Case 3

Presented by Dr James Wilson

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Harrogate and District Foundation Trust

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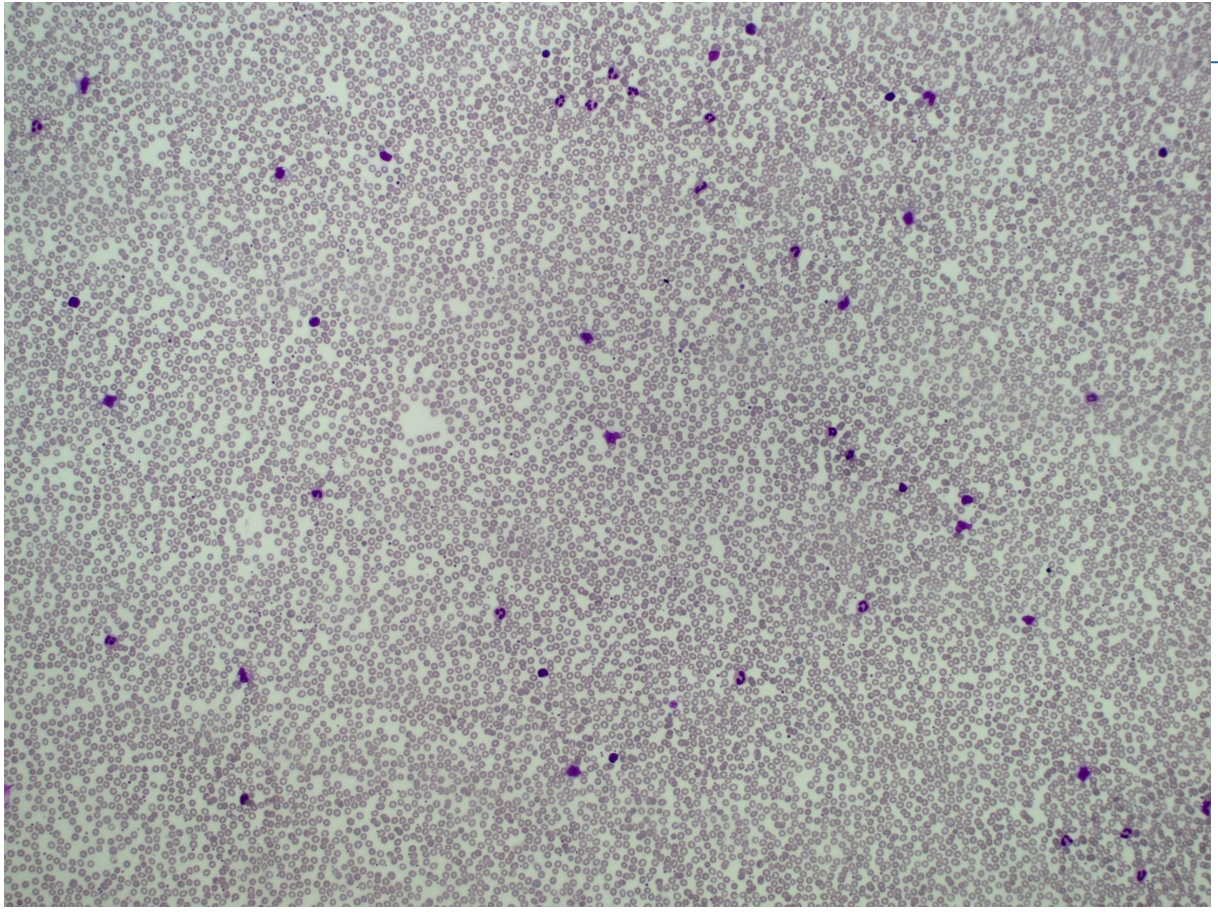
Case 3

- 56 year old male presented to his GP with severe fatigue and night sweats
- PMH: Normally F+W

- FBC: Hb 110, PLT 100, WBC 20

- Slido code BSH2025

Blood Film x 10



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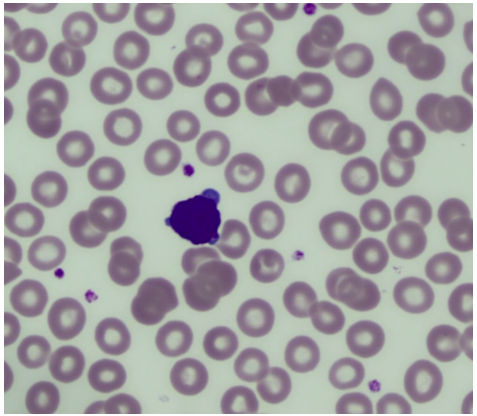
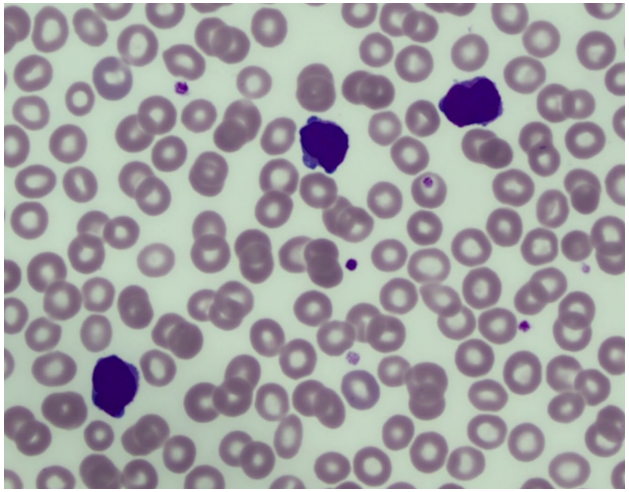
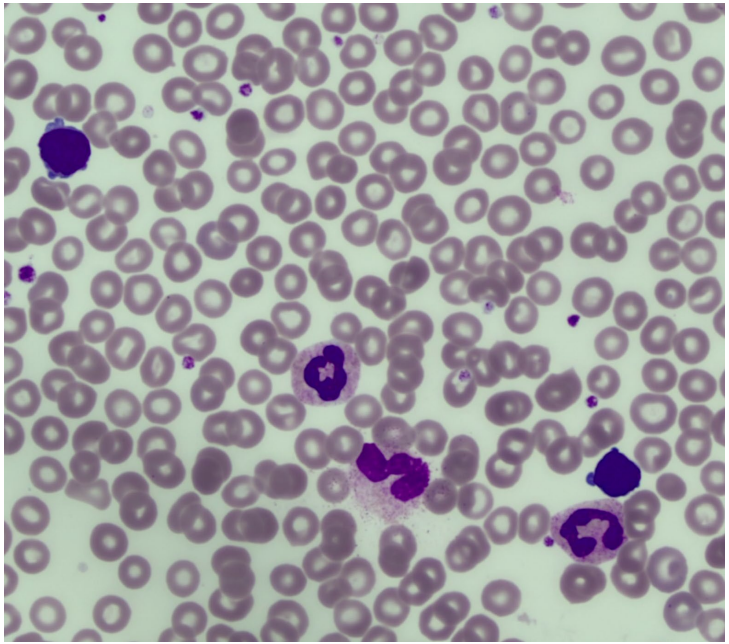
Blood Film x 50







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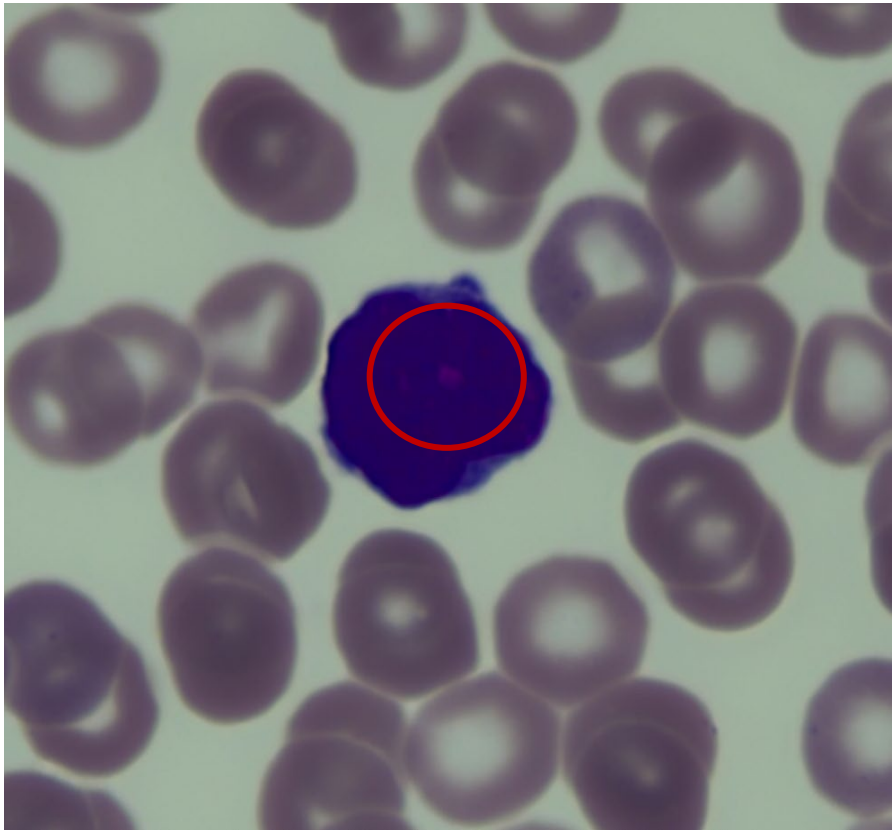
Blood Film x 100



- Lymphocytes
- Very small (similar to a RBC)
- Indistinct central nucleolus
- Basophilic cytoplasm
- Multiple small blebs
- No smear cells

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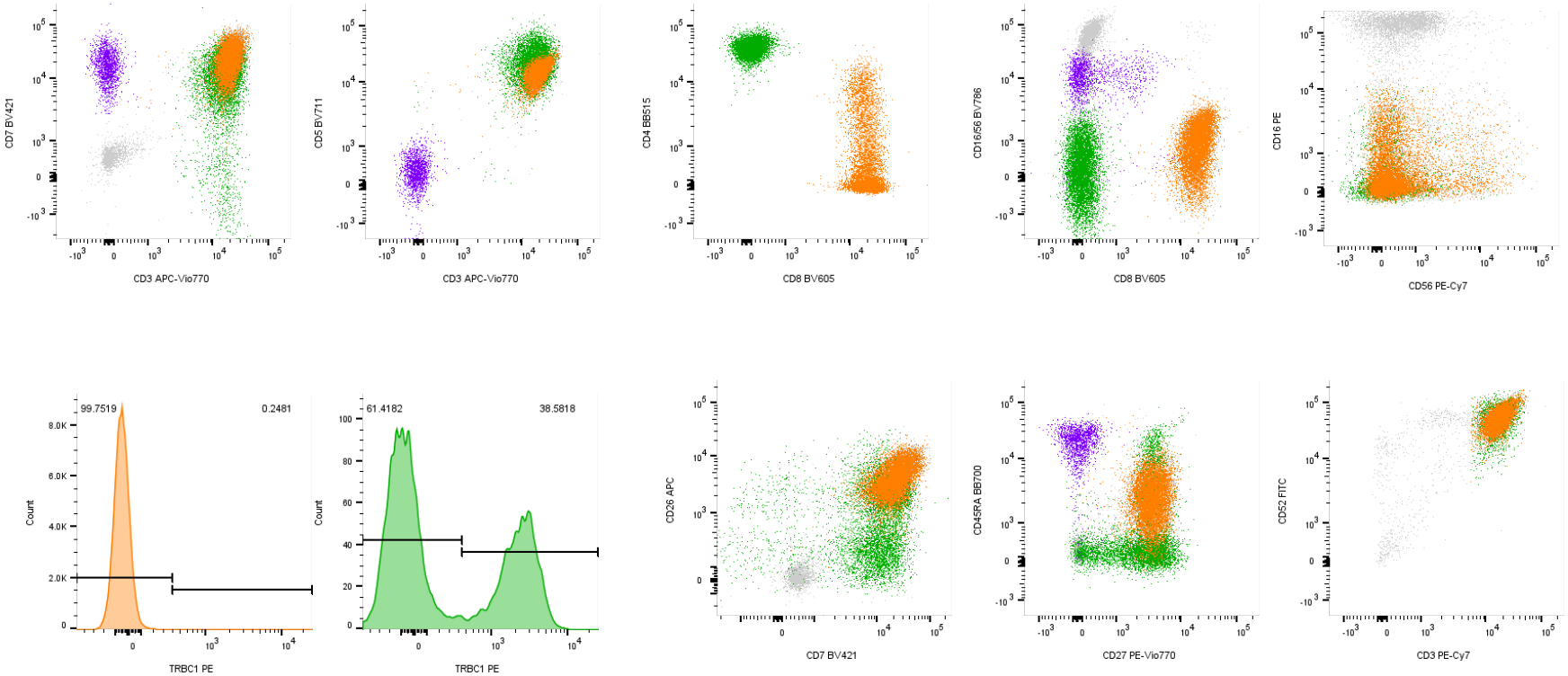
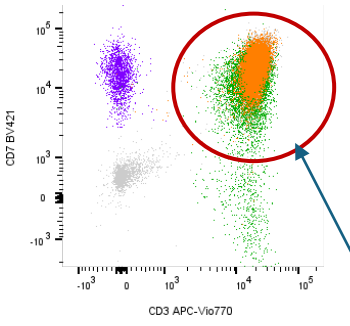
PB Flow Cytometry

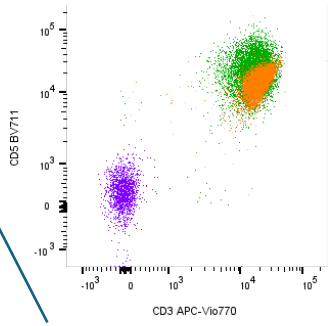


Courtesy of Richard Leach, HMDS

What do people think?

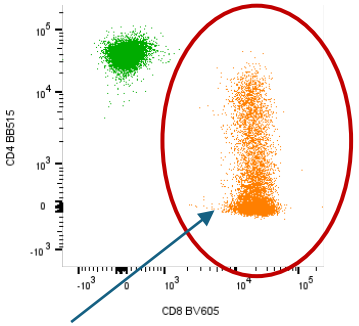
a) Acute T-cell Leukaemia/Lymphoma
b) T-cell Prolymphocytic Leukaemia
c) Sezary syndrome
d) Large Granular Lymphocytic Leukaemia





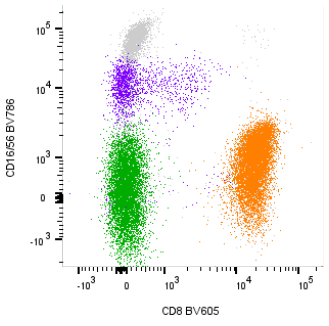
T-cells are identified through expression of CD3, CD5 and CD7. All T-cells show normal expression levels CD3+ CD5+ CD7+/-.

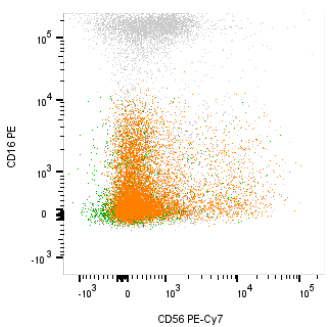
Strong CD7 expression



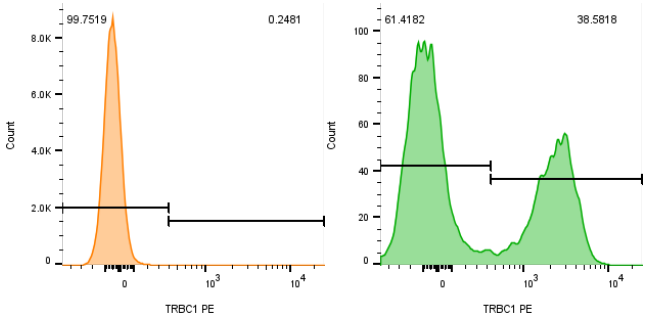
Double positive CD4 / CD8

T-cells are divided into CD4+ and CD8+ subsets. The CD8+ T-cells show some weak CD4 expression

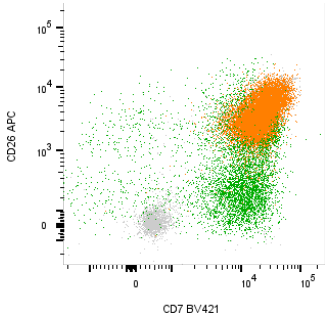


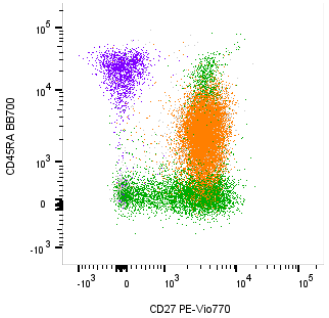


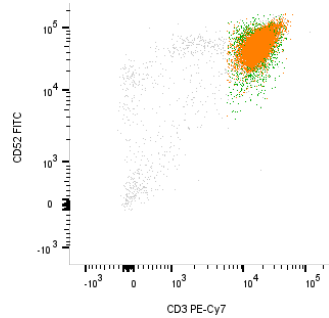
CD16 and CD56 are used to identify NK cells (purple) and any potential NK-T cell populations.



TRBC1 expression is assessed on both the CD4+ and CD8+ T-cell subsets. CD8+ T-cells show TRBC1 restriction indicating a clonal expansion.







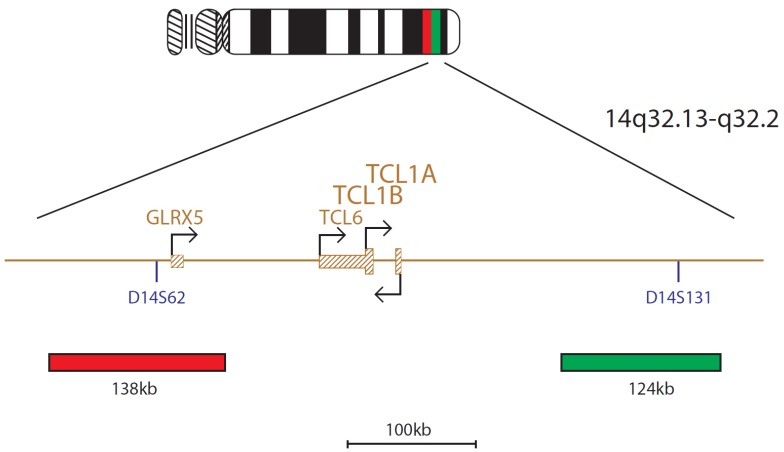
All T-cells show strong CD52 expression. CD52 is the target for campath.

Flow results:

Neoplastic T-cells = 8.9 x 10^9/l, phenotype CD3+CD4+(wk)CD8+ CD2+CD5+CD7+ CD16+(wk)CD56-CD57- TCRab+gd-TRBC1- CD52+CD25-HLADR-CD45RA+(wk)CD26+CD27+ CD1a-CD10-CD30-.

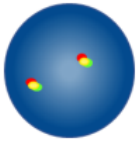
Normal CD3+ T–cells = 0.41 x 10^9/l (low), predominantly CD4+ helper T–cells = 0.36 x 10^9/l (low). NK–cells = 0.089 x 10^9/l (low).

Further tests – TCL1 FISH



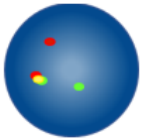
Expected Results

Expected Normal Signal Pattern

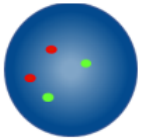


In a normal cell, two red/green fusion signals are expected (2F).

Expected Abnormal Signal Patterns



In a cell with monoallelic TCL1 translocation or inversion, the expected signal pattern will be one red, one green and one fusion (1R, 1G, 1F).



In the event of a biallelic translocation the expected signal pattern will be no fusion, but two red and two green signals (2R, 2G).

Images courtesy of Amy Foster, HMDS

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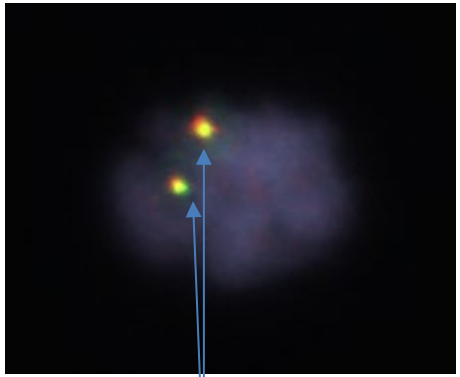
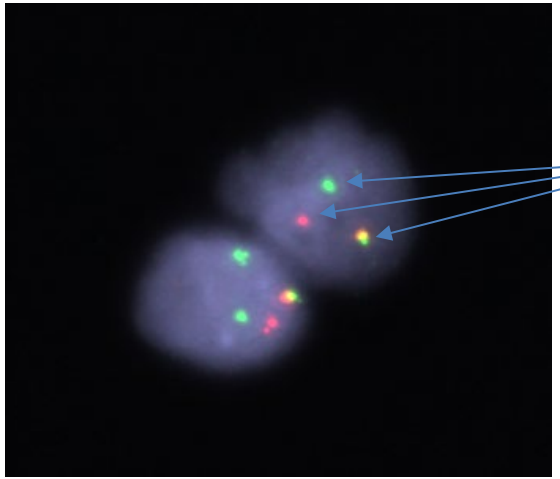
Further tests – TCL1 FISH



2 fusion (yellow) signals
= normal pattern



1 red, 1 green, 1 fusion
= **monoallelic TCL1 rearrangement**

Images courtesy of Amy Foster, HMDS

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Further Tests – T-cell Clonality

T-cell clonality = **TCR gamma^{clonal}**

What do people think now?

a) Acute T-cell Leukaemia/Lymphoma
b) T-cell Prolymphocytic Leukaemia
c) Sezary syndrome
d) Large Granular Lymphocytic Leukaemia

Diagnosis

Diagnostic criteria for T-PLL	
Major criteria	
≥ 5 x 10^9/L cells of with a T-PLL phenotype in the peripheral blood or bone marrow	✓
Evidence of T-cell clonality	✓
Abnormalities of 14q32 or Xq28 or expression of TCL1A, TCL1B or MTCP1	✓
Minor criteria	
Abnormalities involving the chromosome 11 (11q22.3; ATM)	
Abnormalities in chromosome 8: idic (8)(p11), t(8:8), trisomy 8q	
Abnormalities in chromosome 5, del12p, 13, 22 or a complex karyotype	
Involvement of a T-PLL specific site (splenomegaly, effusions, skin and CNS)	

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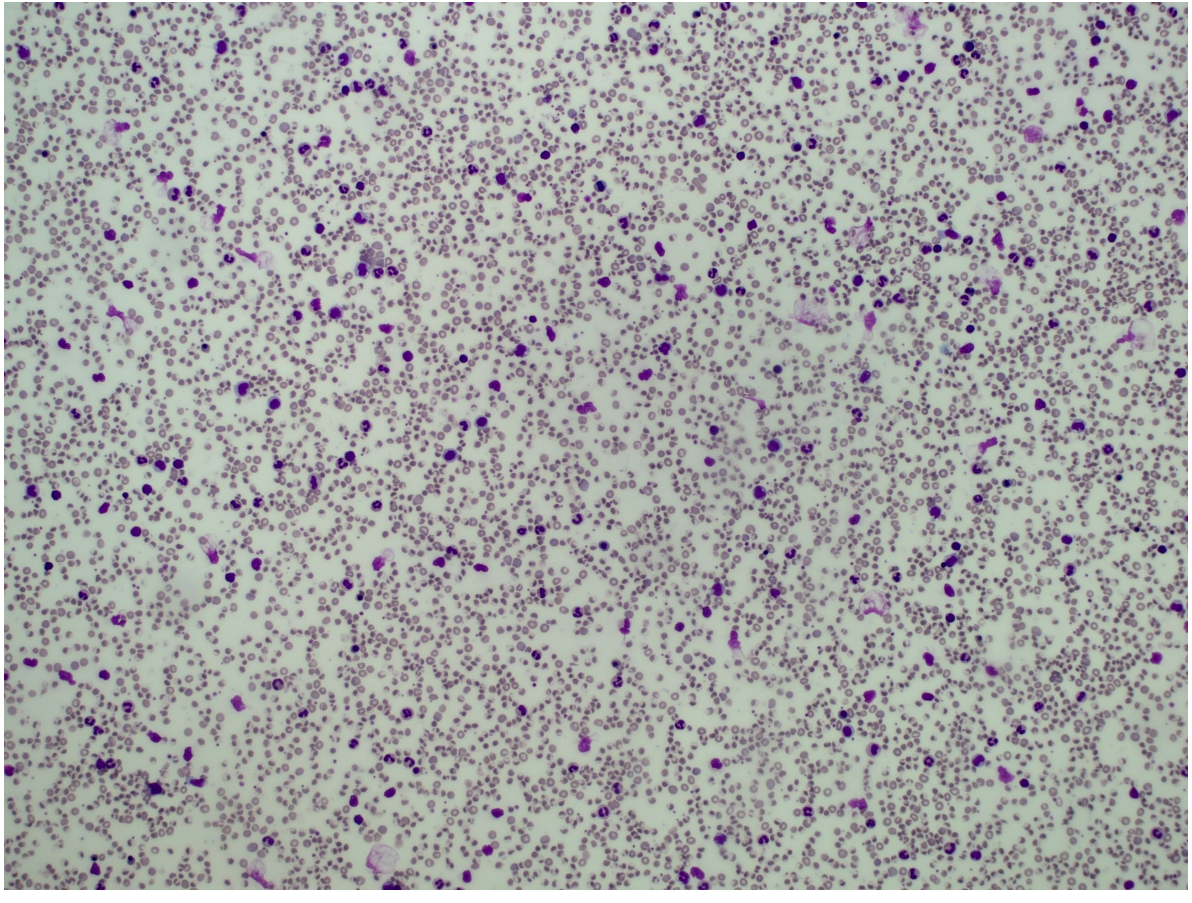
Treatment

- Started treatment with IV Alemtuzumab.
- Plan to consolidate first remission with ALLO transplant.

3 days later… Blood Film x 10



Something has certainly changed…

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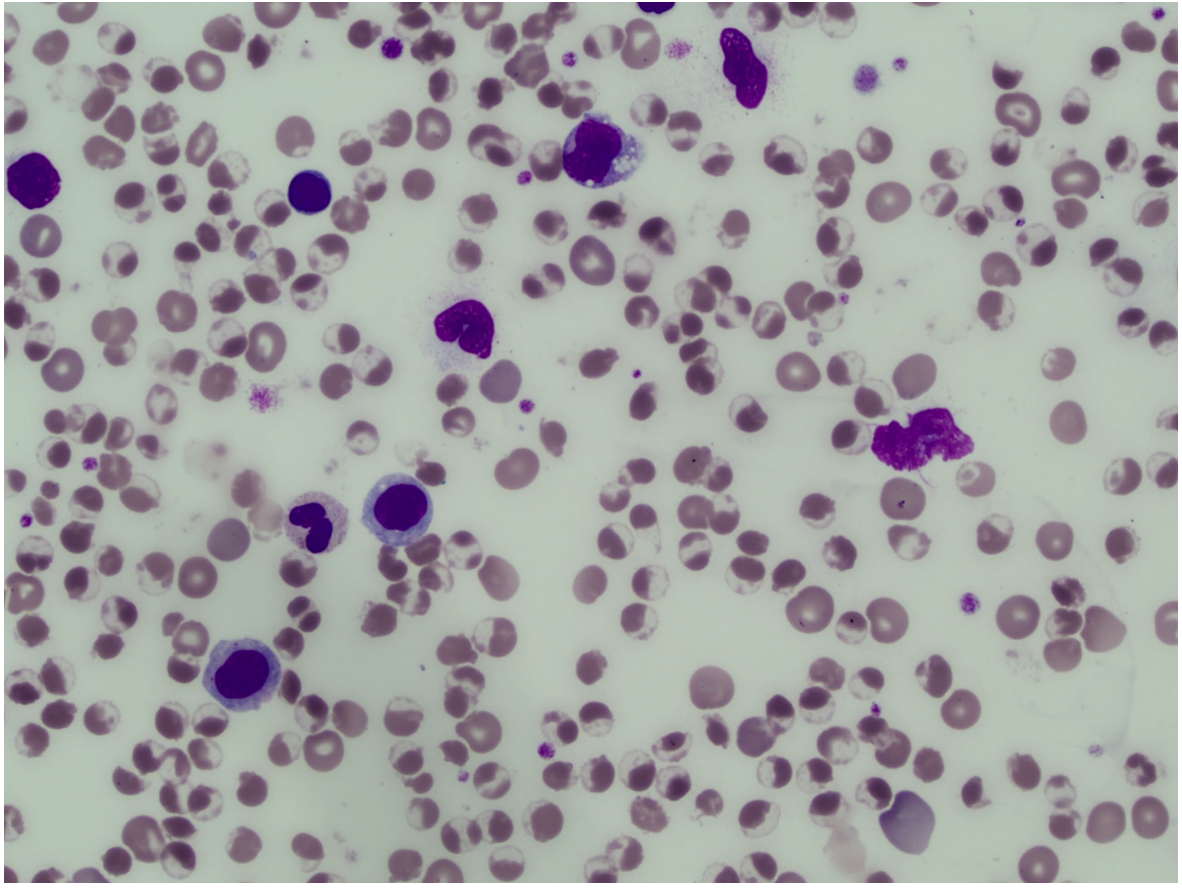
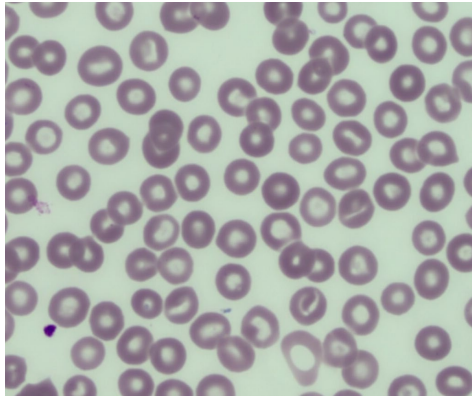
3 days later… Blood Film x 50





Dramatic red cell changes…

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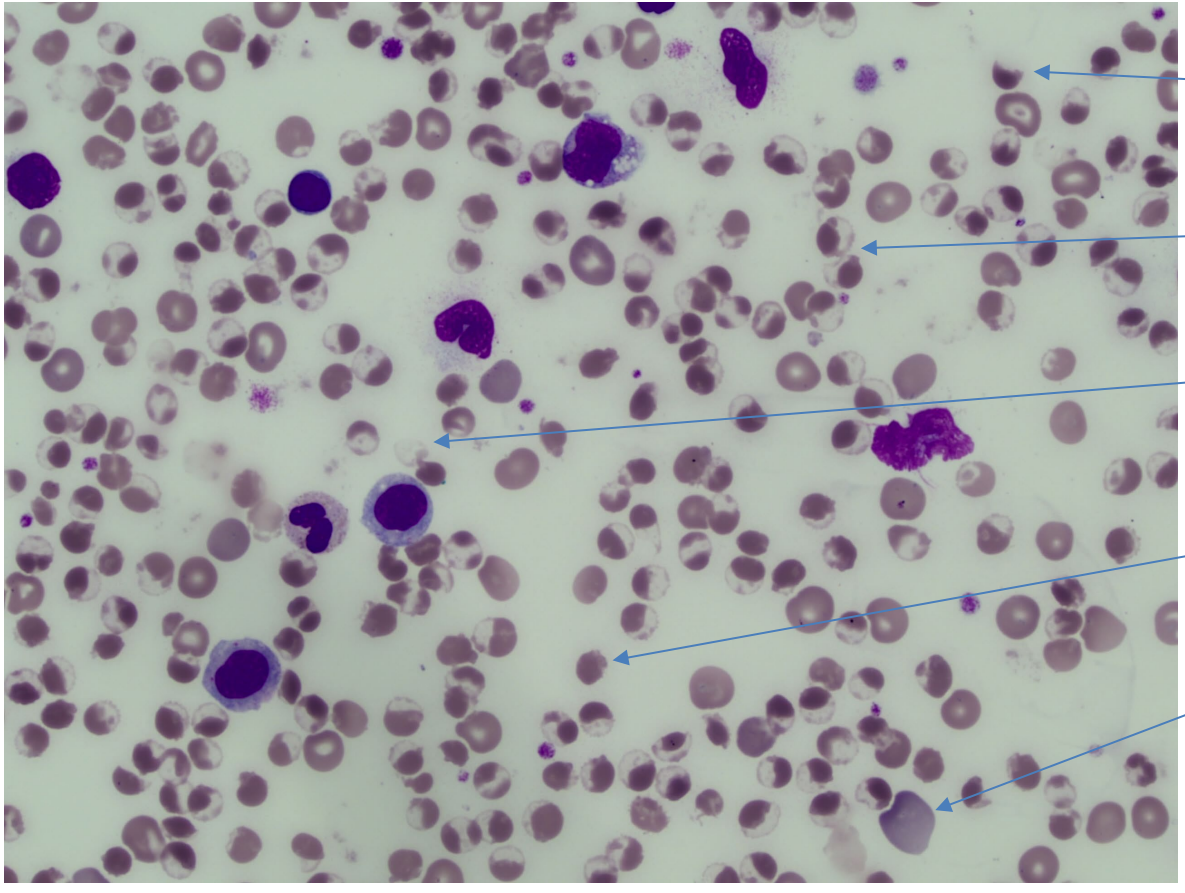
What is going on here?

a) He has developed *Clostridium perfringens* sepsis with haemolysis
b) This is an adverse reaction to his chemotherapy
c) This is oxidative haemolysis from a drug exposure
d) He has developed autoimmune haemolytic anaemia

3 days later… Blood Film x 50



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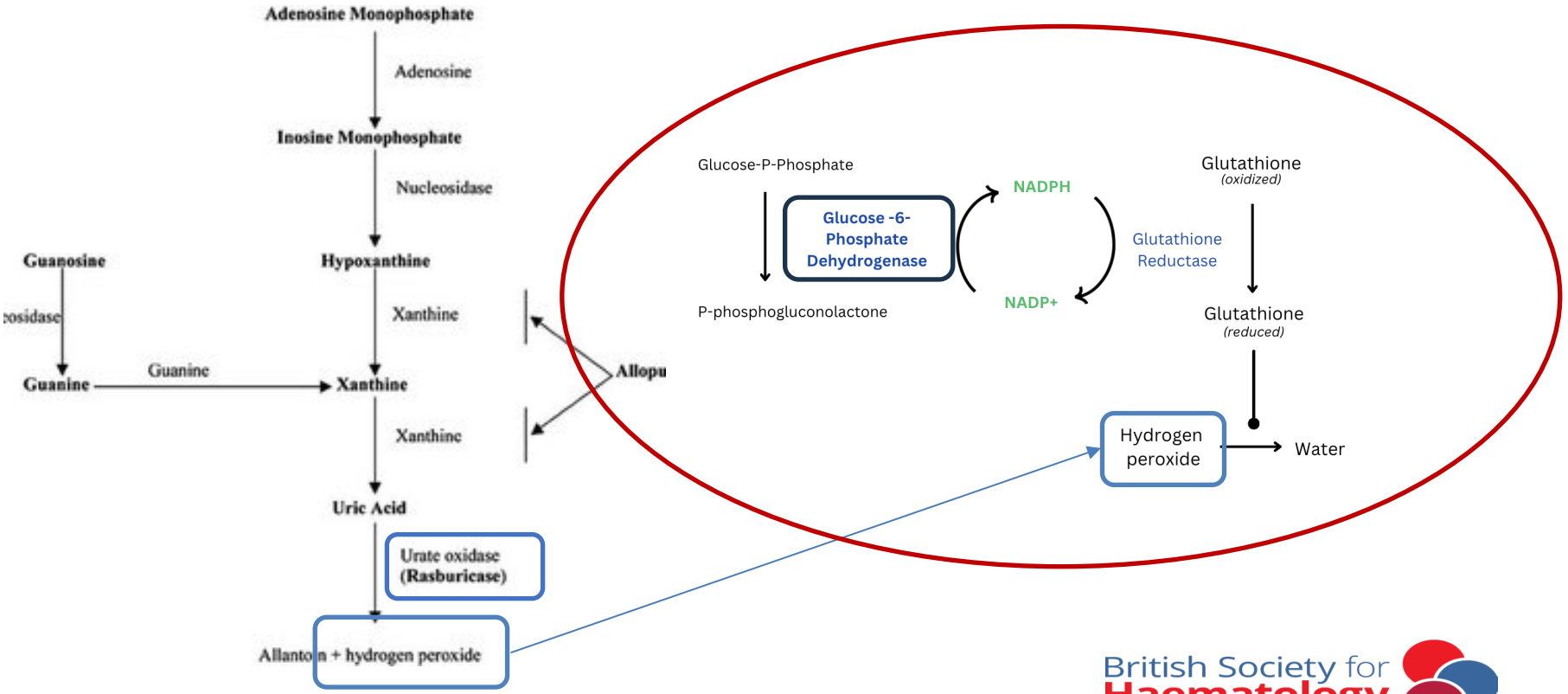
What I didn’t tell you…

- He was of Kurdish/Iraqi ancestry
- Prior to his chemotherapy he received Rasburicase !

Biochemistry…



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Subsequent results…

- G-6-PD confirmed to be low 2.9 iu/gHb

Diagnosis

- *T-PLL*
- *Previously undiagnosed G-6-PD deficiency*
- *Rasburicase induced oxidative haemolysis*

Take home message…

- Always consider the possibility of G-6-PD deficiency, especially in males from at risk ethnic groups and test prior to exposure to Rasburicase.

Acknowledgments

- My thanks to Amy Foster and Richard Leach at HMDS.

Thank you