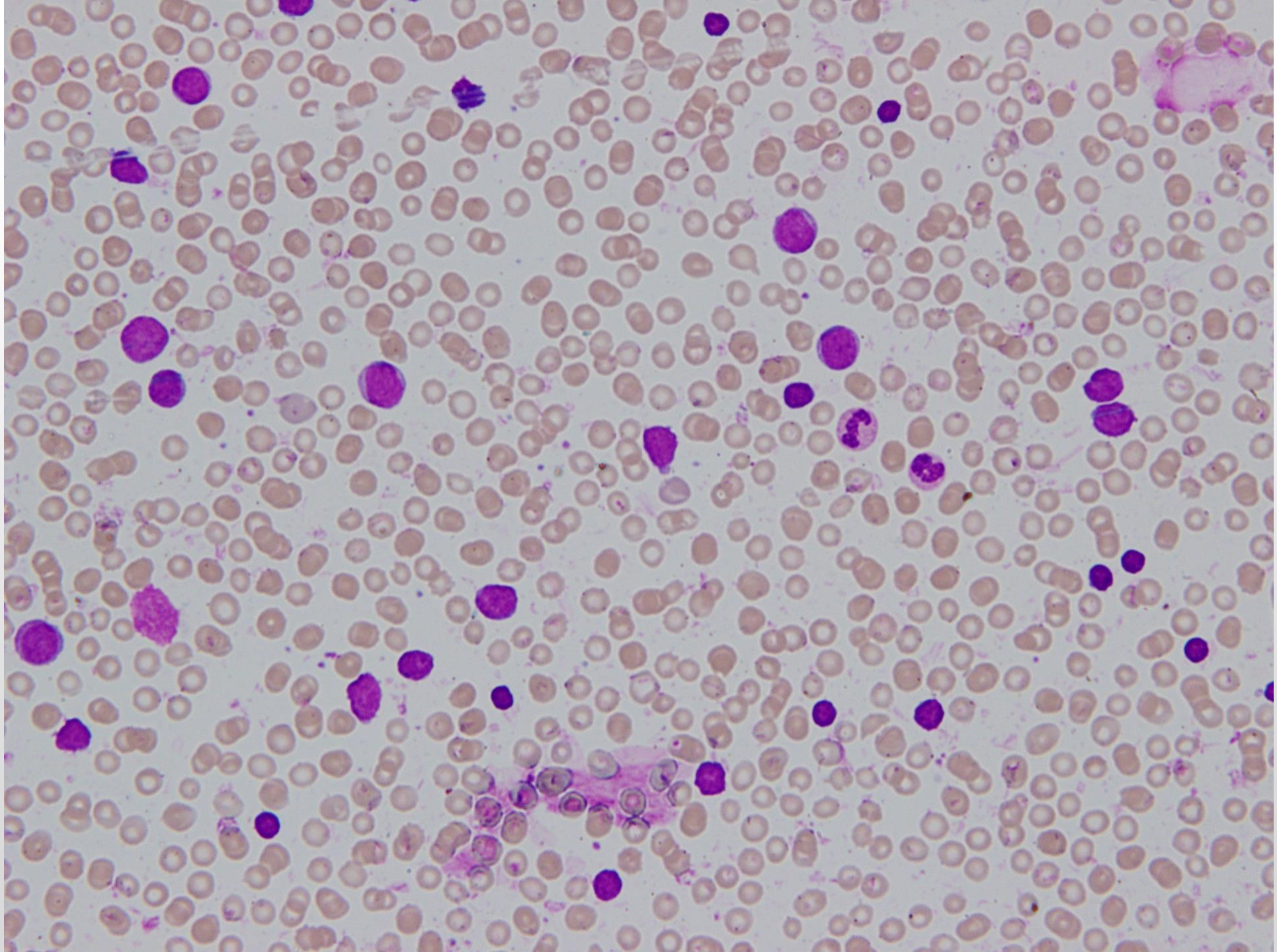
2 separate populations of mononuclear cells



Many medium-sized blasts

Smaller blasts that look almost like mature lymphocytes



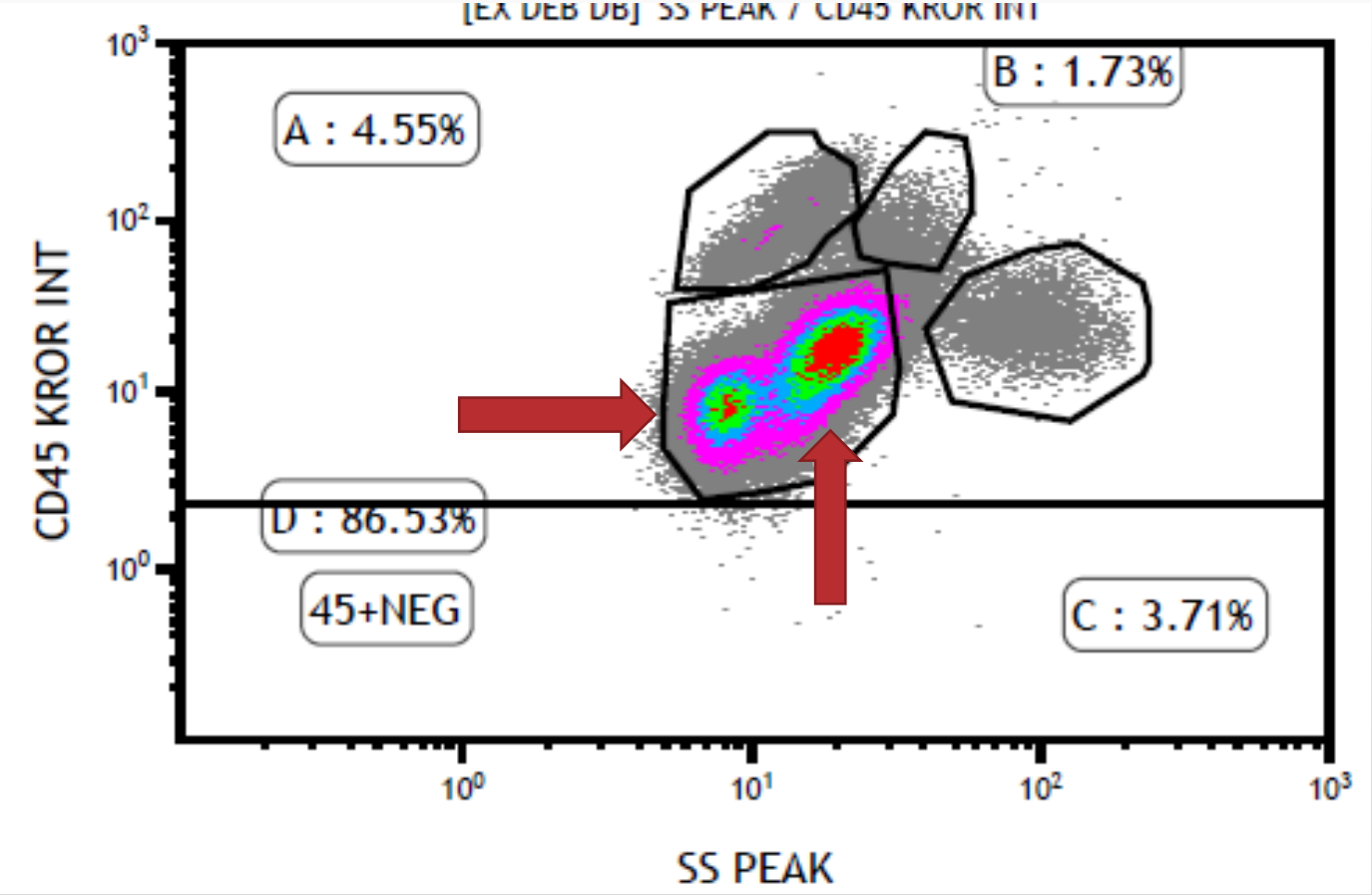


Flow cytometry confirms lineage

- Immature markers CD34, HLA-DR and TdT confirm ‘leukaemia’
- CD19, intracellular CD79a confirms B cell lineage

Diagnosis: B-cell acute lymphoblastic leukaemia

Flow cytometry shows 2 different populations



Marker expression different in the 2 populations

Both B-ALL

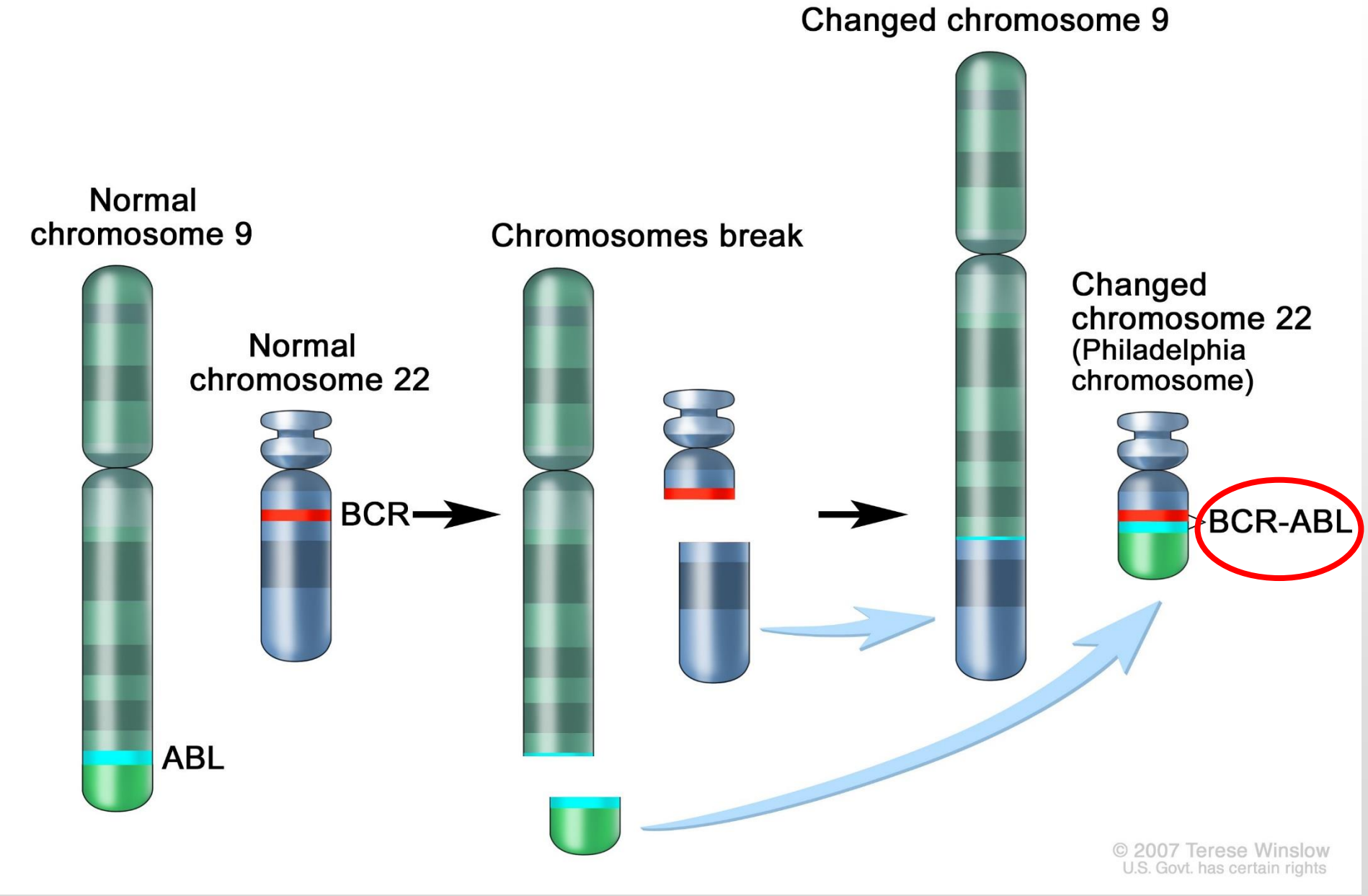
Cytogenetics also shows 2 distinct populations

- 4 cells analysed
- t(9;22)
- Philadelphia translocation (same as seen in CML)

- 15 cells analysed
- t(9;22)
- PLUS an extra 5 abnormalities!!

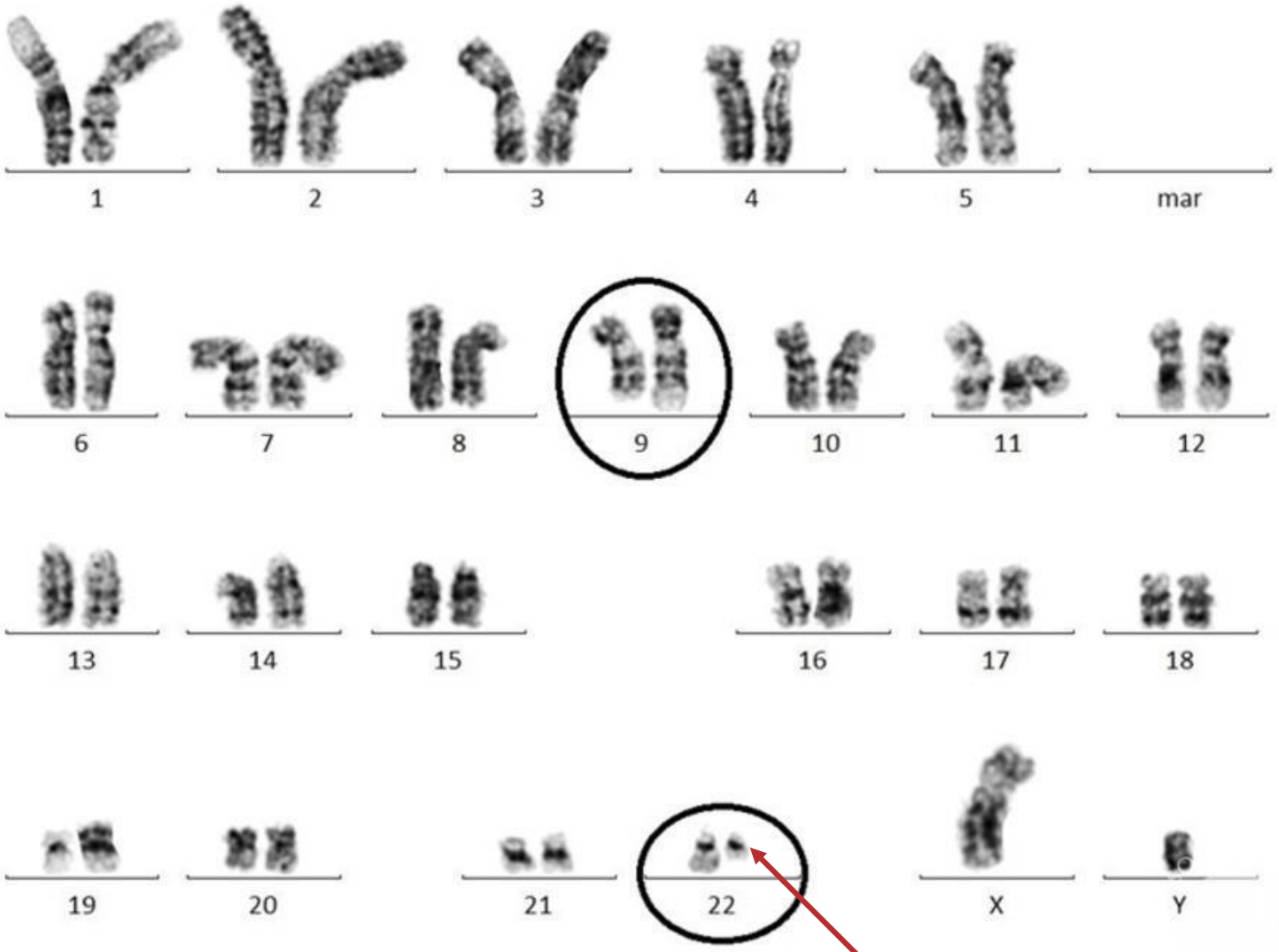
t(9;22) B-ALL has a poor prognosis.

It is treated with chemotherapy plus the tyrosine kinase inhibitors also used in CML (e.g. dasatinib). These drugs greatly improve the outcome.



Used for monitoring response to treatment

A real karyotype!



Final diagnosis

- B-cell acute lymphoblastic leukaemia with t(9;22)